University of Liège, Faculty of Medicine

Doctoral Thesis

Development and Evaluation of a Comprehensive Cancer Risk Model and Mobile Health Application for Public Awareness and Prevention

A thesis submitted in fulfillment of the requirements for the degree of Doctorate in Medical Sciences

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Dedication

Dedicated to Timo Du Four, my best friend and collaborator, whose patience and dedication persisted far longer than anyone could have hoped for. Your support, even when your own passion had dimmed, turned what was merely an idea into a reality. Without you, none of this would have been possible. Thank you for standing by me, even when it was more for my sake than your own.

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Introduction

Cancer, a leading cause of death globally, necessitates proactive measures to educate the public about individual risks and encourage preventive behaviors. This thesis focuses on the development and evaluation of a comprehensive cancer risk model integrated into a mobile health application, named the "Cancer Risk Calculator" (CRC), with the goal of improving public awareness and knowledge of cancer risks and risk factors. It is part of a subsection of eHealth, defined as the use of information and communication technologies for health, called mHealth, defined as the use of mobile technologies for this same purpose.

The thesis addresses the pressing need for accessible and engaging health information tools, particularly in the context of cancer prevention, where individual risk assessment and timely intervention can significantly impact outcomes. While numerous cancer risk prediction models exist, their accessibility and usability for the general public have been limited.

Chapter 1: Interactive Digital Solutions for Health Literacy in Cancer Risk

The first chapter explores how digital tools can enhance health literacy related to cancer risk. It begins by defining health literacy and its critical role in cancer prevention, followed by an analysis of the limitations of traditional approaches. This chapter systematically reviews interactive digital solutions, including web portals and mobile applications, and their potential to empower users by simplifying complex medical information. It concludes with a summary of gaps in current tools and how this thesis addresses them, laying the foundation for the CRC application.

This chapter was the basis for the following publication: *"Westerlinck P, Coucke P. Review of interactive digital solutions improving health literacy of personal cancer risks in the general public. Int J Med Inform. 2021 Oct;154:104564. doi: 10.1016/j.ijmedinf.2021.104564. Epub 2021 Aug 30. PMID: 34492483."*

Chapter 2: Comparative Analysis of Existing Cancer Risk Prediction Models

The second chapter delves into the landscape of existing cancer risk models, offering a comparative analysis of their methodologies, applicability, and effectiveness. It categorizes models by cancer type, evaluates their calibration and discriminatory power, and discusses the factors contributing to their variability. Through this analysis, the chapter identifies critical limitations, such as underrepresentation of specific cancers and lack of external validation, highlighting the need for a more comprehensive and user-friendly model like the CRC.

Chapter 3: Development of the Cancer Risk Calculator and mHealth Application

This pivotal chapter outlines the design and development of the CRC application, emphasizing its comprehensive scope and innovative features. The personalized risk assessment methodology is explained, along with the integration of a wide range of cancer types and risk factors. Ethical considerations, including data privacy and accessibility, are addressed. The chapter provides a detailed walkthrough of the application's functionality, demonstrating how it bridges the gap between clinical precision and public usability.

This chapter was the basis for the following publication: *"Westerlinck P, Coucke P, Albert A. Development of a cancer risk model and mobile health application to inform the public about cancer risks and risk factors. Int J Med Inform. 2024 Sep;189:105503. doi: 10.1016/j.ijmedinf.2024.105503. Epub 2024 May 27. PMID: 38820648."*

Chapter 4: Assessing the Impact of the CRC Application on Cancer Risk Health Literacy

The final chapter evaluates the effectiveness of the CRC application in improving health literacy and promoting preventive behaviors. Through user studies and statistical analyses, it measures the application's impact on knowledge retention, engagement, and behavioral intentions. The findings are discussed in the broader context of public health and digital health literacy, providing insights into the potential scalability and policy implications of mHealth interventions.

This chapter was the basis for the following publication: *"Westerlinck P, Maes N, Coucke P. "Assessing the Effect of a Mobile Application on Cancer Risk Health Literacy: A Cross-Sectional Study Design". Appl Clin Inform. 2025 Jan 15. doi: 10.1055/a-2516-1757. Epub ahead of print. PMID: 39814048."*

Contributions and Implications

This thesis makes significant contributions to cancer prevention by integrating personalized health insights into an accessible digital platform. By addressing the limitations of existing models and evaluating the real-world impact of the CRC application, this research provides a roadmap for future advancements in mHealth and cancer risk communication.

The following chapters will provide a detailed exploration of these themes, guiding the reader through the theoretical underpinnings, methodological rigor, and practical applications of this groundbreaking work.

Chapter 1: Interactive digital solutions improving health literacy of personal cancer risks

Introduction

Health literacy is defined as the possession of literacy skills that are required to make health-related decisions in a variety of different environments (home, community, health clinic). [1] It has now been well established that low health literacy is a major contributing factor to poor health status and outcomes, but also results in higher premature mortality rates, lack of adherence to medical recommendations, and higher direct and indirect health costs. [2], [3] As such, governments of several countries, including the United States and China, have developed national strategies and targets to improve health literacy in their populations [4], [5], [6].

Cancer, as the second leading cause of death globally, responsible for about 1 in 6 deaths [7], could benefit from an improvement in health literacy. Studies have investigated the association of health literacy with cancer-related attitudes, knowledge, and behaviors [8], inquisitiveness after discussions [9] and even self-management capacity [10].

The great majority of reported interventions to improve health literacy have been in clinical settings, and generally focus on its task-directed, functional aspects. The improvement of health literacy in community populations remains poorly studied [11]. The advent of new technology may ameliorate this finding. Relatively simple interventions like use of a web portal and even a brief multimedia presentation have been found to improve attitudes [12], [13]. Digital health technology has been identified as a potential enabler of health care access and literacy [14].

Alongside the more traditional outlets for eHealth, defined as the use of information and communication technologies (ICT) for health [15], we now also have mHealth, which encompasses the use of mobile wireless technologies for public health. In 2016, The WHO acknowledged that mobile technologies were becoming an important resource for health services delivery and public health due to their ease of use, broad reach and wide acceptance [16]. By 2018, after consideration of the report on mHealth, it passed a resolution urging Member States to prioritize the development and greater use of digital technologies in health, as a means of promoting Universal Health Coverage and advancing the Sustainable Development Goals [17].

This chapter attempts to give an overview of the most important digital resources that are available to patients worldwide and could be used to improve the health literacy of patients, whether it results from a personal initiative, or an organized, general and societal approach. Due to the ubiquity of both the internet and mobile phones, there is a pressing need to evaluate these tools. Our hope is that health care professionals can use our findings to tailor their messaging to the resources described. Mobile applications (or ‘apps’) and web applications are listed separately.

Methods

Searches were conducted for both mobile applications and web tools; details are provided in the relevant subsections. Because we wish to focus on tools that might impact health literacy within the general public, we have excluded tools that:

- Could not be widely used by lay people without medical training
- Require complex tests or imaging
- Only provide information on risk factors and do not allow for individual risk calculation
- Were not available in English

●Do not focus on the risk of developing cancer, but rather survival after a cancer diagnosis, risk of recurrence or risks related to specific findings

2.1. Mobile applications

Mobile applications are available through specialized digital distribution platforms developed and maintained by large technology companies and nowadays designed to run on a specific operating system. The two largest platforms, namely Google Play (formerly Android Market) by Google LLS and App Store by Apple Inc., dominate the global app download landscape (mm). We have therefore limited our search to these two platforms. Both platforms only include apps designed to run on a specific operating system. Unsurprisingly, these are the operating systems designed by technology companies that developed the platforms, meaning Android for Google Play and iOS for the App Store.

A search for 'cancer risk calculator' was conducted on both platforms. For Android, this retrieved 250 different apps, 79 of which were medical. Two apps were excluded because they were not available in English, 30 were excluded because they were not focused on cancer, one app was excluded because it was a companion app to a commercial hereditary cancer test and one app was excluded because it was a diagnostic tool. A further 22 apps were excluded because they were not or insufficiently interactive. Finally, 7 apps were excluded because they focused on diagnosis, recurrence, prognosis or mortality, leaving a total of 16 Android applications that are evaluated in this review.

For iOS, this retrieved 10 different apps. One app was excluded because it did not focus on cancer and 2 apps were excluded because they were diagnostic apps for lung nodules, leaving a total of 7 Apple applications that are evaluated in this review. Only three apps were available for both Android and iOS systems. (Table 1)

Table 1. Publicly Available Mobile Tools.

Name	Availability	User score (a)	Developper	Number of cancers included	Cost	Strong points	Weak points	MARS (b)
Melanoma Test	iOS	Not available	Dermatology clinic of the Third Medical Faculty of Charles university	1	Free	- based on ABCDE criteria - provides photographic examples	- requests data	3.9
CORAL: Prostate Cancer Risk and Survival	iOS	Not available	CORAL medical applications	1	Free	- calculators for the relevant risks at every stage of prostate cancer	- completely dependant on PSA values	4.4
BCSC RISK CALCULATOR	iOS	Not available	Breast Cancer Surveillance Consortium	1	Free	- based on their own, published, risk-prediction model (hh) - also available on the BCSC website	/	4.4
ROMA Calculator	iOS	Not available	University of Rochester	1	Free	- based on trademarked algorithm	- completely dependant on	4

			Wilmont Cancer Institute				serum biomarkers CA125 and HE4	
Cancer Risk Calculator	iOS, Android	4.8, 4.5	WestFour	32	Free	- Extremely large number of cancers - Extremely large number of risk factors - Detailed references	/	4.6
CanCell Cancer	iOS, Android	Not available, 3.9	Narodowy Fundusz Zdrowia (National Health Fund of Poland)	2	Free	- developed to direct users to appropriate resources	- large sections only available in Polish	3.2
Rotterdam Prostate Cancer Risk	iOS, Android	4.0, 4.3	Prostate Cancer Research Foundation, Rotterdam (SWOP)	1	One-time purchase	- based on their own, published, risk-prediction model (r)	- dependant on PSA values - not free	4
Lung Cancer Risk Predictor	Android	4.2	Pavel Chtcheprov (private developer)	1	Free	- based on Tammemagi scoring criteria	/	4.1
Breast Cancer Risk Assessment	Android	2.8	mizSoftware	1	Free	/	- requests access to a lot of unnecessary personal information, including the current location, camera, Wifi-connections, device IDs and photos - very low number of risk factors	3
Various Proactiff ‘Cancer Risk Assessment Tool’ applications	Android	Not available	Proactiff	1 per application, total of 9	Free	- Includes more rare cancers	- Non-functional after last update - Account necessary, which requires not just an e-mail address but also a lot of unnecessary personal information	/
Prostate Cancer Calculator	Android	3.7	Borinfer LLC	1	Free	- combines several calculators concerning prostate cancer, including an IPSS (International Prostate	- Several bugs	3.3

						Symptom Score) calculator and PSA Density/ Velocity/Doubling time calculators		
Indonesian prostate cancer risk calculator (IPCRC)	Android	5	Solusi Karya Kita untuk Semesta (SEKATA)	1	Free	- Very easy to use - Prediction risk model of prostate cancer based on the Indonesian population (p)	- completely dependant on PSA values and prostate volume	3.4

a: User rating on App Store (iOS) or Google Play (Android), out of a total of 5. (Accessed May 2021 from Liège Belgium).
b: Mobile Application Rating Scale; App quality mean Score (Stoyanov et al., 2015).

These applications were scored using the Mobile App Rating Scale (MARS), developed by Stoyanov et al. [34], but have also included the user scores for the respective app stores if they were available. The MARS Score is an average of scores on four sections, who are themselves averages of scores on several subsections. They are:

1.Engagement – Entertainment, Interest, Customisation, Interactivity, Target group
2.Functionality – Performance, Ease of use, Navigation, Gestural design
3.Aesthetics – Layout, Graphics, Visual appeal
4.Information – Accuracy of app description, Goals, Quality of information, Quantity, Visual, Credibility, Evidence base

For example, the score for the 'Melanoma Test' application (Annex 1), breaks down as follows:[((1 + 3 + 3 + 4 + 5)/5)+((4 + 4 + 3 + 4)/4)+((5 + 5 + 5)/3)+((3 + 3 + 5 + 4 + 5 + 3 + 2)/7)]/4 = 3.88

2.2. Web tools

I conducted a systematic search of the internet to identify all sites with a risk calculator for any cancer, searching the terms "cancer risk calculator" (without quotes) in each of the following search engines using the Google Chrome browser: Google, Bing, Yahoo! and Baidu. The first 200 hits from each search were visited to determine whether they included a cancer risk calculator.
After excluding non-English sites, duplicate sites, sites that focused on diagnosis, recurrence, prognosis or mortality and sites that did not adequately explain the algorithm, model or source material used a list of 20 sites was generated. (Table 2)

Table 2. Publicly Available Web Tools.

Name	Technology	Link	Developer	Number of cancers included	Strong points	Notes
Your Disease Risk™	Wordpress	https://siteman.wustl.edu/prevention/ydr/	Siteman Cancer Center	12	- Also includes 6 other important chronic diseases - Personalized advice for prevention	- Was known as the Harvard Cancer Risk Index until 2004

Cancer Risk Assessment Tool	Javascript	https://bcrisktool.cancer.gov/calculator.html https://mrisktool.cancer.gov/calculator.html https://ccrisktool.cancer.gov/calculator.html	National Cancer Institute (NCI)	3	- Source code available for download - Detailed references	- The Melanoma calculator is also available as an app for Apple devices. It is not free.
Assessyourrisk	Vue.js JavaScript	https://www.assessyourrisk.org/	Bright Pink	2	- Personalized advice for prevention	- Requests access to a lot of unnecessary personal information, including users' full name, e-mail address and health insurance details
B-RST™	ASP.NET	https://www.breastcancergenescreen.org/	Georgia Center for Oncology Research and Education	2	- Very detailed input of family history	- Very narrow scope; designed to identify who should be referred for cancer genetic counseling
Cleveland Clinic Risk Calculator Library	Express.js	https://riskcalc.org/	Cleveland Clinic	2	- Part of a large library of risk calculators	/
SWOP Prostate Cancer Risk Calculators	PHP	http://www.prostatecancer-riskcalculator.com/seven-prostate-cancer-risk-calculators	Prostate Cancer Research Foundation, Rotterdam (SWOP)	1	- Different calculators depending on the information the user has available and the exact outcome that is desired	/
Lung Cancer Screening Decision Tool	ASP.NET	http://nomograms.mskcc.org/Lung/Screening.aspx	Memorial Sloan Kettering Cancer Center	1	- Displays the risk of dying from lung cancer with and without screening, the chance of saving a life and the number of people like the user that would need to be screened in order for one of them to benefit.	/
Lung Cancer Risk Assessment Tool	ASP.NET	https://www.aats.org/aatsimis/AATSWeb/Resources/Lung_Cancer_Screening/AATSWeb/Association/About/Resources/Lung_Cancer_Risk_Assessment_Tool.aspx	American Association for Thoracic Surgery (AATS)	1	- Shows the risks based on four risk models(Spitz, LLP, Hoggart, PLCO, and Bach)	/
iPrevent	Javascript	https://iprevent.net.au/iprevent/?21	Peter MacCallum Cancer Centre	1	- Detailed disclaimer, particularly concerning people unsuitable for the calculator - Excellent visual representation of results	- Absolutely no information on the impact of risk factors

Breast Cancer Risk Calculator - Princeton Radiology	Wordpress	https://www.princetonradiology.com/	Princeton Radiology	1	- Very detailed familial history component - Intuitive and aesthetically pleasing input screen	- No risk factors other than age and family history are considered - Absolutely no information on the impact of risk factors
Tyrer-Cuzick Risk Assessment Calculator	PHP	https://ibis-risk-calculator.magview.com/	Magview	1	- Allows for downloading of underlying model (IBIS v8 risk assessment model)	/
Omnicalculator	PHP	https://www.omnicalculator.com/	Omni Calculator	2	- Automatically suggests other calculator included on the sites concerning relevant risk factors	/
Lung Cancer Screening	React	https://shouldiscreen.com/	University of Michigan	1	- Provides detailed information on screening efficiency and goals	/
Breast Cancer Risk Assessment Tool for Women With Benign Breast Disease	ASP.NET	https://www.mayoclinic.org/breast-cancer-risk-prediction/itt-20150095#:~:text = The%20BBD%2FAH%2DBC%20model,and%20prevention%20of%20breast%20cancer.	Mayo Clinic	1	- Strictly for women who have had some type of benign breast disease	- Currently non-functional
Snehita Breast Cancer Risk Assessment Tool	Javascript	http://snehita.in/risk	Snehita Women's Health Foundation	1	- Uses the A-J Model, which was made specifically to assess risk for Kerala women	/
Symptom Based Risk Calculator for Head And Neck Cancer Referral	PHP	http://www.orlhealth.com/	(Unknown)	1	- Based on both versions of the HaNC-RC model	/
Prostate Cancer Nomograms	Drupal	https://www.mskcc.org/nomograms/prostate/biopsy_risk_dynamic	Memorial Sloan Kettering Cancer Center	1	- Specifically estimates the risk of high-grade cancer on prostate biopsy	/
Prostate Cancer Risk Calculator	Wordpress	https://www.prostaterisk.ca/prostate-risk-calculator/	Robert Nam, University of Toronto	1	- Includes free:total psa ratio	/
CanRisk Web Tool	Python Javascript	https://canrisk.org/	University of Cambridge	1	- Incorporates the new version of BOADICEA, the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm.	- Requires creation of an account on the website

QCancer	PHP	https://qcancer.org/	Qresearch (collaboration between the University of Oxford and EMIS)	13	- Incorporates general cancer risk and several specific cancer risks	/

Discussion

The overwhelming majority of the calculators focus only on the most common and most lethal cancers, namely breast, prostate and lung cancer. This is not surprising, since these cancers have the best known and validated risk prediction models [18], but the degree to which other cancers have been excluded is nothing short of extreme. In fact, many cancers - namely anal cancer, bladder cancer, cancer of the brain or nervous system, gallbladder cancer, Hodgkin lymphoma, Kaposi's Sarcoma, laryngeal cancer, liver cancer, mesothelioma, myeloma, non-Hodgkin lymphoma, non-melanoma skin cancer (of all kinds), cancer of the oral cavity and pharynx, penile cancer, thyroid cancer and cancer of the vulva or vagina - are only included in the 'Cancer Risk Calculator' app. It is also remarkable that most of these tools only deal with one cancer. And even when tools that discuss more than one cancer are considered, only three of them -namely the 'Cancer Risk Calculator' app, the online Qcancer tool and the online 'Your Disease Risk'™ tool - deal with 10 or more cancer types. Moreover, many of the calculators do not include well-known risk factors and consider only the most frequent ones. It is also notable that there is currently only one calculator for the general risk of developing cancer at any site (QCancer) and that only a minority of calculators even mention mortality.

Some of the applications also raise concerns with data protection, readability standards, lack of references and lack of information updates. More generally, some experts are concerned about the lack of involvement of healthcare professionals in app development. It is well known that their participation and contribution in the elaboration of apps increases content accuracy, app downloads and buy-in [19], [20], whatever the medical specialty.

An encouraging finding is that the size of the reviewed medical applications remains very reasonable, with even the largest app being just 100 Mb in size and most being much smaller. This is good news, since this does not put undue pressure on bandwidth limitations and ensures that these tools remain accessible to a broad audience.

It also seems clear that for the moment, online calculators for cancer risk remain more numerous than mHealth risk calculators. Furthermore, based on the number of tools that are reviewed but not listed here, it seems likely that risk calculators in general -including those that deal with survival after a cancer diagnosis, risk of recurrence or risks related to specific findings- might remain more numerous online than those in mHealth apps. For example, The Cleveland Clinic library of risk calculators contains 67 different, high-quality calculators, 35 of which relate directly to cancer [21]. Other prestigious cancer centers, such as Memorial Sloan Kettering Cancer Center [22] and MD Anderson Cancer Center [23] also have calculators available.

The balance between online and mobile tools will most likely shift in the near future. The ubiquity of mobile phones has reached such a level that there are currently places where people are more likely to have access to a mobile phone than to clean water or electricity [24]. Furthermore, the total number of apps downloaded globally each quarter has doubled in the five years since 2015, reflecting both increased smartphone penetration and the increasingly prominent role of apps in our lives [25].

The economic impact will likely follow a similar trajectory. The global mHealth apps market size is expected to expand at a Compound Annual Growth Rate (CAGR) of 44.7% and is projected to reach USD 236.0 billion by 2026 [26] These numbers might even underestimate the situation, as a 65%

global upswing in medical app downloads in peak COVID-19 lockdown month vs January 2020 has been reported [27].
This is particularly important because traditional health care services appear to be slow in adapting mobile applications. Research has revealed that less than 11% of providers offer proprietary apps that have at least one of the three functions that consumers want the most [28]. When assessing mobile app use among the 100 largest U.S. hospitals, it was found that they only manage to engage 2 percent of patients via mobile apps, putting as much as $100 Million in annual revenue at risk per hospital [29].
However, insight is growing and efforts are underway to push this technology. Even governments are already taking advantage of these innovations, often depending on the specific needs of their populations. In Malaysia, 65% of colorectal cancers are detected at stages III and IV, giving rise to a lower 5-year relative survival by stage as compared with other developed Asian countries. This late detection is thought to be partly because of the low participation in screening among Malaysians. Hence, an initiative has been started to develop a mobile app for community education on colorectal cancer, apparently with encouraging results [30].
Risk calculators are undoubtedly part of this effort. In addition to the general risk calculator apps aimed at specific national communities such as Polish and Indonesian populations mentioned above, an intelligent CRC screening app has been developed in Taiwan based on a data mining approach using decision tree algorithms [31].
Considering the landscape of tools as it stands, we would encourage designers of future tools to do the following. First, to consider focusing their efforts on the types of cancers for which there are currently only limited resources available. Second, to describe the underlying methodology and clearly mention the model and risk factor literature used, with appropriate references as needed. And finally third, to take the time to write not just a disclaimer, but also a detailed privacy policy. Considering not just the current climate of data collection, but also the extremely personal nature of various risk factors for cancers, to do otherwise is simply unconscionable.
Other authors have already emphasized the large potential cancer risk calculators have to provide a public health benefit by educating individuals about their risks, and hence encouraging preventive health behaviors [32].This seems particularly important considering that there are studies linking low health literacy with poor appreciation of health risk analyses and even inadequate screening participation [33]. This, in turn, suggests a large potential for development and utilization of applications in secondary prevention, which could be an interesting field of future research. If developed appropriately with responsible governance, they could play important roles in modern-day cancer management [18].

Limitations

Evaluating digital tools remains challenging for various reasons, limiting the scope of our conclusions. For mobile applications, we have included scores based on the MARS, which has been shown to be multidimensional and flexible, but its rating criteria are based on relatively few peer-reviewed journal articles and interrater reliability of some subsections is poor [34].
As for websites, most of the literature on the evaluation of sites focuses mostly on technical aspects, typically presented as checklists, and while there appears to be agreement about key criteria concepts [35], these invariably assess the site as a whole, rather than any specific tool. In the current context, this would mean that the entire NCI website would have to be evaluated when considering the calculators found there, which poses obvious problems.
It also bears mentioning that some common criteria for the evaluation of tools - like entertainment (through processes like gamification), graphics or probability of repeat usage - may not be suitable when considering the applications presented here and might be downright inappropriate. For instance,

the IPCRC application is a very simple application that is intended to be used once (or at most a handful of times), by a very select group of users for a very specific purpose. Current evaluation criteria are simply not adequate to consider such tools, which is illustrated by the large discrepancy between its relatively poor MARS score and its extremely good user score, a feat all the more impressive when considering that the user score for this application was based on scoring by a very large number of users.

Finally, while we think that the list of mobile applications can be considered complete, the same cannot be definitely stated for the web applications. Due to the vastness of the internet and our relying on various search engines and their underlying algorithms, we cannot exclude the possibility that there are tools that were overlooked.

Summary Points

What was already known on the topic:

- ●Studies link low health literacy with poor appreciation of health risk analyses.
- ●There is a large potential for cancer risk calculators to provide a public health benefit by educating individuals about their risks, and hence encouraging preventive health behaviors.
- ●It has been acknowledged that mobile technologies are becoming an important resource for health services delivery and public health due to their ease of use, broad reach and wide acceptance.

What this study added to our knowledge:

- ●The majority of the calculators focus only on the most common and most lethal cancers, namely breast, prostate and lung cancer.
- ●Most of these tools only deal with one cancer and for many cancers there is only one tool available.
- ●For the moment, online calculators for cancer risk remain more numerous than mobile risk calculators, but this balance will likely shift in the near future.
- ●Mobile applications are poised to impact all aspects of cancer care, with initiatives by both governments and private developers.

Conclusion

The time seems to be ripe for more detailed studies on the impact of cancer risk calculators, preferably in a prospective setting. These risk calculators could improve the health literacy of patients and encourage them to adhere to preventive health measures.

References

[1] D. Nutbeam, Health literacy as a population strategy for health promotion, Japanese Journal of Health Education and Promotion 25 (3) (2017) 210–222.

[2] T.C. Davis, M.V. Williams, E. Marin, et al., Health literacy and cancer communication, CA Cancer J Clin. (2002 May-June;52(3):134–49.).

[3] T.L. Hart, S. Blacker, A. Panjwani, et al., Development of multimedia informational tools for breast cancer patients with low levels of health literacy, Patient Educ Couns. 98 (3) (2015 Mar) 370–377.

[4] Australian Commission on Safety and Quality in Health Care. National statement on health literacy; 2014.
[5] Chinese Ministry of Health, 66 tips of health: Chinese resident health literacy manual, People's Medical Publishing House, Beijing, 2008.
[6] US Department of Health and Human Services, National action plan to improve health literacy, Office of disease prevention and health promotion, Washington DC, 2010.
[7] International Agency for Research on Cancer, World Health Organisation.
[8] D.D. Joyce, D.L. Heslop, J.I. Umoh, et al., Examining the association of health literacy and numeracy with prostate-related knowledge and prostate cancer treatment regret, Urol Oncol. 38 (8) (2020 Aug) 682.e11–682.e19.
[9] K.M. Mazor, D.L. Rubin, D.W. Roblin, et al., Health literacy-listening skill and patient questions following cancer prevention and screening discussions, Health Expect. 19(4) (2016 Aug) 920–934.
[10] J.K. Papadakos, S.M. Hasan, J. Barnsley, et al., Health literacy and cancer self-management behaviors: A scoping review, Cancer. 124 (21) (2018) 4202–4210.
[11] D. Nutbeam, B. McGill, P. Premkumar, Improving health literacy in community populations: a review of progress, Health Promot Int. 33 (5) (2018 Oct 1) 901–911.
[12] A. Austvoll-Dahlgren, A. Bjørndal, J. Odgaard-Jensen, et al., Evaluation of a web portal for improving public access to evidence-based health information and health literacy skills: a pragmatic trial, PLoS One. 7 (5) (2012), e37715.
[13] M. Jay, J. Adams, S.J. Herring, et al., A randomized trial of a brief multimedia intervention to improve comprehension of food labels, Prev Med. 48 (1) (2009) 25–31.
[14] E. Kemp, J. Trigg, L. Beatty, et al., Health literacy, digital health literacy and the implementation of digital health technologies in cancer care: the need for a strategic approach, Health Promot J Austr. 32 (Suppl 1) (2021 Feb) 104–114.
[15] World Health Organization. eHealth at WHO. Available online: https://www.who.int/ehealth/about/en/ (Accessed: 12 Januari 2021).
[16] World Health Organization. EB139/8, 139th session, 27 May 2016, Provisional agenda item 6.6.
[17] World Health Organization. SEVENTY-FIRST WORLD HEALTH ASSEMBLY. WHA71.7 Agenda item 12.4. 26 May 2018. Digital health.
[18] E. Jamnadass, B.P. Rai, D. Veneziano, et al., Do prostate cancer-related mobile phone apps have a role in contemporary prostate cancer management? A systematic review by EAU young academic urologists (YAU) urotechnology group, World J Urol. 38 (10) (2020 Oct) 2411–2431.
[19] N. Pereira-Azevedo, L. Osorio, ´ V. Cavadas, et al., Expert Involvement Predicts mHealth App Downloads: Multivariate Regression Analysis of Urology Apps, JMIR Mhealth Uhealth 4 (2016), e86.
[20] S.D. Gadenz, E. Harzheim, H.G. Amaral, et al., Development and Assessment of a Mobile Nutritional Counseling Tool for Primary Care Physicians, Telemed J E Health. 26 (6) (2020 Jun) 805–811.
[21] https://riskcalc.org/ (Accessed: 12 Januari 2021).
[22] https://www.mskcc.org/nomograms (Accessed: 12 Januari 2021).
[23] https://www.mdanderson.org/for-physicians/clinical-tools-resources/clinical-calculators.html (Accessed: 12 Januari 2021).
[24] The World Bank. (17 July 2012). 'Maximizing Mobile' Report Highlights Development Potential of Mobile Communications. Available online: https://www.worldbank.org/en/news/feature/2012/07/17/maximizing-mobile-development-potential-mobile-communications (Accessed: 12 Januari 2021).
[25] Sensor Tower., 2020 Data Digest. mHealth Apps Market Size , Share & Trends Analysis, Q2.

[26] Research and Markets. mHealth Apps Market Size, Share & Trends Analysis Report By Type (Fitness, Lifestyle Management, Nutrition & Diet, Women's Health, Medication Adherence, Healthcare Providers/Payers), And Segment Forecasts, 2019 - 2026; June 2019.
[27] WeAreSocial. Digital 2020 July Global Statshot Report.
[28] Accenture. Losing Patience: Why Healthcare Providers Need to Up Their Mobile Game; 2015.
[29] Accenture. (6 Januari 2016). 'U.S. Hospitals Engaging Only 2 Percent of Patients via Mobile Apps, Putting as Much as $100 Million in Annual Revenue [Per Hospital] at Risk.' Available online: https://newsroom.accenture.com/news/us-hospitals-engaging-only-2-percent-of-patients-via-mobile-apps-putting-as-much-as-100-million-in-annual-revenue-per-hospital-at-risk-accenture-finds.htm (Accessed: 12 Januari 2021).
[30] M.F. Mohamad Marzuki, N.A. Yaacob, N.M. Bin Yaacob, et al., Usable Mobile App for Community Education on Colorectal Cancer: Development Process and Usability Study, JMIR Hum Factors. 6 (2) (2019 Apr 16), e12103.
[31] H.C. Wu, C.J. Chang, C.C. Lin, et al., Developing screening services for colorectal cancer on Android smartphones, Telemed J E Health. 20 (8) (2014) 687–695.
[32] A.G. Levy, S.S. Sonnad, J.E. Kurichi, et al., Making sense of cancer risk calculators on the web, J Gen Intern Med. 23 (3) (2008) 229–235.
[33] C.H. Huang, Y.J. Lo, K.M. Kuo, et al., Health literacy and cancer screening behaviors among community-dwelling female adults in Taiwan, Women Health. (2021 May-Jun;61(5):408–419.).
[34] Stoyanov S, Hides L, Kavanagh D, et al., Mobile App Rating Scale: A New Tool for Assessing the Quality of Health Mobile Apps. JMIR Mhealth Uhealth 2015;3(1):e27.
[35] A. Baumel, M.L. Birnbaum, M. Sucala, A Systematic Review and Taxonomy of Published Quality Criteria Related to the Evaluation of User-Facing eHealth Programs, J Med Syst. 41 (8) (2017 Aug) 128.

Annex 1: Quality Rating – ‘Melanoma Test’ app

The Rating scale assesses app quality on four dimensions. All items are rated on a 5-point scale from “1.Inadequate” to “5.Excellent”. Circle the number that most accurately represents the quality of the app component you are rating. Please use the descriptors provided for each response category.

SECTION A

Engagement – fun, interesting, customisable, interactive (e.g. sends alerts, messages, reminders, feedback, enables sharing), well-targeted to audience

1. **Entertainment: Is the app fun/entertaining to use? Does it use any strategies to increase engagement through entertainment (e.g. through gamification)?**

   1 Dull, not fun or entertaining at all
   2 Mostly boring
   3 OK, fun enough to entertain user for a brief time (< 5 minutes)
   4 Moderately fun and entertaining, would entertain user for some time (5-10 minutes total)
   5 Highly entertaining and fun, would stimulate repeat use

2. **Interest: Is the app interesting to use? Does it use any strategies to increase engagement by presenting its content in an interesting way?**

   1 Not interesting at all
   2 Mostly uninteresting
   3 OK, neither interesting nor uninteresting; would engage user for a brief time (< 5 minutes)
   4 Moderately interesting; would engage user for some time (5-10 minutes total)
   5 Very interesting, would engage user in repeat use

3. **Customisation: Does it provide/retain all necessary settings/preferences for apps features (e.g.**

sound, content, notifications, etc.)?

   1 Does not allow any customisation or requires setting to be input every time
   2 Allows insufficient customisation limiting functions
   3 Allows basic customisation to function adequately
   4 Allows numerous options for customisation
   5 Allows complete tailoring to the individual’s characteristics/preferences, retains all settings

4. **Interactivity: Does it allow user input, provide feedback, contain prompts (reminders, sharing options, notifications, etc.)? Note: these functions need to be customisable and not overwhelming in order to be perfect.**

1 No interactive features and/or no response to user interaction
2 Insufficient interactivity, or feedback, or user input options, limiting functions
3 Basic interactive features to function adequately
4 Offers a variety of interactive features/feedback/user input options
5 Very high level of responsiveness through interactive features/feedback/user input options

5. **Target group: Is the app content (visual information, language, design) appropriate for your target audience?**

1 Completely inappropriate/unclear/confusing
2 Mostly inappropriate/unclear/confusing
3 Acceptable but not targeted. May be inappropriate/unclear/confusing
4 Well-targeted, with negligible issues
5 Perfectly targeted, no issues found

A. Engagement mean score = _____3.2_____

SECTION B

Functionality – app functioning, easy to learn, navigation, flow logic, and gestural design of app

6. **Performance: How accurately/fast do the app features (functions) and components (buttons/menus) work?**

1 App is broken; no/insufficient/inaccurate response (e.g. crashes/bugs/broken features, etc.)
2 Some functions work, but lagging or contains major technical problems
3 App works overall. Some technical problems need fixing/Slow at times
4 Mostly functional with minor/negligible problems
5 Perfect/timely response; no technical bugs found/contains a 'loading time left' indicator

7. **Ease of use: How easy is it to learn how to use the app; how clear are the menu labels/icons and instructions?**

1 No/limited instructions; menu labels/icons are confusing; complicated
2 Useable after a lot of time/effort
3 Useable after some time/effort
4 Easy to learn how to use the app (or has clear instructions)
5 Able to use app immediately; intuitive; simple

8. **Navigation: Is moving between screens logical/accurate/appropriate/ uninterrupted; are all necessary screen links present?**

    1 Different sections within the app seem logically disconnected and random/confusing/navigation

    is difficult

    2 Usable after a lot of time/effort

    3 Usable after some time/effort

    4 Easy to use or missing a negligible link

    5 Perfectly logical, easy, clear and intuitive screen flow throughout, or offers shortcuts

9. **Gestural design: Are interactions (taps/swipes/pinches/scrolls) consistent and intuitive across all components/screens?**

    1 Completely inconsistent/confusing

    2 Often inconsistent/confusing

    3 OK with some inconsistencies/confusing elements

    4 Mostly consistent/intuitive with negligible problems

    5 Perfectly consistent and intuitive

B. Functionality mean score = ____3.75_____

SECTION C

Aesthetics – graphic design, overall visual appeal, colour scheme, and stylistic consistency

10. **Layout: Is arrangement and size of buttons/icons/menus/content on the screen appropriate or zoomable if needed?**

    1 Very bad design, cluttered, some options impossible to select/locate/see/read device display not optimised

    2 Bad design, random, unclear, some options difficult to select/locate/see/read

    3 Satisfactory, few problems with selecting/locating/seeing/reading items or with minor screensize problems

    4 Mostly clear, able to select/locate/see/read items

    5 Professional, simple, clear, orderly, logically organised, device display optimised. Every design component has a purpose

11. **Graphics: How high is the quality/resolution of graphics used for buttons/icons/menus/content?**

    1 Graphics appear amateur, very poor visual design - disproportionate, completely stylistically inconsistent

    2 Low quality/low resolution graphics; low quality visual design – disproportionate, stylistically inconsistent

3 Moderate quality graphics and visual design (generally consistent in style)

4 High quality/resolution graphics and visual design – mostly proportionate, stylistically consistent

5 Very high quality/resolution graphics and visual design - proportionate, stylistically consistent throughout

12. Visual appeal: How good does the app look?

1 No visual appeal, unpleasant to look at, poorly designed, clashing/mismatched colours

2 Little visual appeal – poorly designed, bad use of colour, visually boring

3 Some visual appeal – average, neither pleasant, nor unpleasant

4 High level of visual appeal – seamless graphics – consistent and professionally designed

5 As above + very attractive, memorable, stands out; use of colour enhances app features/menus

C. Aesthetics mean score = ____5_____

SECTION D

Information – Contains high quality information (e.g. text, feedback, measures, references) from a credible source. Select N/A if the app component is irrelevant.

13. Accuracy of app description (in app store): Does app contain what is described?

1 Misleading. App does not contain the described components/functions. Or has no description

2 Inaccurate. App contains very few of the described components/functions

3 OK. App contains some of the described components/functions

4 Accurate. App contains most of the described components/functions

5 Highly accurate description of the app components/functions

14. Goals: Does app have specific, measurable and achievable goals (specified in app store description or within the app itself)?

N/A Description does not list goals, or app goals are irrelevant to research goal (e.g. using a game for educational purposes)

1 App has no chance of achieving its stated goals

2 Description lists some goals, but app has very little chance of achieving them

3 OK. App has clear goals, which may be achievable.

4 App has clearly specified goals, which are measurable and achievable

5 App has specific and measurable goals, which are highly likely to be achieved

15. **Quality of information: Is app content correct, well written, and relevant to the goal/topic of the app?**

N/A There is no information within the app

1 Irrelevant/inappropriate/incoherent/incorrect

2 Poor. Barely relevant/appropriate/coherent/may be incorrect

3 Moderately relevant/appropriate/coherent/and appears correct

4 Relevant/appropriate/coherent/correct

5 Highly relevant, appropriate, coherent, and correct

16. **Quantity of information: Is the extent coverage within the scope of the app; and comprehensive but concise?**

N/A There is no information within the app

1 Minimal or overwhelming

2 Insufficient or possibly overwhelming

3 OK but not comprehensive or concise

4 Offers a broad range of information, has some gaps or unnecessary detail; or has no links to more information and resources

5 Comprehensive and concise; contains links to more information and resources

17. **Visual information: Is visual explanation of concepts – through charts/graphs/images/videos, etc. – clear, logical, correct?**

N/A There is no visual information within the app (e.g. it only contains audio, or text)

1 Completely unclear/confusing/wrong or necessary but missing

2 Mostly unclear/confusing/wrong

3 OK but often unclear/confusing/wrong

4 Mostly clear/logical/correct with negligible issues

5 Perfectly clear/logical/correct

18. **Credibility: Does the app come from a legitimate source (specified in app store description or within the app itself)?**

1 Source identified but legitimacy/trustworthiness of source is questionable (e.g. commercial business with vested interest)

2 Appears to come from a legitimate source, but it cannot be verified (e.g. has no webpage)

3 Developed by small NGO/institution (hospital/centre, etc.) /specialised commercial business, funding body

4 Developed by government, university or as above but larger in scale

5 Developed using nationally competitive government or research funding (e.g. Australian Research Council, NHMRC)

19. **Evidence base: Has the app been trialled/tested; must be verified by evidence (in published scientific literature)?**

N/A The app has not been trialled/tested

1 The evidence suggests the app does not work

2 App has been trialled (e.g., acceptability, usability, satisfaction ratings) and has partially positive outcomes in studies that are not randomised controlled trials (RCTs), or there is little or no contradictory evidence.

3 App has been trialled (e.g., acceptability, usability, satisfaction ratings) and has positive outcomes in studies that are not RCTs, and there is no contradictory evidence.

4 App has been trialled and outcome tested in 1-2 RCTs indicating positive results

5 App has been trialled and outcome tested in ≥ 3 high quality RCTs indicating positive results

D. Information mean score = ____3.57_____ *

* Exclude questions rated as "N/A" from the mean score calculation.

Scoring

App quality scores for

SECTION

A: Engagement Mean Score = _____**3.2**_____

B: Functionality Mean Score = _____**3.75**_____

C: Aesthetics Mean Score = _____**5**_____

D: Information Mean Score = _____**3.57**_____

App quality mean Score = _____3.88_____

Chapter 2: Comparative Analysis of Existing Predictive Models for Individual Cancer Risk

Introduction

The genesis of cancer risk prediction models dates back several decades, with pioneering efforts aimed at identifying individuals at higher risk of developing chronic diseases. Among the first of these was the Framingham Coronary Risk Prediction Model introduced in 1976 [1], which utilized a combination of clinical and biological factors to estimate the risk of heart disease. This model set the precedent for future endeavors in risk prediction, demonstrating the utility of incorporating multiple risk factors into a cohesive model to inform clinical decision-making. Its success paved the way for the development of models focused on cancer risk, beginning in earnest in the late 1980s and early 1990s. These early models primarily targeted breast cancer, integrating known risk factors such as age, reproductive history, and family history to calculate an individual's absolute risk of developing the disease over a specified timeframe.

The interest in and reliance on cancer risk prediction models have only intensified since. Today, the proliferation of digital platforms, from informational websites to comprehensive handbooks and professional society resources, underscores the growing public and professional interest in these tools. This is further evidenced by the emergence of companies offering genetic risk profiling services and the prioritization of risk prediction research by leading cancer institutions like the National Cancer Institute (NCI). The NCI, recognizing the significance of risk prediction in cancer research, has highlighted it as an area of "extraordinary opportunity" [2].

However, as the number of cancer types studied and the sophistication of predictive models have expanded, so too has the variability in their development, application, and evaluation. The proliferation of models has led to a landscape marked by significant disparities in the number and type of models available for different cancer types. This uneven distribution raises important questions about the factors driving these disparities and the implications for cancer risk prediction across the spectrum of disease. It underscores the need for a comprehensive examination of the current state of cancer risk prediction modeling, with a focus on understanding the diversity of approaches and the challenges and opportunities they present.

This chapter aims to delve into these issues, providing a thorough analysis of the existing landscape of cancer risk prediction models. By examining the differences in the number and nature of models developed for various cancer types, it seeks to shed light on the complexities of predicting cancer risk and the implications for clinical practice, public health policy, and future research directions.

Materials and Methods

Study Selection

We evaluated cancer risk prediction models by searching PubMed, Web of Science, and Scopus up to December 2023. Inclusion criteria mandated studies to be peer-reviewed, detailed risk models of cancer. Diagnostic models were included, but diagnostic testing studies were excluded, as were feasibility studies and cost-benefit studies. Models for the development of a second cancer were

included, but prognostic models for the risk of cancer relapse, metastasis or cancer-specific survival were excluded.

Data Extraction and Synthesis

For each study, we extracted comprehensive data including model name, year, type, targeted population, geographical area, follow-up duration, number of subjects, derivation set size, validation metrics, discrimination power, factors incorporated, TRIPOD level, data sources, data collection years, participant age, prediction rule risk thresholds, study design, methods, applicability, strengths, limitations, risk measures, calibration, accuracy (sensitivity/specificity), independent testing, inclusion/exclusion criteria, prognostic/diagnostic focus, validation efforts, and reproducibility.

Results

Type of cancer

Our comprehensive analysis encompassed a wide array of cancer types, each represented by distinct models focusing on risk prediction. The models spanned across 22 cancer types (Table 1). This diverse collection illustrated the breadth of research efforts aimed at developing predictive models that incorporate a range of risk factors.

Table 1: Division of models across cancers and articles.

Cancer Type	Number of Articles	Number of Models
Bladder	17	29
Breast	103	143
Colorectal	94	144
Oesophagus	23	47
Blood	6	9
Kidney	25	39
Head & Neck	16	23
Liver	33	46
Lung	40	65
Ovary	14	14
Pancreas	35	48
Prostate	68	97
Melanoma	35	62
Stomach	17	19
Testis	2	2
Thyroid	4	6
Cervix	4	4
Endometrium	16	17
General	3	4
Non-melanoma skin cancer	7	10
Eye	1	1
Gallbladder	1	3

We did not find any model for Cancer of the brain or nervous system, Kaposi sarcoma, Mesothelioma, Penis cancer, Anal cancer, Vaginal cancer, Bone sarcoma, Soft tissue sarcoma, Small intestine cancer, and Sinonasal cancer. There are several possible reasons for this.First, some cancers, such as Kaposi

sarcoma and Sinonasal cancer, are relatively rare, making it challenging to gather sufficient data for model development. Second, several of these cancers might have complex pathophysiologies that may complicate risk prediction modeling. And third, there may be less research focus or funding for certain cancers compared to more prevalent types like breast or lung cancer. In any case, the research focus is clearly skewed towards the most frequent cancers [3] and particularly towards cancers for whom early diagnosis might be the most feasible and beneficial. Efforts are now underway to have such models inform screening [4].

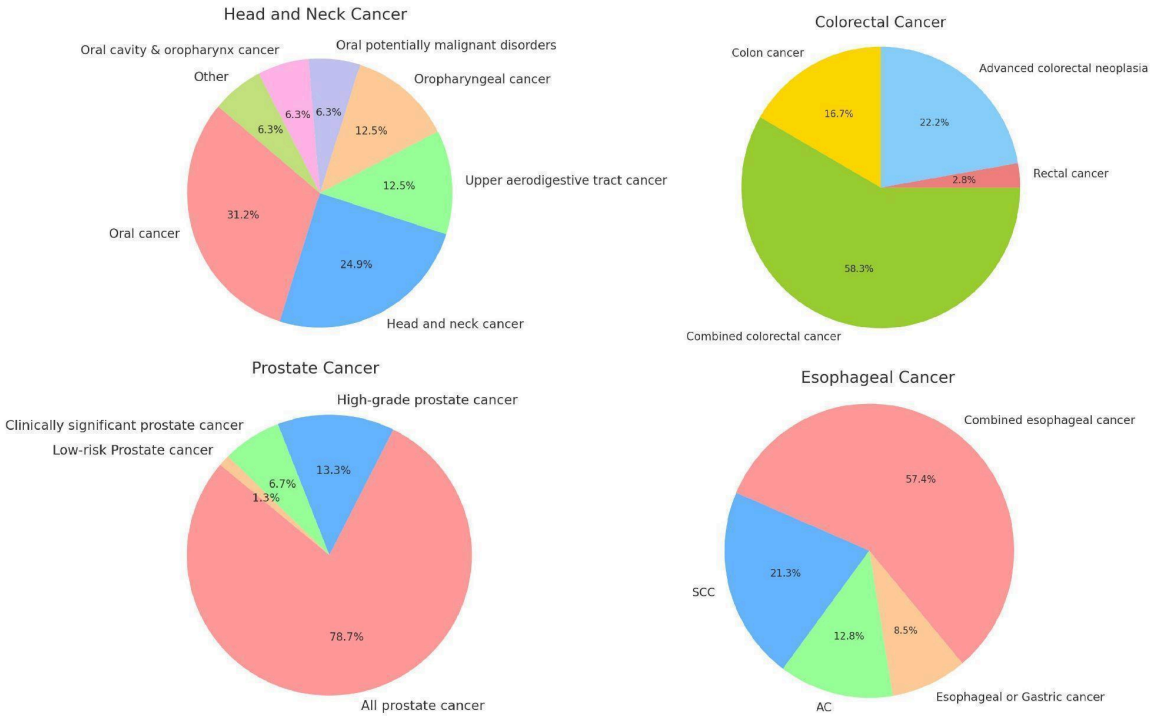


Figure 1: Representation of subtypes in models for Head and Neck cancer, Colorectal cancer, Prostate cancer and Esophageal cancer. (SCC: Squamous cell carcinoma, AC: Adenocarcinoma)

The integration of subtype-specific data into cancer risk prediction models offers a nuanced approach that may significantly enhance the accuracy and clinical utility of these models. We have provided an overview of the different subtypes for the cancers for whom it was most relevant, namely colorectal cancer, esophageal cancer, head and neck cancer, and prostate cancer (Figure 1). The underlying logic for the development of specific models within these cancers is somewhat different for each.

Colorectal cancer encompasses 2 distinct subtypes based on location, with notable differences between colon cancer and rectal cancer in terms of location, progression, and response to treatment. Esophageal cancer subtypes are distinguished by their cellular origins (adenocarcinoma and squamous cell carcinoma), presenting unique challenges in risk prediction. The subtype analysis helps in understanding the etiological differences — primarily tied to acid reflux and smoking or alcohol consumption, respectively. H&N cancers are notable for their large number of subsites, making it difficult to include sufficient patients for each specific subsite. Prostate cancer models are primarily divided by clinical relevance. These distinctions are useful, since they can significantly influence the

management strategies. Indolent tumors might require active surveillance, whereas aggressive forms demand more intensive treatment modalities.

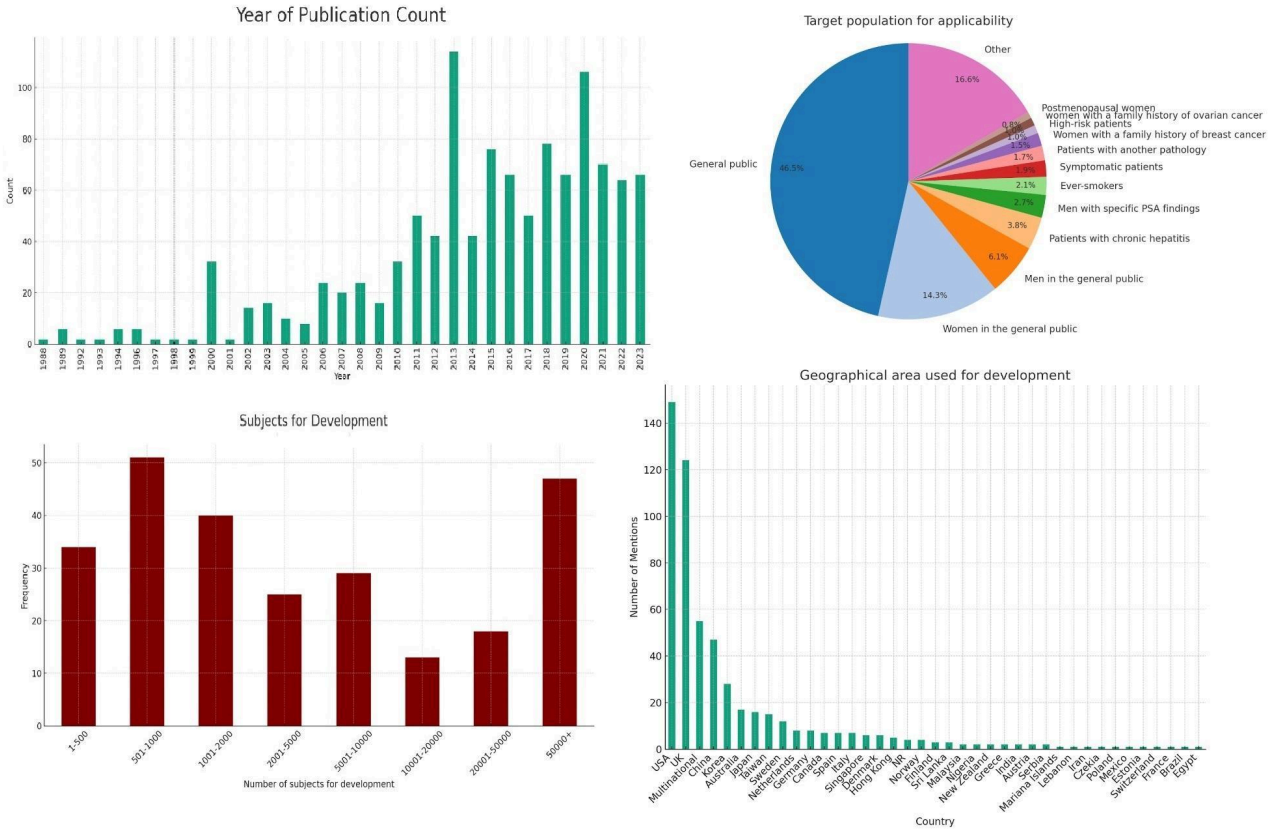


Figure 2: Division of models for year of publication, target population, size of the development group and country of development.

Year of publication

The earliest model we identified was published in 1988 and models have continued to be published up until the present (Figure 2). Upon examining the frequency of publications over these years, we see steadily rising interest in the field, although we also observe a non-uniform distribution. The late 1980s and early 1990s show sporadic activity with a few publications, signaling the nascent stages of cancer risk modeling. This period likely represents the foundational research efforts, characterized by pioneering studies exploring the feasibility and methodologies for cancer risk prediction. A good example of this is the Gail model for breast cancer [5] which was published in 1989 and has not only been adapted to specific populations [6], but has also led to the development of other models that have tried to imitate its unique methodology [7–9]. Starting in 2000, we see a noticeable uptick in the number of publications, which could be attributed to advances in computational methods, increased availability of epidemiological data, and a growing recognition of the potential for predictive models in personalizing cancer screening and prevention strategies. This continued interest is likely driven by the integration of new technologies (e.g., machine learning, big data analytics) into risk modeling, the identification of new risk factors through genomic studies, and a push towards more personalized and precise oncology.

Applicability

The examination of target populations for the applicability of newly developed cancer risk prediction models reveals a broad spectrum of demographics and clinical conditions, reflecting the diverse nature of cancer risk factors and tailored preventive strategies (Figure 2). For this analysis, we did not take ethnic background or nationality into account, since this is inherent in the development population. We did not represent age criteria to allow for easier representation of the data. Without considering such age criteria, roughly half of the prediction models were applicable to the general public. The pronounced emphasis on gender-specific cancer risk prediction models can be largely attributed to the prevalence of breast and prostate cancers, which are the most common cancers among women and men, respectively. This focus is not only reflective of the high incidence rates but also underscores the significant impact these cancers have on public health.

Models tailored to chronic hepatitis (3.8%), other medical conditions (1.7%) and symptomatic patients (1.9%) highlight the integration of clinical indicators in risk prediction and a move towards more personalized medicine.

Targeted models for high-risk groups, including those with a family history of breast (1.6%) or ovarian cancer (1.0%), point towards the use of genetic information and family medical history as critical components in predicting cancer risks. These models are crucial for early intervention strategies in populations known to carry higher genetic risks.

Population used for development

Our analysis of the geographical areas utilized for the development of such models reveals a concentrated effort across a select number of countries, with the United States (USA) and the United Kingdom (UK) leading in terms of the volume of contributions (Figure 2). This distribution highlights the significant engagement of these countries in cancer research and particularly their pivotal role in the development of large databases that are critical in the development of risk prediction models.

The geographical distribution of cancer risk prediction model development efforts also reflects a targeted approach, often dictated by the incidence rates of specific cancers within regions. This targeted focus is not arbitrary but a strategic alignment with the pressing needs of each region, informed by the prevalent cancer types. For example, liver cancer, which has a markedly higher incidence in Asia compared to Western countries, sees a proportionately larger number of predictive models developed within Asian countries. This regional concentration in model development is driven by the imperative to address the most significant cancer threats affecting the population, leveraging local research capacities and clinical insights to devise accurate predictive tools.

The emphasis on developing region-specific models based on prevalent cancer types does not necessarily detract from the global utility of these models. Instead, it highlights the complexity of cancer as a global health challenge and underscores the importance of a multifaceted approach in prediction model development. However, what might pose a potential limitation in the global applicability of these models is the underrepresentation of many other countries and regions. This slant towards data from predominantly Western and Asian populations might limit the effectiveness of the prediction models when applied to populations with different genetic backgrounds, lifestyles, and environmental exposures.

The integration of data from multinational studies into these models serves to bridge the gap between regional specificity and global applicability. This approach ensures that the models are not only

reflective of the unique cancer profiles of different regions but are also versatile enough to be adapted across various global contexts.

The development of robust cancer risk prediction models is critically dependent on the demographic and statistical characteristics of the subjects included in the development cohorts. An analysis of the cohort sizes used across various studies provides insights into the statistical power and potential generalizability of the resulting models (Figure 2).

A significant number of studies rely on relatively small cohorts. While these studies can offer highly detailed data on specific populations, they may lack the statistical power necessary for broader applicability and may be more prone to overfitting. Larger cohorts can provide the robust data needed to account for a variety of genetic, environmental, and lifestyle factors that influence cancer risk. They also typically provide a more reliable basis for developing predictive models due to their greater diversity and statistical power. However, the feasibility of assembling such large cohorts often limits their availability. Therefore, strategies that combine data from multiple smaller studies (meta-analysis) or the use of synthetic data augmentation techniques may be necessary to enhance the predictive accuracy and generalizability of risk models.

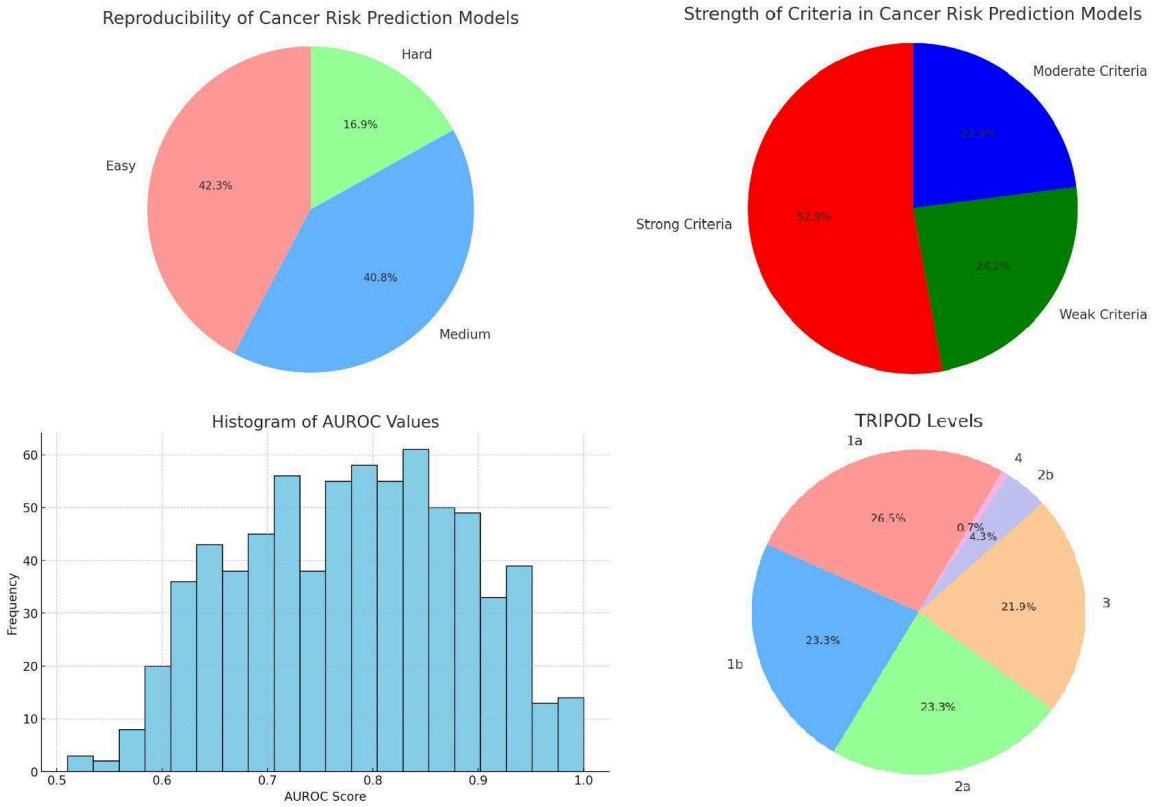


Figure 3: Division of models for reproducibility, strength of criteria, discrimination and TRIPOD level.

Inclusion/exclusion criteria

Inclusion and exclusion criteria of the population used to develop a model is critical, as they directly influence the model's applicability, accuracy, and generalizability. We scored the inclusion and

exclusion criteria for its specificity and comprehensiveness. Based on the content and specificity of the descriptions, criteria were classified into three categories (Figure 3).

Strong criteria were often detailed and tailored to the study's specific cancer type or risk factor. For example, criteria such as "Patients aged ≥18 years referred for haematuria investigations" and "Previous history of bladder cancer" reflect a focused approach to participant selection, aiming to isolate effects of specific variables on cancer risk.

Moderate criteria, while still significant, offered less granularity. These included conditions like general cancer histories or broader demographic specifications, e.g., "No prior history of cancer (except nonmelanoma skin cancer)" or "African-American ethnicity aged 35–64 years." Such criteria help refine the study population but do not delve into as much detail as strong criteria.

Weak criteria were noted to be the least specific, sometimes due to incomplete data or overly broad definitions, such as participants described simply by lack of certain diagnostic data or minimal demographic details without further health specifications.

The strength of inclusion and exclusion criteria is pivotal in determining the precision and relevance of cancer risk prediction models. Strong criteria enhance the model's predictive power by ensuring that the cohort closely matches the intended population. However, overly restrictive criteria can limit the generalizability of the results. Therefore, it is important to clearly define criteria without diluting the predictive accuracy due to a less targeted participant pool.

Reproducibility

In the context of cancer risk prediction models, user-friendliness and accessibility are essential for ensuring that these tools can be widely adopted and effectively utilized across various clinical and research settings, particularly because automated tools remain relatively rare [10]. We used a scoring system, with each entry categorized according to its implied ease of use based on several indicators:

- Easy: Models that allowed for straightforward usage by including elements such as scoring tables, nomograms or simple formulas. Models that were supported by a website or mobile application were also included here.
- Medium: Models that required a working knowledge of statistics or dedicated software to reproduce were included here to reflect a moderate level of user accessibility.
- Hard: Models involving advanced methods like machine learning or missing significant information.

This analysis reveals a significant proportion of cancer risk prediction models that are user-friendly, potentially facilitating broader adoption and application in diverse settings (Figure 3). We consider this to be of critical importance, particularly because we have attempted to reproduce a large number of these models by way of a mobile application [11], thereby facilitating access to them. However, the considerable number of models with moderate or challenging ease of use highlights the ongoing need for improved design and documentation practices to make these tools more accessible.

Discrimination power

Discriminatory power, measured by the Area Under the Receiver Operating Characteristic Curve (AUROC), is crucial for the clinical utility of cancer risk models. Our dataset comprises AUROC values derived from various studies or models focused on cancer risk prediction. A total of 716 AUROC values were extracted and analyzed after appropriate data cleaning, including conversion of percentage values and removal of entries before validation (Figure 3). The concentration of scores around the upper end of the spectrum (0.85-0.89) suggests that most cancer risk prediction models perform well in distinguishing between high-risk and low-risk individuals [12]. This high level of performance is essential for models used in clinical settings where the cost of false negatives (failing to identify at-risk individuals) can be significant.

A small number of models exhibit AUROC values below 0.7, which, while still considered acceptable, indicate lower predictive accuracy. These models may require further refinement or might be specific to cancers that are inherently more challenging to predict due to overlapping symptoms with other conditions or less distinct biomarker profiles.

The histogram's wide spread also raises important considerations regarding the variability in model construction, such as differences in underlying algorithms, training datasets, and the specific cancer types being predicted. For instance, models trained on large, well-annotated datasets or those utilizing more advanced machine learning techniques may demonstrate higher AUROC values.

TRIPOD level

The Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) statement, which came out in 2015 [13], encompasses a checklist of 22 essential items, designed to standardize the reporting of studies that develop, validate, or update multivariable prediction models, irrespective of the diagnostic or prognostic aim.

The primary thrust of the TRIPOD guidelines is to foster transparency in reporting prediction model studies. This is achieved by mandating detailed disclosures regarding model development, statistical analysis, validation processes, and performance metrics. Specifically, the guidelines advocate for the explicit reporting of external validation efforts, which are indispensable for gauging a model's generalizability and performance in real-world scenarios. The initiative categorizes predictive models based on their developmental and validation stages into distinct levels: 1a, 1b, 2a, 2b, 3, and 4. A more detailed explanatory figure is added as an addendum.

In analyzing the distribution of TRIPOD levels within our dataset, it is evident that the practices surrounding the development and validation of predictive models vary significantly across studies (Figure 3). We can say that roughly one quarter of the published models rely solely on apparent performance, one quarter exclusively use resampling techniques, one quarter randomly split the data in development and validation sets and one quarter tries to externally validate the model. In other words, for a clear majority of the models attempts were to validate them, although one a minority externally validated them. A larger focus on external validation would be welcome, since this is crucial for determining the generalizability and applicability of predictive models across different populations and settings. Furthermore, for almost a quarter of the models, no validation efforts were made. This is unfortunate, since techniques such as bootstrapping or cross-validation are possible even when data are limited, while still mitigating overfitting and providing a more robust estimate of model performance. The observed distribution reflects a growing recognition within the scientific

community of the need for rigorous evaluation methods to ensure the reliability and generalizability of prediction models.

It should be noted that no additional searches were made for independent validations of the models, which explains the low number of level 4 publications, and that many of the studies that externally validated their data also used resampling techniques beforehand.

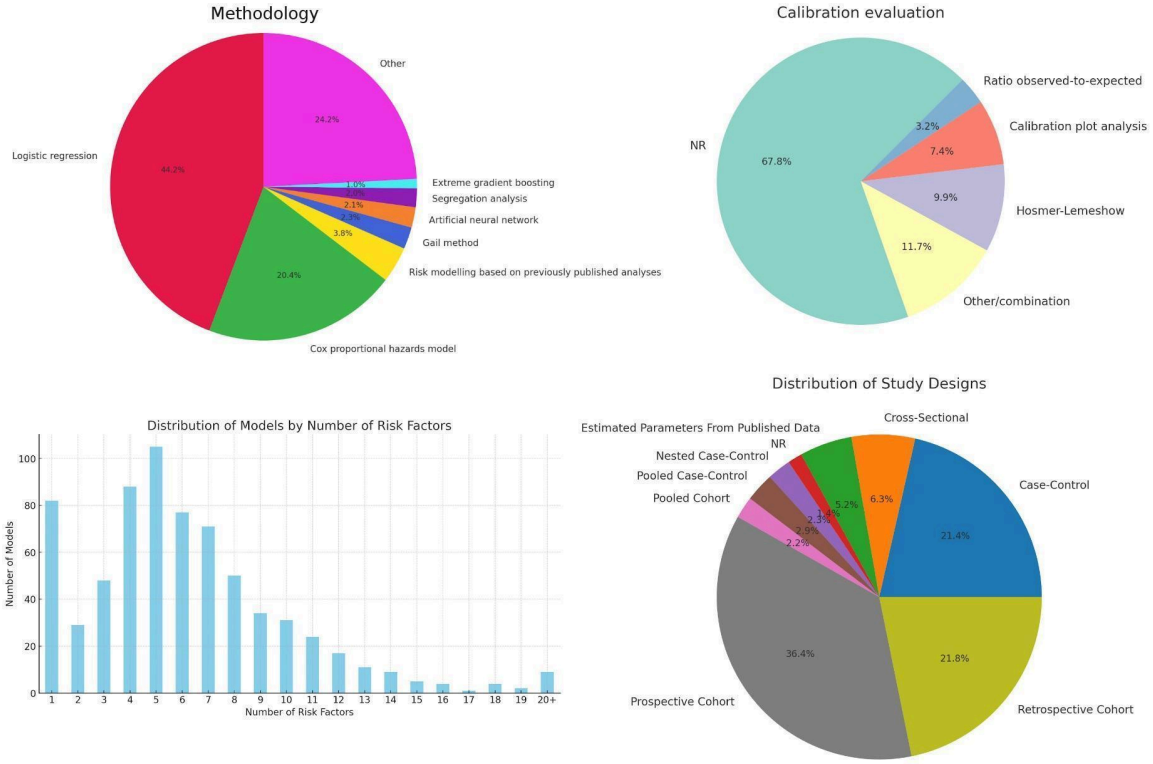


Figure 4: Division of models for methodology, calibration, number of risk factors and study design.

Data for development

The dataset shows a significant reliance on prospective cohort studies (36.4%), valued for their ability to establish temporal sequences between risk factors and cancer outcomes (Figure 4). Retrospective cohort studies (21.8%) offer cost-effective exploration of large populations and historical data, crucial for hypothesis generation. Case-control studies (21.4%) are efficient for studying rare cancers by comparing individuals with and without cancer to identify risk factors.
Interestingly, the dataset also includes Pooled Cohort and Pooled Case-Control studies, signifying a collaborative effort to enhance statistical power and generalize findings across different populations. These pooled analyses, though less common, demonstrate the research community's commitment to overcoming individual study limitations and variability in risk factor exposure across populations.

Model methodology

The analysis shows a clear preference for "Logistic regression" and "Cox proportional hazards model" designs, making up almost two-thirds of the models. Logistic regression, used in 44.2% of the cases, is favored for its straightforward interpretation of binary outcomes like cancer presence, aiding

clinical decision-making (Figure 4). Cox proportional hazards model, at 20.4%, excels in survival analysis, crucial for assessing variables affecting time to events such as recurrence or mortality, thanks to its ability to handle censored data and time-dependent variables. The aggregation category "Other", which constitutes approximately 24.2% of the studies, was used to group modeling strategies that occurred 5 times or less. Its significant size demonstrates the willingness among researchers to innovate and tailor approaches to complex cancer-related questions. Of note, 2.3% of models relied on the Gail method, which was developed specifically for cancer risk prediction [5].

Calibration

Calibration ensures cancer risk prediction models' predicted probabilities match observed outcomes, enhancing model reliability and clinical decision-making [14]. Calibration was primarily evaluated using calibration plot analysis, the Hosmer-Lemeshow test and calculating the observed-to-expected ratio (Figure 4).

The high number of “NR” (Not Reported) entries indicate that calibration is underreported, particularly when compared to discrimination. The common use of the Hosmer-Lemeshow test and calibration plot analysis indicates their popularity in assessing model calibration. The 'Other/combination' category reflects mixed reporting practices, highlighting the need for standardized reporting.

Factors incorporated

As depicted in the accompanying bar graph, there is a significant variance in the number of risk factors utilized across different models (Figure 4). The majority of models incorporate between 4 and 10 risk factors, suggesting a preference for models that balance predictive power and model simplicity.

Notably, the models employing exactly 5 risk factors represent the peak in our distribution, indicating a common model configuration that may offer an optimal balance between complexity and ease of interpretation. This could be reflective of the fact that beyond a certain point, adding more risk factors can lead to diminishing returns in terms of predictive accuracy and model usability.

A notable observation from the analysis of cancer risk prediction models is the relatively large number of models that utilize only one risk factor. This phenomenon may initially seem counterintuitive given the complex nature of cancer, but two key factors contribute to its prevalence. First, the single risk factor in question is often a score of some sort that relies on several elements. These are usually high-resolution imaging and sophisticated genetic sequencing techniques, allowing for comprehensive insights. Second, the models in question were usually developed for highly selected target groups, which is clear from the intended inclusion and exclusion criteria for their development cohort.

The presence of models with 20 or more risk factors highlights an approach where extensive data collection and analysis are prioritized. These models, although less common, were usually models employing machine learning or where highly individualized clinical information was available. The risk factors in these models might include genetic markers, lifestyle factors, and detailed medical histories, which can significantly enhance predictive accuracy at the cost of increased data requirements and computational complexity.

Still, this accounts for a relatively modest number of models, suggesting a threshold beyond which the inclusion of additional risk factors may not be practical or beneficial in everyday clinical practice.

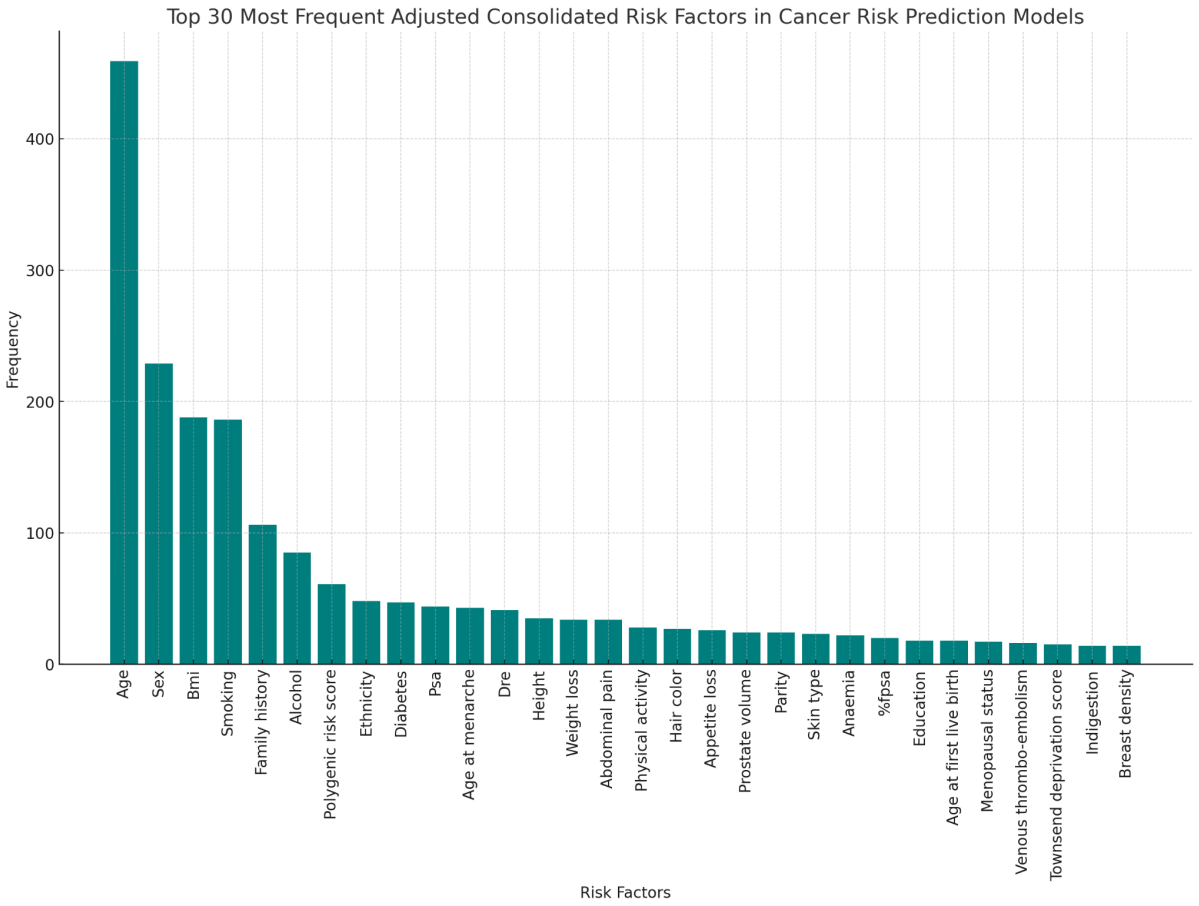


Figure 5: Most frequent risk factors in models.

The analysis of the most frequently incorporated risk factors across various models offers a revealing glimpse into the current priorities and methodologies in cancer risk assessment (Figure 5).

The most prominent risk factors are:

1. Age and Gender: Unsurprisingly, age remains the most commonly cited risk factor, reflecting its fundamental influence on cancer susceptibility across multiple types. Similarly, gender is frequently considered, underlining specific cancer risks that are prevalent in either males or females, such as prostate and breast cancers, respectively.
2. Genetic Markers: The inclusion of genetic markers, notably Polygenic Risk Scores and SNPs (Single Nucleotide Polymorphisms), highlights a significant shift towards genetic profiling in cancer prediction. These factors are crucial for assessing hereditary risks and are increasingly used to personalize screening and prevention strategies.
3. Family History: This risk factor, often broken down into specific cancers such as lung cancer, underscores the importance of genetic predispositions in cancer risk assessments. The recurrence of family history across various models indicates a general consensus about its predictive value for hereditary cancer types.
4. Lifestyle Factors (Smoking, Alcohol): Lifestyle choices such as smoking and alcohol consumption are well-represented in cancer risk models. These modifiable risk factors are critical for public health strategies and are actionable in preventative measures.
5. Ethnicity: The inclusion of ethnicity and race as consolidated factors reflects the recognition of different cancer risks and outcomes among ethnic groups, possibly due to genetic, socioeconomic, or environmental variations.

6. Medical History & Symptoms: Conditions like diabetes have been linked to an increased risk of certain cancers, illustrating the interconnected nature of chronic diseases and cancer risk.

The diversity of these risk factors across models points to a multi-faceted approach to cancer risk prediction, where both genetic and environmental factors are considered. This broad spectrum of risk factors aids clinicians in developing more accurate risk assessments and tailored prevention strategies. Moreover, it emphasizes the need for interdisciplinary research to further refine the impact of each risk factor on cancer development.

Discussion

We have mapped the landscape of cancer risk prediction models, illustrating a diversity of approaches that span traditional epidemiological factors and emerging methodologies. The variation in model development, validation, and performance metrics across different cancer types highlights the multifaceted nature of cancer risk prediction and the ongoing evolution of research methodologies in this field.

A key observation from our analysis is the nuanced manner in which risk factors are integrated into predictive models. While genetic markers, including polygenic risk scores, play a role in certain models, it is evident that the most robust models incorporate a blend of genetic, environmental, lifestyle, and clinical factors. This comprehensive approach mirrors the complex etiology of cancer, suggesting that an interplay of diverse risk factors contributes to the disease's development.

This paper underscores a prevalent challenge in the external validation of risk prediction models. Many models have not undergone rigorous testing in diverse populations, which raises questions about their generalizability and utility in broader clinical and public health contexts. Addressing this challenge requires a concerted effort to standardize validation practices and ensure models are tested across varied demographic groups, enhancing their applicability and impact.

The methodological diversity observed among the included models calls for a move towards harmonization. Establishing consensus on methodological best practices, including the selection and weighting of risk factors, could improve the reliability and reproducibility of predictive models. Future research should also prioritize the exploration of underrepresented cancer types and risk factors, broadening the scope of predictive modeling to encompass a wider array of cancers.

The potential impact of these predictive models on cancer prevention and early detection is substantial. Tailored risk assessment can guide personalized screening strategies, potentially leading to earlier detection and more effective interventions for high-risk individuals. However, the translation of these models into clinical practice necessitates not only methodological rigor but also careful consideration of the ethical implications associated with risk prediction, particularly regarding data privacy and the potential for health disparities.

Conclusion

The analysis underscored the progress and challenges within the field of cancer risk prediction. While significant strides have been made, gaps remain, particularly in model validation and in covering a broader spectrum of cancer types. Our findings suggest an ongoing need for rigorous external

validation to ascertain models' applicability and for continued research to fill the existing gaps, thereby enhancing the predictive accuracy and utility of cancer risk models in personalized medicine and public health.

Highlights

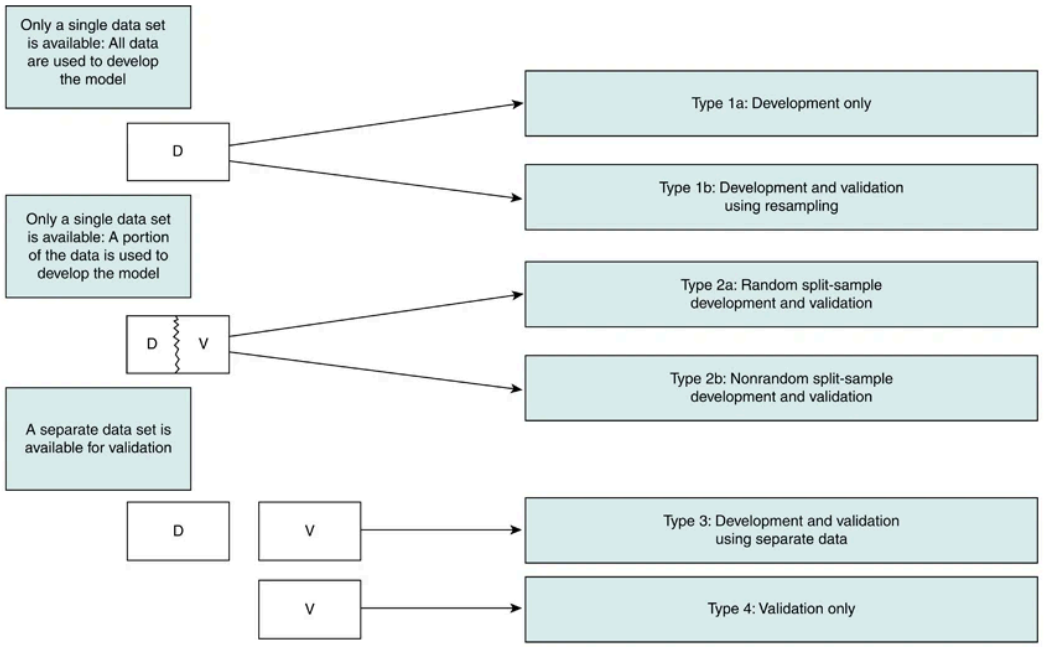
- Identified significant disparities in model development for 22 cancer types, with some cancers lacking models entirely.
- Gives overview of model publication years, geographical spread, applicability and incorporated risk factors.
- Found an increasing scientific interest, largely complementing clinical needs with clear regional research efforts.
- Scored models on reproducibility, discrimination, calibration, TRIPOD level, methodology, development data and in/exclusion criteria.
- Highlighted the need for more external validation and standardized reporting to enhance model reliability.

References

[1] Kannel WB, McGee D, Gordon T. A general cardiovascular risk profile: The Framingham study. Am J Cardiol 1976;38:46–51. https://doi.org/10.1016/0002-9149(76)90061-8.
[2] National Cancer Institute (2006) The nation's investment in cancer research. A plan and budget proposal for the fiscal year 2006. n.d.
[3] Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024. CA Cancer J Clin 2024;74:12–49. https://doi.org/10.3322/caac.21820.
[4] Jeter LK, Morello R, Rivere AE, Fuhrman GM, Mackey AM, Corsetti RL, et al. Impact of Launching A High-Risk Breast Cancer Screening Program Using the Tyrer-Cuzick Model. Am Surg 2023;89:1077–8. https://doi.org/10.1177/0003134820956922.
[5] Gail MH, Brinton LA, Byar DP, Corle DK, Green SB, Schairer C, et al. Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. J Natl Cancer Inst 1989;81:1879–86. https://doi.org/10.1093/jnci/81.24.1879.
[6] Gail MH, Costantino JP, Pee D, Bondy M, Newman L, Selvan M, et al. Projecting individualized absolute invasive breast cancer risk in African American women. J Natl Cancer Inst 2007;99:1782–92. https://doi.org/10.1093/jnci/djm223.
[7] Cassidy A, Myles JP, van Tongeren M, Page RD, Liloglou T, Duffy SW, et al. The LLP risk model: an individual risk prediction model for lung cancer. Br J Cancer 2008;98:270–6. https://doi.org/10.1038/sj.bjc.6604158.
[8] Wu X, Lin J, Grossman HB, Huang M, Gu J, Etzel CJ, et al. Projecting individualized probabilities of developing bladder cancer in white individuals. J Clin Oncol Off J Am Soc Clin Oncol 2007;25:4974–81. https://doi.org/10.1200/JCO.2007.10.7557.
[9] Fears TR, Guerry D, Pfeiffer RM, Sagebiel RW, Elder DE, Halpern A, et al. Identifying individuals at high risk of melanoma: a practical predictor of absolute risk. J Clin Oncol Off J Am Soc Clin Oncol 2006;24:3590–6. https://doi.org/10.1200/JCO.2005.04.1277.
[10] Westerlinck P, Coucke P. Review of interactive digital solutions improving health literacy of personal cancer risks in the general public. Int J Med Inf 2021;154:104564. https://doi.org/10.1016/j.ijmedinf.2021.104564.
[11] Westerlinck P, Coucke P, Albert A. Development of a cancer risk model and mobile health application to inform the public about cancer risks and risk factors. Int J Med Inf 2024;189:105503. https://doi.org/10.1016/j.ijmedinf.2024.105503.

[12] Çorbacıoğlu ŞK, Aksel G. Receiver operating characteristic curve analysis in diagnostic accuracy studies: A guide to interpreting the area under the curve value. Turk J Emerg Med 2023;23:195–8. https://doi.org/10.4103/tjem.tjem_182_23.
[13] Collins GS, Reitsma JB, Altman DG, Moons KGM. Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD): the TRIPOD statement. Ann Intern Med 2015;162:55–63. https://doi.org/10.7326/M14-0697.
[14] Huang Y, Li W, Macheret F, Gabriel RA, Ohno-Machado L. A tutorial on calibration measurements and calibration models for clinical prediction models. J Am Med Inform Assoc JAMIA 2020;27:621–33. https://doi.org/10.1093/jamia/ocz228.

Addendum - TRIPOD Levels



Analysis Type	Description
Type 1a	Development of a prediction model where predictive performance is then directly evaluated using exactly the same data (apparent performance).
Type 1b	Development of a prediction model using the entire data set, but then using resampling (e.g., bootstrapping or cross-validation) techniques to evaluate the performance and optimism of the developed model. Resampling techniques, generally referred to as 'internal validation', are recommended as a prerequisite for prediction model development, particularly if data are limited (6, 14, 15).
Type 2a	The data are randomly split into two groups: one to develop the prediction model, and one to evaluate its predictive performance. This design is generally not recommended or better than type 1b, particularly in case of limited data, because it leads to lack of power during model development and validation (14, 15, 16).
Type 2b	The data are nonrandomly split (e.g., by location or time) into two groups: one to develop the prediction model and one to evaluate its predictive performance. Type 2b is a stronger design for evaluating model performance than type 2a, because it allows for nonrandom variation between the 2 data sets (6, 13, 17).
Type 3	Development of a prediction model using one data set and an evaluation of its performance on separate data (e.g., from a different study).
Type 4	The evaluation of the predictive performance of an existing (published) prediction model on separate data (13).

Types 3 and 4 are commonly referred to as 'external validation studies.' Arguably, type 2b is as well, although it may be considered an intermediary between internal and external validation.

Reproduced from: Collins, G.S., Reitsma, J.B., Altman, D.G. et al. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD Statement. BMC Med 13, 1 (2015). https://doi.org/10.1186/s12916-014-0241-z

Chapter 3: Development of a cancer risk model and mobile health application to inform the public about cancer risks and risk factors

Objective

The need to improve e-health literacy has been emphasized and continuously discussed among health literacy experts and healthcare stakeholders. Health literacy is crucial in navigating the many risk factors for cancer. Low health literacy is associated with low adherence to medications, poor health status, and increased healthcare costs. The development of a mobile application called ‘Cancer Risk Calculator’ (CRC) is described to educate the public on both the risks of developing cancer and the risk factors impacting them. The model underlying the mobile application is also discussed.

Background and Significance

In the evolving landscape of healthcare, the paradigm shift towards patient-centered care has spotlighted the critical role of health literacy. The surge of mobile health (mHealth) technologies has opened new avenues for disseminating health information, but their impact on health literacy, particularly in the realm of oncology, remains an area ripe for exploration.

Health literacy, defined as the degree to which individuals can obtain, process, and understand basic health information and services needed to make appropriate health decisions, is fundamental in the context of disease prevention and management. In the digital age, the intersection of health literacy and technology presents both opportunities and challenges. While digital tools can democratize access to health information, the complexity of the content and the interface design can either facilitate or hinder effective comprehension, especially in areas as intricate as cancer risk assessment.

Cancer, a leading cause of mortality worldwide, presents a public health challenge exacerbated by the general population's often limited understanding of cancer risks and prevention strategies. The complexity of cancer etiology, encompassing genetic, environmental, and lifestyle factors, makes it imperative for health communication tools to not only provide information but also enhance users' understanding and ability to use that information effectively. Digital health technologies can reduce health disparities in cancer care with benefits of digital health technology depending partly on the digital health literacy of the users [1].

A thorough review was conducted on the currently available tools designed to educate the public about individual cancer risk and associated risk factors. This included both mobile applications and online resources. The review confirmed the unique position of the Cancer Risk Calculator application. It stands out as a comprehensive tool, including more types of cancers and risk factors than any other tool. Moreover, it was found to be the only available tool for many cancers [2].

The application presented in this section estimates an individual's general risk of cancer for any single individual and the risk of 38 different cancer types with an additional 18 subtypes, based on approximately 790 risk factors documented in the scientific literature. This tool represents a significant stride in health informatics, marrying complex data algorithms with user-friendly

interfaces to deliver personalized risk assessments. By offering risk information for different timeframes and providing detailed references for each risk factor, the application stands at the forefront of personalized healthcare, empowering users with knowledge that is traditionally limited to the medical community.

Materials and Methods

This section describes the creation of an app for mobile cell phones and tablets to inform the public about cancer risks. The project was conducted in four phases.

Phase 1. Identifying the technical features and necessary content for a comprehensive mobile application

Reliable data from various sources on general cancer risks were reviewed. Guidelines for the identification and possible selection of risk factors were discussed and agreed upon (and are discussed in detail in Phase 3). Features and functions of useful applications were examined with the help of thematic content analysis. Common extracted features and functions were selected and the initial model of the application designed accordingly.

Phase 2. Including average risks of cancer

The probabilities of developing 26 cancers were based on data from the *Surveillance, Epidemiology, and End Results (SEER) Program,* collected since 1973 by the National Cancer Institute (NCI), Bethesda, Maryland, USA, and since 1995 by the Centers for Disease Control and Prevention (CDC) National Program of Cancer Registries (NPCR). This was done by using *Devcan* (version 6.8.0), specifically the most recent version when this application was created. These figures provided a baseline individual risk of cancer according to sex, racial background, and age cohort by decade. An aggregate risk of developing invasive cancer at any site, as reported by SEER, was also provided.

The probabilities of 12 other cancers were not available in the SEER database and were approximated by figures available in the scientific literature. These included penile cancer [3], basocellular skin cancer [4], spinocellular skin cancer [4], anal cancer [5], vaginal/vulvar cancer [6], gallbladder cancer [7], soft tissue sarcoma , bone and joint sarcoma [8], cancer of the small intestine [8], Merkel cell carcinoma [9], cancer of the eye and orbit [10] and sinonasal cancer [11]. Lastly, 18 subtypes of various cancers with separate risk profiles were also identified and added, bringing the total number of separate cancers to 56 (Table 1), each with their own risk calculation. (Summarised under ‘Cancer Algorithms’)

Table 1. List of all cancers included in the application

Cancer Risk	Subtypes
Overall cancer risk	
Bladder cancer	
Brain or nervous system cancer	
Breast cancer	
Colorectal cancer	Colon cancer
	Rectum cancer
Esophageal carcinoma	Esophageal adenocarcinoma (EAC)
	Esophageal squamous-cell carcinoma (ESCC)
Hodgkin lymphoma	
Kaposi's Sarcoma	
Kidney and renal pelvis cancer	

Laryngeal cancer	
Leukemia	Acute lymphoblastic leukemia
	Acute myelogenous (or myeloblastic) leukemia
	Chronic lymphocytic leukemia
	Chronic myelogenous (or myeloblastic) leukemia
	Other leukemia
Liver cancer	
Lung cancer	
Mesothelioma	
Myeloma	
Non-Hodgkin lymphoma	
Oral cavity and pharynx cancer	Tongue Cancer
	Oral Cavity Cancer
	Other oral or pharyngeal cancer
	Nasopharynx cancer
	Oropharynx cancer
	Hypopharynx cancer
Ovarian cancer	
Pancreatic cancer	
Prostate cancer	
Melanoma of the skin	
Stomach cancer	Cancer of the stomach cardia
	Cancer of the rest of the stomach
Testicular cancer	
Thyroid cancer	
Uterine cervix cancer	Adenocarcinoma of the cervix
	Squamous cell carcinoma of the cervix
Uterine corpus cancer	
Penile cancer	
Basal cell carcinoma of the skin	
Squamous cell carcinoma of the skin	
Cancer of the eye and orbit	
Anal cancer	
Cancer of the vulva or vagina	
Gallbladder cancer	
Bone or joint sarcoma	
Soft Tissue sarcoma	
Small intestine cancer	
Sinonasal cancer	
Merkel-cell carcinoma	

Phase 3. Creating the model

The development of the novel cancer risk model was primarily driven by the objective to educate people about the various risk factors contributing to their personal risk of cancer and to provide a quantifiable understanding of the factor impacts. To this end, an approach was devised inspired by the '*Harvard Cancer Risk Index*' [12], initially conceived and drafted as a set of pencil and paper quizzes but has since been adapted into the online '*Your Disease Risk*' tool. This tool has gone through many changes in its 20-year existence [13] but the core methodology of the Harvard Index has remained consistent. The creation of the Index involved classifying risk factors based on evidence strength, assigning relative risk categories, and translating these into cancer risk points for comparison against

averages, which were then transformed into a factor used to multiply the SEER-derived 10-year estimated risk of cancer to obtain a numerical value for the likelihood of cancer diagnosis during the next 10 years.

In constructing the model, we took a somewhat different approach, albeit with similar basic principles. We began by identifying the proportion of cancer cases attributable to modifiable risk factors, as reported in the literature [14,15] This was a crucial step as it grounded the model in empirical evidence and ensured that it was reflective of the latest scientific understanding. Once we had identified these changeable risk factors, we then applied the relative risks associated with each factor. This process was instrumental in establishing relative risk categories for the model. These categories, much like those in the Harvard Index, provided a framework for understanding the impact of each risk factor in relation to others (Table 2).

Table 2. Risk levels and multipliers for the Cancer Risk Calculator and the Harvard Cancer Risk Index

Cancer Risk Calculator Heuristic		Harvard Cancer Risk Index		
Level of risk	Risk multiplier	Risk score ratio	Level of risk	SEER multiplier
Below average risk	0.2	<0	Very much below average risk	0.2
Possibly below average risk	0.2-0.9	0 or < 0.5	Much below average risk	0.4
		0.5 < 0.9	Below average risk	0.7
On average	0.9-1.1	0.9 < 1.1	About average risk	1
Possibly above average risk	1.1-5.0	1.1 < 2.0	Above average risk	1.5
		2.0 < 5.0	Much above average risk	3
Above average risk	5	5.0 or more times	Very much above average risk	5

Only risk factors with a quantifiable risk were included and risk factors requiring complex tests not available to the average clinician were excluded, leading to a total of around 790 risk factors. These factors were divided into 11 different categories for ease of use (Summarised under ‘Layout’).

Meta-analyses were given preference when available. If none existed, preference was given to studies that were either more recent, included larger patient cohorts, were published in journals with high impact factors, or included age-adjusted and/or multivariate relative risks. Where possible, multivariate analyses that were the basis for other models were incorporated, such as the Tammemagi model for lung cancer. [16] Particular interactions between risk factors, such as a history of gallstones with or without a cholecystectomy impacting the risk of primary liver cancer [17], were also included.

This approach to cancer risk was chosen for several reasons.

1. Comprehensiveness of Risk Factors: Focusing on including all known risk factors in the model ensures a comprehensive approach. This is particularly important in the context of cancer, where multiple factors - genetic, environmental, lifestyle, and others - contribute to the risk. By incorporating a broad range of risk factors, the model provides a more holistic view of cancer risk, which is crucial for patient education.

2. Educational Value: The primary purpose of this model is educational. It aims to inform people about the various factors that could increase their risk of cancer. From a public health perspective, awareness and understanding of these risk factors are vital. They empower individuals to make informed decisions about lifestyle changes and preventive measures. A model focused solely on statistical discrimination might not provide the same level of detailed, factor-specific information useful for education.
3. Evidence-Based Approach: By basing the model on scientifically recognized risk factors and categorizing them according to the strength of evidence, the model maintains scientific integrity. This evidence-based approach is crucial in healthcare and public health, ensuring that the information provided to users is reliable and grounded in current scientific understanding.
4. Broad Applicability: The model is designed to be applicable to a wide range of cancers. This is achieved by including a diverse array of risk factors that are relevant to multiple cancer types. Such a broad scope ensures that the model can provide valuable insights regardless of the specific type of cancer being considered. This aspect is particularly significant considering that for many cancers specific risk assessment tools are either limited or non-existent.
5. Individualized Risk Assessment: While statistical models focusing on discrimination, like those using c-statistics, are excellent for predicting outcomes within a population, they may not always convey individual risk factors effectively. A model that details all known risk factors can provide more personalized information to users, helping them understand which specific factors are relevant to their situation.
6. Public Health Strategy: From a public health standpoint, the model aligns with strategies aimed at prevention and early detection. By educating individuals about all known risk factors, the model supports broader public health goals, like reducing the incidence of cancer through informed lifestyle choices and increased vigilance for early symptoms.
7. Adaptability and Updating: As new research data emerge and our understanding of cancer risk factors evolves, a model that focuses on including all known risk factors can be more easily updated. This adaptability ensures that the model remains relevant and continues to provide value over time.

However, while the present comprehensive risk model focuses on educating users about all known cancer risk factors, it is important to acknowledge the significant advantages of more traditional risk models based on statistical methods such as Cox proportional hazards modeling and logistic regression. Recognizing these advantages, we have included these traditional models alongside our comprehensive model, offering a complementary strategy that leverages the strengths of both methodologies (Table 3).

Table 3. Most important differences between the Cancer Risk Calculator and the Harvard Cancer Risk Index

	Cancer Risk Calculator Application	Harvard Cancer Risk Index
Number of included cancers	38 (+ 18 subtypes)	14
Number of included risk factors	790	57
Risk factors selection	Published literature (including meta-analyses)	Expert consensus
Allows for interaction between	Yes	No

risk factors		
Validated	No	Yes [12,18]
Includes screening examinations	Yes	Only those aimed at reducing cancer incidence
Type of Classifiers for risk factors	Varied (Numerical, Categorical, etc.)	Mostly binary (Yes/No, Threshold reached/not reached)
Includes other validated models	Yes	No

Phase 4. Construction of the mobile application

The application was developed using the JavaScript framework Angular and built with Cordova for the Android and iOS platforms. To reach a broad audience, it was made available in English, Dutch and French (Figure 1).

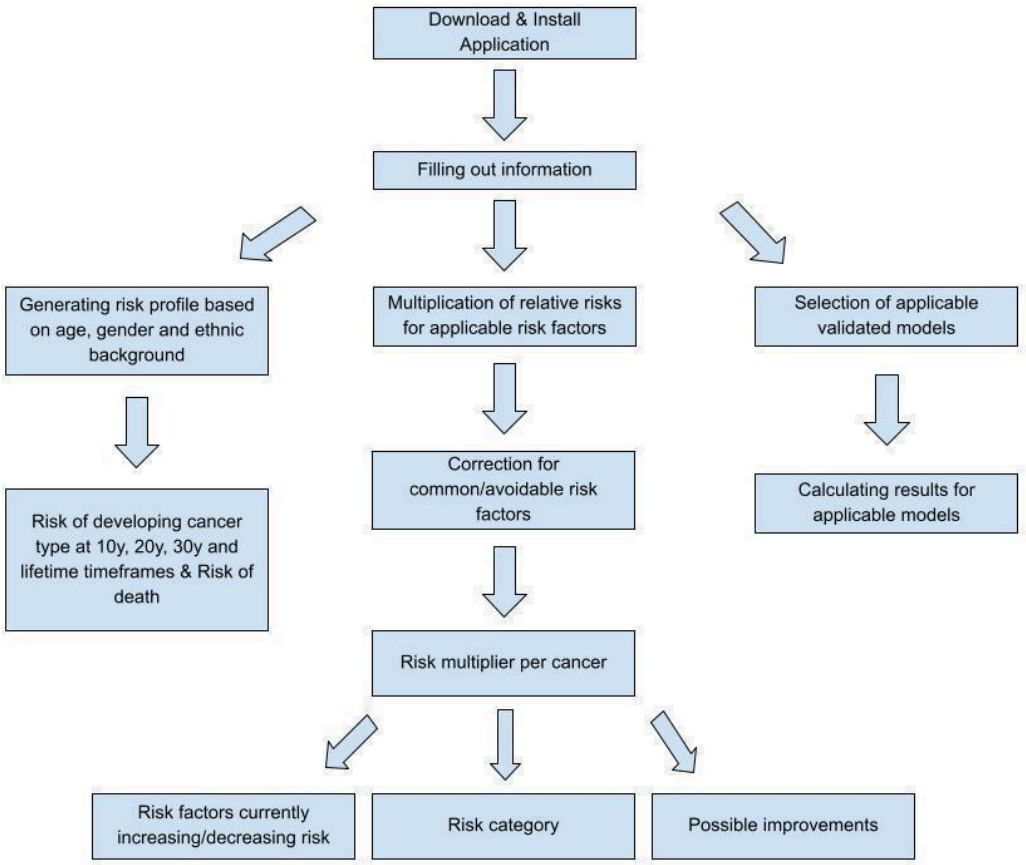


Figure 1. Flow of app functions

Results

Results were displayed as average 10-year, 20-year and 30-year risks, with a separate adaptation based on the fraction of cancers that might be avoidable. For cancers based on the SEER database, lifetime risk and the risk of death due to the relevant cancer in the relevant time frame were also displayed. A note was added stating that results were not applicable to organs that have already been affected by cancer, but for paired organs, the risk factors for the healthy contralateral organ are still relevant. A color-coded list of risk factors was shown, with risk factors reducing risk shown in green, risk factors increasing risk shown in red, and a separate list of changeable risk factors that a user might change to reduce their risk if they desire (Figure 2).

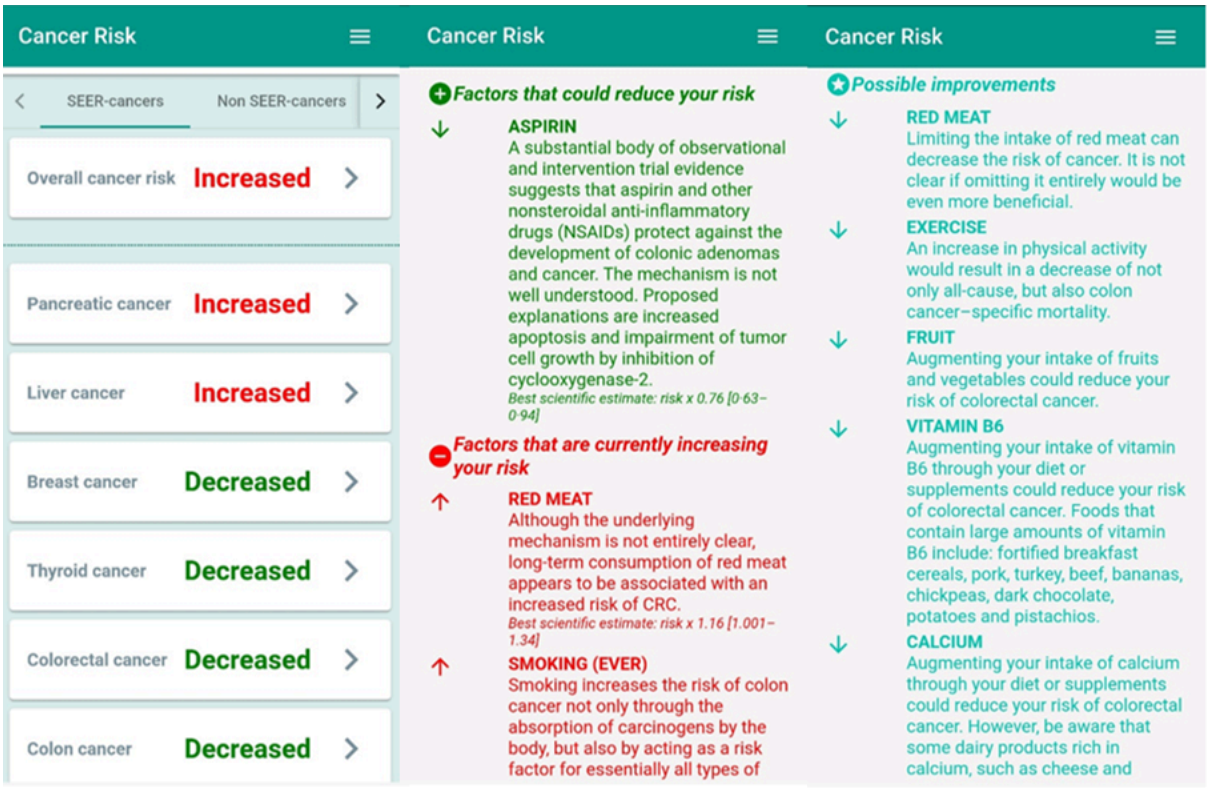


Figure 2. Illustration of the presentation of cancers and various types of risk factors.

Finally, since the model cannot be validated due to the exceedingly large number of risk factors, a considerable effort was made to include a great number of validated risk models for various cancers. Of these, 5 were models for bladder cancer, 14 were models for breast cancer, 35 were models for colorectal cancer, 12 were models for oesophageal cancer, 1 was a model for myeloma, 2 were models for renal cancer, 9 were models for head and neck cancer, 43 were models for liver cancer, 19 were models for lung cancer, 1 was a model for ovarian cancer, 7 were models for pancreatic cancer, 51 were models for pancreatic cancer, 11 were models for skin melanoma, 6 were models for gastric cancer, 6 were models for endometrial cancer, 7 were models for non-melanoma skin cancer, 1 was a model for retinal melanoma and 2 were models for gallbladder cancer. Some of these models grouped several cancers (such as ‘Upper aerodigestive cancer’) and some of them gave multiple results (such as for both ‘Prostate cancer’ and ‘High-grade prostate cancer’), for a total of 244 separately included validated models. These are summarized under ‘Included risk models’ as an appendix.

These were summarized into an additional tab, specifying which models were applicable for the current user based on the submitted information. Clicking through shows not just the results for the model but also when it was published, for which population it was derived, and which risk factors were included (Figure 3).

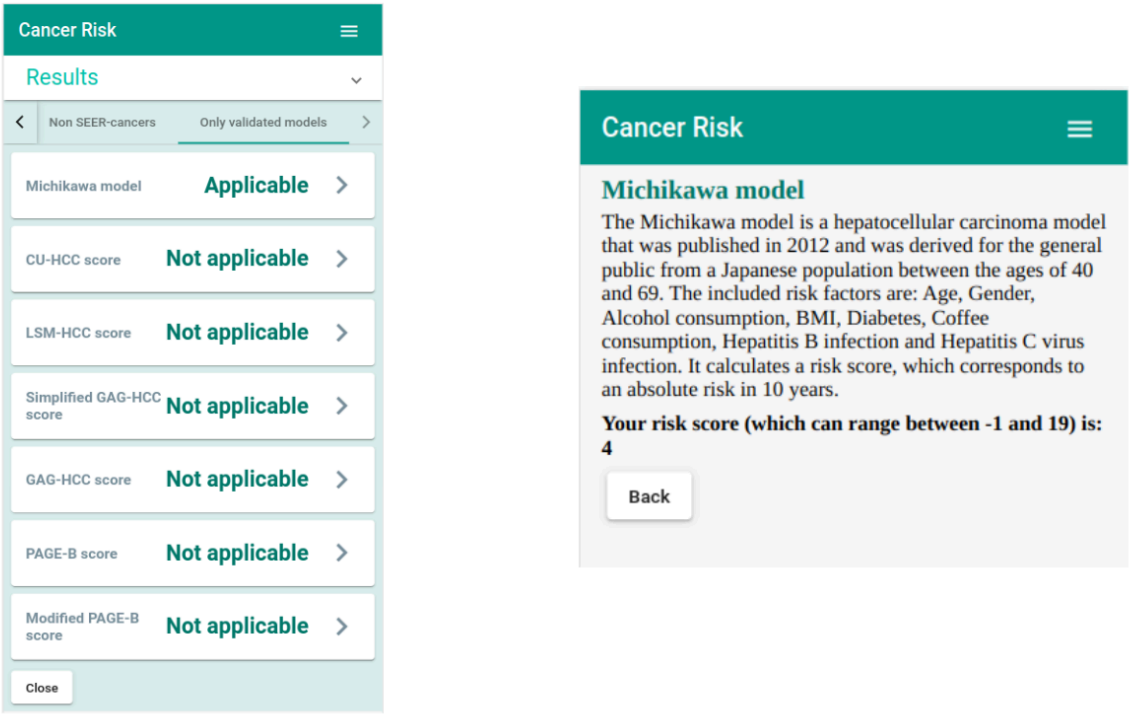


Figure 3. Illustration of the presentation of validated models.

Ethical Concerns

Due to ethical concerns and issues, two documents were drafted to properly inform users. These documents were made publicly available and incorporated in the application. They consisted of the following elements.

1. A comprehensive privacy policy clearly specifying that:
    a. all personal information will strictly be used for the calculation of the risks;
    b. names and pseudonyms provided will only be used for identifying the correct user profile;
    c. personal and medical information submitted by users in the forms of the application will only be stored on the device and will not be collected;
    d. links to the privacy policies of third-party service providers used by the applications will be encrypted
2. A disclaimer emphasizing that:

a. the application should be considered strictly educational and that all information contained within cannot and should not replace assessment by a physician;
b. evaluations presented represent best efforts to conveniently assess cancer risk, so any figures should therefore be regarded as indicative, but not precise, and a cautious or even skeptical interpretation is encouraged;
c. the effect of some risk factors on certain cancers is so large these effects cannot be eliminated from basic probability;
d. even for risk factors that are undoubtedly influencing the risk of cancer, large-scale prospective studies are not always available.

Certification

CE Marking

The CE mark is a conformity mark which all European medical devices must have before they can be marketed. It is seen as a declaration by the manufacturer that the product meets all the appropriate provisions of the relevant legislation including those related to safety and, where required, has been assessed in accordance with these. Under current regulations, our application would either fall out of the scope of the medical devices regulation or be considered a medical device with a low risk. As such, we have followed the Class I conformity assessment procedures as described in Annex VII Module A, EC Declaration of Conformity.

FDA Label

In their guidelines, the FDA encourages the development of mobile medical apps that improve healthcare and provide consumers and healthcare professionals with valuable health information. As such, for many mobile apps that may meet the regulatory definition of a “device” but pose minimal risk to patients and consumers, the FDA will exercise enforcement discretions and will not expect manufacturers to submit premarket review applications or to register and list their apps with the FDA. Our app seems to fall into this category. For more information, please visit the relevant section the official FDA website: https://www.fda.gov/medical-devices/mobile-medical-applications/examples-mobile-apps-which-fda-will-exercise-enforcement-discretion.

Discussion

Since the development of the first prominent breast cancer model by Gail et al. in 1989 [19], many cancer risk prediction models have been proposed. These include models not just for various types of cancer, but with wildly different goals and target populations. For example, there are models that aim to optimize screening strategies [20], models for patients with chronic infections [21], models to assess risk after negative cytology for cancer [22], models for patients with high-risk behaviors [16], models for patients with positive family histories [23], models for patients of distinct ethnic groups [24], models for patients with distinct radiological findings [25], and models for patients with specific symptoms [26]. However, using these models to educate the public about their risk of developing cancer has been difficult and other currently available tools have been found to be lacking for a variety of reasons [2]. The development of this mobile application, which calculates the risk of a wide range of cancers based on individual risk factors, therefore represents a major leap forward in personalized healthcare. It offers numerous advantages, including tailored cancer risk assessments,

facilitating early detection strategies, empowering users with personalized health insights, enhancing patient engagement in preventive healthcare, providing accessible health education, supporting decision-making in cancer screening, and potentially reducing the overall burden of cancer through informed preventive measures.

The concept of personalized risk assessment tools, particularly in the form of mobile applications, aligns with the growing emphasis on personalized medicine. Such tools can significantly enhance the accuracy of risk prediction by incorporating a range of individual risk factors, including genetics, lifestyle, and environmental exposures. This approach is crucial when considering cancer, where risk varies greatly among individuals. Since cancer is not predicted by a single factor, a combination of non-clinical, clinical, and genetic risk factors together provide a more comprehensive and accurate assessment of risk for each individual and efficient prevention therapy strategies will need to rely on such comprehensive risk assessment tools for targeted intervention [27].

The use of mobile health (mHealth) technologies in cancer care has been a growing area of research. Prospective surveys have already confirmed that users of mobile health applications have a higher level of health literacy than those who do not actively use it [28]. The integration of risk calculation models into these platforms can further empower users by providing them with personalized health information. Randomized controlled trials have already confirmed that utilizing cancer risk prediction models may help among individuals maintain healthy lifestyles [29]. And such help seems badly needed, as research has consistently demonstrated that despite the significant advances in understanding the causes and risk factors of various cancers, public awareness remains relatively low. Many individuals are not fully informed about the lifestyle and environmental factors that can increase their risk of developing cancer [30–32]. Even worse, misconceptions about risk factors seem to be common, even for straightforward links and specific medical interventions. For example, a 2020 survey of Australian adults found that only 18% of respondents were aware that human papillomavirus (HPV) vaccination confers a protective effect, while 17% paradoxically believed that it increases risk [33]. The lack of awareness can lead to missed opportunities for prevention. For instance, adopting healthier lifestyle choices, such as a balanced diet and regular exercise, can significantly reduce the risk of certain types of cancer. Increasing public education and awareness about these risk factors is therefore essential. Educational campaigns, healthcare provider counseling, and accessible information resources play key roles in enhancing public understanding of cancer risks. Additionally, integrating cancer education into broader health promotion programs can help in building a more informed and health-conscious society [31]. Ultimately, a well-informed public is better equipped to make decisions that can reduce cancer risk and support early detection efforts, contributing to better health outcomes and potentially reducing the burden of cancer on individuals and healthcare systems.

Another interesting avenue is the role of mHealth interventions in screening programs. Regular screening and self-exams for certain cancers, such as breast, cervical, and colorectal cancers, can also lead to early detection, when the disease is more treatable. Screening specifically has been shown to reduce disease-specific mortality for several cancers, leading many countries to implement population-based screening programs. For instance, the Norwegian Breast Cancer Screening Program observed a 43% reduction in mortality among women who attended the program [34]. Interest in mHealth is growing in this context because of their promising role in promoting cancer screening participation [35].

Looking forward, the integration of such risk calculation tools in routine clinical practice poses both opportunities and challenges. The widespread adoption of mHealth tools in clinical settings requires overcoming barriers related to technology acceptance, integration with existing healthcare systems, and ensuring clinical accuracy and reliability. Continued research and collaboration between technologists, healthcare providers, and policymakers are essential to address these challenges.

We have described the creation of an app that has been downloaded worldwide and which at the time of writing has been downloaded tens of thousands of times, being favorably reviewed on both the Android [36] and iOS [37] platforms. When the application was tested by oncology patients, two-thirds of respondents found the application useful and reported learning something new, but most impressively, more than half indicated a willingness to change their habits based on the information provided. These results are discussed in detail in the next chapter. We therefore consider the project to be a preliminary success and believe that it and other similar educational apps can significantly improve health literacy in the 21st century.

Conclusion

This exploration underscores the dynamic and multifaceted nature of personalized cancer risk assessment and the role of mobile technology in transforming cancer care. By continuing to refine these tools and approaches, there is significant potential to enhance cancer prevention and treatment strategies, ultimately leading to better health outcomes.

References

[1] Kemp E, Trigg J, Beatty L, Christensen C, Dhillon HM, Maeder A, et al. Health literacy, digital health literacy and the implementation of digital health technologies in cancer care: the need for a strategic approach. Health Promot J Aust Off J Aust Assoc Health Promot Prof 2021;32 Suppl 1:104–14. https://doi.org/10.1002/hpja.387.
[2] Westerlinck P, Coucke P. Review of interactive digital solutions improving health literacy of personal cancer risks in the general public. Int J Med Inf 2021;154:104564. https://doi.org/10.1016/j.ijmedinf.2021.104564.
[3] Hernandez BY, Barnholtz-Sloan J, German RR, Giuliano A, Goodman MT, King JB, et al. Burden of invasive squamous cell carcinoma of the penis in the United States, 1998-2003. Cancer 2008;113:2883–91. https://doi.org/10.1002/cncr.23743.
[4] Muzic JG, Schmitt AR, Wright AC, Alniemi DT, Zubair AS, Olazagasti Lourido JM, et al. Incidence and Trends of Basal Cell Carcinoma and Cutaneous Squamous Cell Carcinoma: A Population-Based Study in Olmsted County, Minnesota, 2000 to 2010. Mayo Clin Proc 2017;92:890–8. https://doi.org/10.1016/j.mayocp.2017.02.015.
[5] Johnson LG, Madeleine MM, Newcomer LM, Schwartz SM, Daling JR. Anal cancer incidence and survival: the surveillance, epidemiology, and end results experience, 1973-2000. Cancer 2004;101:281–8. https://doi.org/10.1002/cncr.20364.
[6] Shah CA, Goff BA, Lowe K, Peters WA, Li CI. Factors affecting risk of mortality in women with vaginal cancer. Obstet Gynecol 2009;113:1038–45. https://doi.org/10.1097/AOG.0b013e31819fe844.
[7] Duffy A, Capanu M, Abou-Alfa GK, Huitzil D, Jarnagin W, Fong Y, et al. Gallbladder cancer (GBC): 10-year experience at Memorial Sloan-Kettering Cancer Centre (MSKCC). J Surg Oncol 2008;98:485–9. https://doi.org/10.1002/jso.21141.
[8] SEER 21 2013–2017 n.d.
[9] Albores-Saavedra J, Batich K, Chable-Montero F, Sagy N, Schwartz AM, Henson DE. Merkel cell carcinoma demographics, morphology, and survival based on 3870 cases: a

population based study. J Cutan Pathol 2010;37:20–7.
https://doi.org/10.1111/j.1600-0560.2009.01370.x.
[10] Cheng C-Y, Hsu W-M. Incidence of eye cancer in Taiwan: an 18-year review. Eye Lond Engl 2004;18:152–8. https://doi.org/10.1038/sj.eye.6700619.
[11] Turner JH, Reh DD. Incidence and survival in patients with sinonasal cancer: a historical analysis of population-based data. Head Neck 2012;34:877–85.
https://doi.org/10.1002/hed.21830.
[12] Colditz GA, Atwood KA, Emmons K, Monson RR, Willett WC, Trichopoulos D, et al. Harvard report on cancer prevention volume 4: Harvard Cancer Risk Index. Risk Index Working Group, Harvard Center for Cancer Prevention. Cancer Causes Control CCC 2000;11:477–88.
https://doi.org/10.1023/a:1008984432272.
[13] Colditz GA, Dart H. Commentary: 20 years online with "Your Disease Risk." Cancer Causes Control CCC 2021;32:5–11. https://doi.org/10.1007/s10552-020-01356-3.
[14] Islami F, Goding Sauer A, Miller KD, Siegel RL, Fedewa SA, Jacobs EJ, et al. Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. CA Cancer J Clin 2018;68:31–54. https://doi.org/10.3322/caac.21440.
[15] O'Sullivan DE, Brenner DR, Villeneuve PJ, Walter SD, Demers PA, Friedenreich CM, et al. The current burden of non-melanoma skin cancer attributable to ultraviolet radiation and related risk behaviours in Canada. Cancer Causes Control CCC 2021;32:279–90.
https://doi.org/10.1007/s10552-020-01382-1.
[16] Tammemagi CM, Pinsky PF, Caporaso NE, Kvale PA, Hocking WG, Church TR, et al. Lung cancer risk prediction: Prostate, Lung, Colorectal And Ovarian Cancer Screening Trial models and validation. J Natl Cancer Inst 2011;103:1058–68. https://doi.org/10.1093/jnci/djr173.
[17] Liu Y, He Y, Li T, Xie L, Wang J, Qin X, et al. Risk of primary liver cancer associated with gallstones and cholecystectomy: a meta-analysis. PloS One 2014;9:e109733.
https://doi.org/10.1371/journal.pone.0109733.
[18] Kim DJ, Rockhill B, Colditz GA. Validation of the Harvard Cancer Risk Index: a prediction tool for individual cancer risk. J Clin Epidemiol 2004;57:332–40.
https://doi.org/10.1016/j.jclinepi.2003.08.013.
[19] Gail MH, Brinton LA, Byar DP, Corle DK, Green SB, Schairer C, et al. Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. J Natl Cancer Inst 1989;81:1879–86. https://doi.org/10.1093/jnci/81.24.1879.
[20] Ma GK, Ladabaum U. Personalizing colorectal cancer screening: a systematic review of models to predict risk of colorectal neoplasia. Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc 2014;12:1624-1634.e1. https://doi.org/10.1016/j.cgh.2014.01.042.
[21] Kim JH, Kim YD, Lee M, Jun BG, Kim TS, Suk KT, et al. Modified PAGE-B score predicts the risk of hepatocellular carcinoma in Asians with chronic hepatitis B on antiviral therapy. J Hepatol 2018;69:1066–73. https://doi.org/10.1016/j.jhep.2018.07.018.
[22] Cai Q-C, Chen Y, Xiao Y, Zhu W, Xu Q-F, Zhong L, et al. A prediction rule for estimating pancreatic cancer risk in chronic pancreatitis patients with focal pancreatic mass lesions with prior negative EUS-FNA cytology. Scand J Gastroenterol 2011;46:464–70.
https://doi.org/10.3109/00365521.2010.539256.
[23] Lee A, Mavaddat N, Cunningham A, Carver T, Ficorella L, Archer S, et al. Enhancing the BOADICEA cancer risk prediction model to incorporate new data on RAD51C, RAD51D, BARD1 updates to tumour pathology and cancer incidence. J Med Genet 2022;59:1206–18.
https://doi.org/10.1136/jmedgenet-2022-108471.
[24] Gail MH, Costantino JP, Pee D, Bondy M, Newman L, Selvan M, et al. Projecting individualized absolute invasive breast cancer risk in African American women. J Natl Cancer Inst 2007;99:1782–92. https://doi.org/10.1093/jnci/djm223.
[25] Chen J, Pee D, Ayyagari R, Graubard B, Schairer C, Byrne C, et al. Projecting absolute invasive breast cancer risk in white women with a model that includes mammographic density. J Natl Cancer Inst 2006;98:1215–26. https://doi.org/10.1093/jnci/djj332.
[26] Matulewicz RS, Rademaker A, Meeks JJ. A simplified nomogram to assess risk of bladder cancer in patients with a new diagnosis of microscopic hematuria. Urol Oncol 2020;38:240–6.
https://doi.org/10.1016/j.urolonc.2019.12.010.

[27] Zhang Z, Bien J, Mori M, Jindal S, Bergan R. A way forward for cancer prevention therapy: personalized risk assessment. Oncotarget 2019;10:6898–912. https://doi.org/10.18632/oncotarget.27365.
[28] Sariyildiz AY, Aksoy Y, Samanci M. The Effect of Mobile Health Applications on the Health Literacy of Individuals. Pak J Med Health Sci 2022;16:552–5. https://doi.org/10.53350/pjmhs22163552.
[29] Sherratt FC, Marcus MW, Robinson J, Field JK. Utilizing Lung Cancer Risk Prediction Models to Promote Smoking Cessation: Two Randomized Controlled Trials. Am J Health Promot AJHP 2018;32:1196–205. https://doi.org/10.1177/0890117116673820.
[30] Ryan AM, Cushen S, Schellekens H, Bhuachalla EN, Burns L, Kenny U, et al. Poor awareness of risk factors for cancer in Irish adults: results of a large survey and review of the literature. The Oncologist 2015;20:372–8. https://doi.org/10.1634/theoncologist.2014-0453.
[31] Redeker C, Wardle J, Wilder D, Hiom S, Miles A. The launch of Cancer Research UK's "Reduce the Risk" campaign: baseline measurements of public awareness of cancer risk factors in 2004. Eur J Cancer Oxf Engl 1990 2009;45:827–36. https://doi.org/10.1016/j.ejca.2008.10.018.
[32] Al-Azri M, Al-Rasbi K, Al-Hinai M, Davidson R, Al-Maniri A. Awareness of risk factors for cancer among Omani adults--a community based study. Asian Pac J Cancer Prev APJCP 2014;15:5401–6. https://doi.org/10.7314/apjcp.2014.15.13.5401.
[33] Lizama N, Jongenelis M, Slevin T. Awareness of cancer risk factors and protective factors among Australian adults. Health Promot J Aust Off J Aust Assoc Health Promot Prof 2020;31:77–83. https://doi.org/10.1002/hpja.248.
[34] Hofvind S, Ursin G, Tretli S, Sebuødegård S, Møller B. Breast cancer mortality in participants of the Norwegian Breast Cancer Screening Program. Cancer 2013;119:3106–12. https://doi.org/10.1002/cncr.28174.
[35] Ruco A, Dossa F, Tinmouth J, Llovet D, Jacobson J, Kishibe T, et al. Social Media and mHealth Technology for Cancer Screening: Systematic Review and Meta-analysis. J Med Internet Res 2021;23:e26759. https://doi.org/10.2196/26759.
[36] https://play.google.com/store/apps/details?id=be.tdf_it.cancerrisk&hl=en n.d.
[37] https://apps.apple.com/be/app/cancer-risk-calculator/id1452067400#see-all/reviews n.d.

Layout

- Personal information
    - Name
    - Date of birth [Age]
    - Gender at birth
    - Transgender
        - With Hormonal Therapy?
        - With surgery?
    - Race [White,Hispanic, Asian/Pacific Islander, African, Native American]
    - Number of years of education (after age 6)
    - Relationship status: Married/Never married/No longer living together/Divorced
    - Family wealth
- Physical characteristics
    - Length
    - Weight
    - [automatic BMI calculation]
    - Blood type
    - Fitzpatrick type
    - Hair Color [Dark, Red, Blonde, Light Brown]
    - Eye color [Green, Blue, Light Brown , Dark]
    - Freckles
        - Freckles poor
    - Birthmarks
        - Ordinary
            - How many?
        - Atypical
            - How many?
- Male History
    - Klinefelter syndrome
    - Prostatitis
    - Prostate cancer
    - Circumcision
    - Medical conditions of the testicles
        - Cryptorchidism (testicular malposition)
        - Contralateral testicular cancer
        - Orchiectomy (castration)
        - Testicular microlithiasis
    - Medical conditions of the penis
        - Hypospadias
        - Penis tear
        - Penis rash.
        - Penile injury
        - Inflammation of the penis
        - Stricture of the urethra
        - Smegma.
        - Phimosis.
    - How many female sexual partners?
    - Genital Warts.
    - Frequent urinary tract infections.
    - History of genital herpes
    - Confirmed HPV infection of the genitals.
    - History of zoophilia.
    - Medical conditions of the prostate
        - Digital rectal examination
        - Prostate examination
            - Hypoechoic lesions
            - Prostate volume

        - Prostate biopsies
            - Date of first negative biopsy
            - Date of last negative biopsy
            - New biopsy planned?
                - How many cores?
            - [automatic calculation: Sampling density]
            - History of High-grade prostatic intraepithelial neoplasia

- Female History
    - Menarche
        - What age?
        - Infertility
        - Ever been pregnant?
            - How many times?
            - Age at first pregnancy?
            - Age at last pregnancy?
            - 2 or more times in the last 2 years?
            - Ever breastfed?
                - How long?
                - During the last 5 years?
        - Menopause
            - What age?
                - [automatically calculate number of years of menstruation]
            - Average weight without PMH
            - Postmenopausal hormone therapy
                - How long?
                - Current user?
                - Standard (estrogen+progesterone)
                    - How long?
                - estrogen without progesterone
                    - How long?
                - Other PMH?
                    - How long?
                    - Tibolone
                - Average weight with PMH
    - Have you ever been sexually active?
        - Number of sexual partners
        - Age at first sexual contact
        - Current partner who is circumcised?
    - Oral contraceptives?
        - Current?
            - Stopped for how long?
        - How long?
    - Intrauterine contraceptive?
    - Endometriosis
    - Fibroma
    - Polycystic ovary syndrome
    - Endometrial cancer
        - Before 50 years of age?
    - Breast examination?
        - Lobular involution
            - Partial
        - Dense mammary gland tissue
        - Flat epithelial atypia
        - Columnar cell alteration tissue
        - Proliferative disease
            - Number of atypical foci
            - Atypical Hyperplasia
            - Usual ductal hyperplasia

            - Intraductal papillomas
                - Solitary
                - Multiple
            - Sclerosing adenosis
            - Radial scars
            - Fibroadenomas
    - Unilateral salpingo-oophorectomy (USO)
        - Bilateral?
    - Hysterectomy
    - IVF treatment
    - HPV positive on the cervix
    - Pap smear within the last three years
    - HPV vaccine
    - Genital talc

- Living habits
    - Ever smoked?
        - Do you still smoke now?
            - How long have you stopped?
        - How long have you smoked?
        - On average, how long does it take you to produce a pack of cigarettes (or the equivalent?)
        - [automatic calculation of number of pack years]
    - Chewing tobacco
    - Use snuff.
    - Nutrition
        - Animal products
            - Red meat
            - White meat
            - Processed meat
            - Fish
            - Eggs
            - Dairy [How often?]
            - Milk
        - Vegetables
            - Frequency
            - Green vegetables frequency
            - Tomatoes
            - Soya
            - Eating mushrooms:
                - 1–2 times/week
                - ≥3 times/week
        - Fruit
            - Frequency
            - Citrus fruits 2x/week or more
        - Grains [How often?]
        - Fiber-rich food
        - Salty food
        - Fried food
        - Pickled food
        - Mediterranean diet
    - Drink
        - Ever Alcohol?
            - How many glasses on an average day?
            - Have you stopped?
                - How long have you stopped?
            - How long have you been drinking alcohol?
        - Coffee
            - how many cups on average per day?
        - Green tea

        - Black tea
        - Hot drinks?
        - 2.5l per day or more
        - Chlorinated drinking water
        - Sugary drink intake 1 or more per day
        - Fruit juice
    - Marijuana
    - To play sports
    - Frequency of bathing/showering
    - Chew Betel nuts
    - Brush teeth daily
    - Filled/missing teeth
    - Night work
- Family history
    - Cancer
        - Breast carcinoma
            - 1 first-degree relative with breast cancer
                - age at diagnosis <30
                - age at diagnosis >36
            - 2 first-degree relatives with breast cancer
        - Prostate cancer
            - Brother
        - Endometrial carcinoma
        - Testicular Carcinoma
            - 1 first degree relative
        - Pancreatic carcinoma
            - 1 first-degree relative with pancreatic cancer
            - 2 first-degree relatives with pancreatic cancer
            - 3 first-degree relatives with pancreatic cancer
        - Bladder carcinoma
            - Older
            - Brother sister
        - Thyroid carcinoma
            - Older
            - Brother sister
        - Mesothelioma
            - Older
            - Brother or sister
        - Skin cancer
            - BCC
            - SCC
            - Melanoma
                - Older
                    - Multiple melanomas?
                - Brother or sister
                - 2 first-degree relatives
        - Hodgkin lymphoma
            - How old was the family member at the time of diagnosis?:
                - Less than 30
                - 30-59
                - 60 or more
            - Who?:
                - with parent or child
                - with sister
                - with brother
                - Multiple first-degree relatives
                - Identical twins
        - Colon carcinoma

        - 1 first-degree relative
        - family member diagnosed with colorectal carcinoma before age 45
        - multiple family members diagnosed with colorectal carcinoma
        - 1 first-degree relative diagnosed with colorectal polyp
    - Renal carcinoma
        - Brother sister
    - Liver cancer
- Sarcoidosis
- Ulcerative colitis

- Medical history
- Cancer
    - Cancer in childhood
    - Non -melanoma skin cancer
        - Basocellular skin carcinoma
            - How many?
    - Leukemia
    - Mesothelioma
    - Thyroid cancer
        - treated with radioactive iodine
    - Multiple myeloma
- Stomach ulcers
- History of caustic damage to the esophagus
- Gallstones
    - smaller than 3 cm
    - larger than 3 cm
- Kidney stones
- Actinic skin damage
- Past infections
    - Epstein-Barr
    - infectious diseases in childhood
    - infection with Helicobacter pylori
    - Gonorrhea or syphilis
    - History of pneumonia
- Chronic/permanent condition
    - Gastrointestinal Problems
        - Stomach lesions
            - Gastritis
            - Atrophic gastritis
            - Intestinal metaplasia
            - Dysplasia
        - Celiac disease
        - Chronic pancreatitis
        - Hereditary pancreatitis
        - Ulcerative colitis
            - Single proctitis
            - Generalized
            - Left-sided only
        - Crohn's disease
            - Disease only in terminal ileum
            - Disease in terminal ileum and parts of colon
            - Disease only in colon
            - If diagnosed at age <30 years with colon involvement
        - Achalasia
        - HPV positivity in esophagus
        - Gastroesophageal reflux
            - Weekly or daily complaints
            - Barrett's esophagus
        - Familial Adenomatous Polyposis

        - MUTYH-associated polyposis
            - Biallelic
            - Monoallelic
        - Primary sclerosing cholangitis
        - Primary biliary cholangitis
        - Esophagitis
        - Esophageal stricture
        - Hiatal hernia
    - Diagnosed syndrome
        - Howel-Evans syndrome [Tylosis]
        - Peutz-Jeghers syndrome
        - Lynch syndrome
        - Cowden syndrome
        - Rothmund-Thomson syndrome
        - Nevoid basal cell carcinoma syndrome
    - Polycystic kidney disease
        - Development of polycystic kidney disease after dialysis
        - Hereditary polycystic kidney disease
    - Chronic infections
        - Tuberculosis
        - Salmonella
        - Hepatitis B
            - Genotype
                - B
                - C
                - B+C
        - Hepatitis C
            - Treated with interferon
            - Treated with ribavarin
            - Sustained virological response
            - Genotype G1B
        - HIV
            - with treatment?
    - Rheumatic disorders
        - Ankylosing spondylitis
        - Rheumatic fever / rheumatic heart diseases
        - Psoriatic/enteropathic arthropathies
        - Sjogren's syndrome
        - Rheumatoid arthritis
        - Systemic lupus erythematosus
        - Rheumatism, unspecified
    - Other Conditions
        - Asthma
        - Ascites
            - Uncontrolled ascites
        - Alpha-1 antitrypsin deficiency
        - Allergy
        - Chronic edema of the lower extremities
        - Cirrhosis
            - Alcoholic/Metabolic
            - Autoimmune
            - Viral
            - Other
        - Steatohepatitis
        - COPD
        - Hypertension
        - Hypercholesterolemia
        - Diabetes

                - Type 1
                - Is it newly diagnosed?
                    - BG at diagnosis
                    - BG 1 year before diagnosis
            - Eczema
            - Hemochromatosis
            - Multiple sclerosis
            - Cystic fibrosis
            - MGUS
            - Neurofibromatosis Type 1
            - Paget Bone Disease
            - Sarcoidosis
            - Xeroderma pigmentosum
            - Parkinson's
            - Epidermolysis bullosa
            - Coronary heart disease
            - Guillain-Barre syndrome
            - Bullous disorders
            - Necrotizing vasculopathies
            - Autoimmune hepatitis
            - Allergic rhinitis
            - Graves'/autoimmune thyroiditis
            - Idiopathic thrombocytopenic purpura
            - Lichen Planus
            - Myasthenia Gravis
            - Myositis
            - Psoriasis
            - Genital warts
            - Pulmonary fibrosis
    - Treatments
        - PUVA
        - High doses of alkylating drugs
            - Cyclophosphamide
        - Cholecystectomy
        - Local corticoid use
            - Cranial radiotherapy
            - Abdominal radiotherapy
        - Organ transplantation
            - Kidney transplantation
        - Permanent bladder catheter in place
        - Treatment with GnRH agonist
        - Esophageal fundoplication

- Gene mutations
    - ATM gene variant
    - BARD1
    - BRCA1
    - BRCA2
    - BRIP1
    - CDH1
    - CDKN2A
    - CHEK2
    - HOBX13
    - MC1R
    - MLH1
    - MSH6
    - MSH2
    - NBN

- PALB2
- PTEN
- RAD51C (+info)
- RAD51D
- TP53 (+info)
- α5-nAChR (rs 16969968) AA
- CYP 2E1 (rs 2031920) TT/TC
- Interleukin-18 (rs 360721) CC
- Interleukin-8 (rs 4073) TT 1.5
- Interleukin 1B (rs 16944) GG
- ITGA11 (rs 2306022) AA
- N-Acetylcysteine transferase 2 (rs 1799930) GG
- α1-Antichymotrypsin (rs 4934) GG
- Cerberus 1 (rs 10115703) AA/AG
- DAT1 (rs 6413429) GT/TT
- TNFR1 (TNFRSF1A) (rs 1139417) AA
- TLR9 (rs 5743836) CC
- P73 (TP73) (rs 2273953) CC
- SOD3 (rs 1799895) GG/GC
- ITGB3 (rs 2317676) GG/GA
- DRD2 (rs 1799732) CDel/Del.Del
- BCL2 (rs 2279115) AA
- XPD (ERCC2) (rs 13181) GG
- REV1 (REV1L) (rs 3087386) CC
- FasL (TNFSF6) (rs 763110) TT
- Rs2736100
- Rs402710
- Rs4083914
- Rs4488809

- Medication
    - Any use of long term (> 1year) medications
        - Aminophylline
        - Amiodarone
        - Anticholinergics
        - Captopril
        - Enalapril
        - Beta blocker
            - Sotalol
        - Verapamil
        - Methyldopa
        - Aromatase inhibitors
        - Benzodiazepines
        - Beta adrenergic agonists
        - Carbamazepine
        - Corticosteroid
        - Diuretics
            - Bumetanide
            - Furosemide
            - Thiazide diuretics
                - Bendroflumethiazide
        - Dutasteride
        - Finasteride
        - Metformin
        - Methotrexate
        - Nitroglycerin
        - NSAIDS
            - More than 10 years?
            - Aspirin

        - Diclofenac
        - Indomethacin
    - Paracetamol
    - Arzoxifene
    - Lasofoxifene
    - Raloxifene
    - Tamoxifen
        - How long?
    - Statins
        - Simvastatin
    - Sildenafil
    - Tolbutamide
    - Valproate
    - Multivitamin
- Any use of short term medications
    - Acitretin
    - Acyclovir
    - Ciprofloxacin
    - Doxycycline
    - Hydroxychloroquine
    - Isotretinoin
    - Ketoconazole
    - Levofloxacin
    - Sulfamethazole with trimethoprim
    - Tetracycline
    - Vemurafenib
    - Voriconazole

- Supplements
- Selenium
- Zinc
- Calcium
- Magnesium
- Vitamin B6
- Vitamin B9 (Folic acid)
- Vitamin B12
- Vitamin D
- Vitamin E
- Omega-3 fatty acids

- Environmental factors
- Exposure
    - Smoke (from living with a smoker)
    - Hours a day in room with smoke
    - Asbestos
        - Certainly
            - How long?
        - Probably
    - Arsenic
    - Cadmium
    - Petrol
    - Diesel
    - Diazinon
    - Other petroleum products
    - Officer Orange
    - High doses of electromagnetic radiation
    - Aflatoxins
    - Chlordecone

        - Dry-cleaning solvents
        - Paint fabric
        - Aluminum
        - Benzene
        - Beryllium
        - Chromium
        - Formaldehyde
        - Nickel
            - High exposure
        - Polycyclic aromatic hydrocarbons
        - Silica
            - High exposure
        - Trichloroethylene
        - Tungsten carbide-cobalt
        - Ethylene oxide
        - Lead
        - 1,3-Butadiene
        - Acid fog
            - High exposure
        - Bis Chloromethyl ether
        - Wood dust
        - Lindane
        - Dichloromethane
    - Living on a farm
    - Work
        - Airplane flight crew
        - Rubber industry
        - Glass industry
        - Barber
        - Welder
        - Cook
        - Working in the blast furnace of the coke oven industry
        - Working in the iron and steel industry
        - Working in a uranium mine
            - How many years?
    - Solar exposure
        - Chronic/intermittent/total/low
    - History of sunburn
        - First before age 15?
        - First brown, then burnt
        - Childhood sunburn
    - Use sunbed
        - How long?

- Complaints & Tests
    - Complaints
        - Abdominal distension
        - Abdominal pain
        - Appetite loss
        - Back pain
        - Black stool
            - How often?
        - Change in bowel habits
        - Constipation
        - Cough
        - Defecation frequency
        - Dysphagia
        - Haematemesis
        - Haemoptysis

    - Heartburn
    - Hepatic encephalopathy
        - Severe hepatic encephalopathy
    - Indigestion
    - Neck lump
    - Neck pain
    - Night sweats
    - Rectal bleeding
    - Retrosternal pain
    - Suspicious melanocytic lesions
    - Urinary complaints
        - Retention
            - How often over the past month? (0%, <20%, <50%, about 50%, >50%, about 100%)
        - Frequency
            - How often over the past month? (0%, <20%, <50%, about 50%, >50%, about 100%)
        - Urinary Intermittency
            - How often over the past month? (0%, <20%, <50%, about 50%, >50%, about 100%)
        - Urinary Straining
            - How often over the past month? (0%, <20%, <50%, about 50%, >50%, about 100%)
        - Urinary Urgency
            - How often over the past month? (0%, <20%, <50%, about 50%, >50%, about 100%)
        - Weak urinary stream
            - How often over the past month? (0%, <20%, <50%, about 50%, >50%, about 100%)
        - Nocturia
            - How often?
        - Haematuria
    - Weight loss
        - How much
- Blood test
    - Anti-H. pylori IgG
    - AFP
    - Albumin
    - Alpha-1 globulin
    - ALT
    - AST
    - Bilirubin
    - CEA
    - CRP
    - Estradiol
    - Gastrin 17
    - GGT (γ-glutamyltransferase)
    - HBeAG
    - HBsAG
    - HBV DNA viral load level
    - HBV A1762T/G1764A core promoter mutation
    - Hemoglobin
    - Hemoglobin A1c
    - Human kallikrein 2
    - INR
    - Mean corpuscular volume (MCV),
    - NM23A
    - NMP22
    - NNMT
    - LCP1
    - Pepsinogen I
    - Pepsinogen II
    - PSA
        - Intact PSA

        - Free PSA
        - [%fPSA]
        - PSA slope
    - Platelets
    - RBC count
    - [automatic calculation: AST/ALT ratio]
    - [automatic calculation: PG I/II ratio]
- Imaging
    - Liver stiffness measurement
    - Liver fibrosis
    - Barium enema
    - Pelvic X-ray photos
    - High bone density
    - Diagnosed pancreatic cysts
- Colon cancer screening
    - Fecal immunochemical test
    - Colonoscopy
        - Most distal finding
            - No polyps
            - Hyperplasia
            - Tubular adenoma < 1cm
            - Tubular adenoma 1cm or more
            - Advanced lesion
        - Large (>1 cm) adenomatous colonic polyps or polyps with villous or tubulovillian histology or high-grade dysplasia
            - Multiple?

Adjusted risk

All cancers: risk x 0.58

Cancer	Risk x (95% CI), %
Men	
Kaposi's sarcoma	0.001 (0.061-0)
Melanoma (skin)	0.040 (0.048-0.032)
Lung, bronchus, trachea	0.112 (0.130-0.100)
Anus	0.119 (0.185-0.052)
Larynx	0.156 (0.193-0.122)
Oral cavity, pharynx, nasal cavity, paranasal sinus	0.177 (0.200-0.151)
Esophagus	0.253 (0.277-0.229)
Liver	0.259 (0.319-0.213)
Colorectum	0.418 (0.460-0.381)
Penis	0.431 (0.542-0.314)
Stomach	0.464 (0.495-0.435)
Kidney, renal pelvis, ureter	0.476 (0.528-0.435)
Urinary bladder	0.506 (0.528-0.484)
Gallbladder	0.671 (0.719-0.619)
Pancreas	0.740 (0.768-0.710)
Myeloid leukemia	0.829 (0.852-0.804)
Non-Hodgkin lymphoma	0.859 (0.894-0.827)
Thyroid	0.885 (0.906-0.862)
Multiple myeloma	0.891 (0.919-0.858)
Hodgkin lymphoma	0.920 (0.943-0.897)
Women	
Cervix	0.001 (0.032-0)
Kaposi's sarcoma	0.001 (0.165-0)
Melanoma (skin)	0.063 (0.073-0.053)
Anus	0.117 (0.166-0.069)
Lung, bronchus, trachea	0.172 (0.186-0.157)
Larynx	0.215 (0.272-0.149)
Corpus uteri	0.290 (0.344-0.240)
Esophagus	0.325 (0.368-0.280)
Oral cavity, pharynx, nasal cavity, paranasal sinus	0.343 (0.373-0.313)
Vagina	0.354 (0.446-0.260)
Liver	0.374 (0.431-0.320)
Stomach	0.394 (0.432-0.360)
Kidney, renal pelvis, ureter	0.436 (0.483-0.389)
Colorectum	0.492 (0.526-0.459)
Urinary bladder	0.609 (0.629-0.588)
Vulva	0.611 (0.659-0.569)
Gallbladder	0.635 (0.682-0.589)
Breast	0.713 (0.740-0.683)
Pancreas	0.755 (0.784-0.722)
Thyroid	0.872 (0.896-0.851)
Myeloid leukemia	0.875 (0.893-0.857)
Multiple myeloma	0.882 (0.911-0.850)
Ovary	0.957 (0.972-0.942)
Non-Hodgkin lymphoma	0.976 (0.985-0.967)
Hodgkin lymphoma	0.985 (0.991-0.977)

Reference: Islami F, Goding Sauer A, Miller KD, Siegel RL, Fedewa SA, Jacobs EJ, McCullough ML, Patel AV, Ma J, Soerjomataram I, Flanders WD, Brawley OW, Gapstur SM, Jemal A. Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. CA Cancer J Clin. 2018 Jan;68(1):31-54. doi: 10.3322/caac.21440. Epub 2017 Nov 21. PMID: 29160902.

Prostate cancer: risk x 0.995 (95% CI, 0.998-0.991)
Reference: Bhindi B, Wallis CJD, Nayan M, et al. The Association Between Vasectomy and Prostate Cancer: A Systematic Review and Meta-analysis. JAMA Intern Med. 2017;177(9):1273-1286. doi:10.1001/jamainternmed.2017.2791

	Risk x		
	M	F	Both Sexes
Oral cavity (C00–C06)	0.471	0.660	

Nasopharynx (C11)	0.147	0.157	
Pharynx (C09, C10, C12–C14)	0.098	0.185	
Mesothelioma (C45)	0.030	0.175	
Leukemia (C91-C95)	0.885	0.869	
Brain & other central nervous system (C70–C72)			0.975

Reference: Brown KF, Rumgay H, Dunlop C, Ryan M, Quartly F, Cox A, Deas A, Elliss-Brookes L, Gavin A, Hounsome L, Huws D, Ormiston-Smith N, Shelton J, White C, Parkin DM . The fraction of cancer attributable to modifiable risk factors in England, Wales, Scotland, Northern Ireland, and the United Kingdom in 2015. Br J Cancer. 2018 Apr;118(8):1130-1141. doi:10.1038/s41416-018-0029-6. Epub 2018 Mar 23. PMID: 29567982; PMCID: PMC5931106.

BCC: Risk x 0.195
SCC: Risk x 0.170
Reference: O'Sullivan DE, Brenner DR, Villeneuve PJ, Walter SD, Demers PA, Friedenreich CM, King WD; ComPARe Study Team. The current burden of non-melanoma skin cancer attributable to ultraviolet radiation and related risk behaviors in Canada. Cancer Causes Control. 2021 Mar;32(3):279-290. doi:10.1007/s10552-020-01382-1. Epub 2021 Jan 4. PMID: 33394206.

Merkel cell cancer: no data available, so no risk adjustment made
Testicular cancer: no data available, so no risk adjustment made
Bone and joint sarcoma: no data available, so no risk adjustment made
Soft tissue sarcoma: no data available, so no risk adjustment made

Cancer algorithms

Thi section of the thesis provides detailed descriptions of the specific formulae developed to calculate the risk of various cancers. Each subsection focuses on a particular type of cancer, such as bladder carcinoma, breast carcinoma, or liver cancer. These algorithms incorporate data about risk factors—genetic, lifestyle, environmental, or demographic—to assess the likelihood of developing a specific cancer type.

All cancer - General Cancer Risk

-BMI

<22.5	22.5-24.9 (reference group)	25-27.4	27.5-29.5	≥30
0.99 (0.97-1.01)	1.00 (0.98-1.02)	1.01 (0.99-1.03)	1.04 (1.01-1.06)	1.12 (1.10-1.15)

Reference: Reeves GK, Pirie K, Beral V, et al. Cancer incidence and mortality in relation to body mass index in the Million Women Study: cohort study. BMJ. 2007;335(7630):1134. doi:10.1136/bmj.39367.495995.AE

- Habits

- Alcohol:

25 g/day [range]	50 g/day [range]	100 g/day [range]
1.01 [0.90–1.05]	1.22 [1.11–1.27]	1.91 [1.77–2.06]

Reference: Bagnardi V, Blangiardo M, La Vecchia C, Corrao G. Alcohol consumption and the risk of cancer: a meta-analysis. Alcohol Res Health. 2001;25(4):263-270.

- Smoking:

- Former smokers	risk x	1.32	(1.18-1.47)
- Current smokers	risk x	1.71	(1.54-1.89)

Reference: Andreotti G, Freedman ND, Silverman DT, Lerro CC, Koutros S, Hartge P, Alavanja MC, Sandler DP, Freeman LB. Tobacco Use and Cancer Risk in the Agricultural Health Study. Cancer Epidemiol Biomarkers Prev. 2017 May;26(5):769-778. doi: 10.1158/1055-9965.EPI-16-0748. Epub 2016 Dec 29. PMID: 28035020; PMCID: PMC5413369.

- Physical activity:

Leisure time physical activity (metabolic equivalents of energy-hours/week)

10	risk x	0.93	(0.91-0.95)
20	risk x	0.91	(0.88-0.93)
40	risk x	0.90	(0.88-0.91)
60	risk x	0.89	(0.87-0.92)
80	risk x	0.89	(0.85-0.94)

Reference: Liu L, Shi Y, Li T, Qin Q, Yin J, Pang S, Nie S, Wei S. Leisure time physical activity and cancer risk: evaluation of the WHO's recommendation based on 126 high-quality epidemiological studies. Br J Sports Med. 2016 Mar;50(6):372-8. doi: 10.1136/bjsports-2015-094728. Epub 2015 Oct 23. Erratum in: Br J Sports Med. 2016 Apr;50(8):487. PMID: 26500336.

-Nutrition

Fish eaters	Vegetarians	Vegans
0.88 (0.80-0.97)	0.89 (0.83-0.96)	0.81 (0.66-0.98)

Reference: Key TJ, Appleby PN, Crowe FL, Bradbury KE, Schmidt JA, Travis RC. Cancer in British vegetarians: updated analyzes of 4998 incident cancers in a cohort of 32,491 meat eaters, 8612 fish eaters, 18,298 vegetarians, and 2246 vegans. Am J Clin Nutr. 2014 Jul;100 Suppl 1(1):378S-85S. doi: 10.3945/ajcn.113.071266. Epub 2014 Jun 4. PMID: 24898235; PMCID: PMC4144109.

- Fruit consumption	risk x	0.93	(0.89-0.97)
- Vegetable intake	risk x	0.96	(0.93-0.98)
- Whole grain intake	risk x	0.91	(0.87-0.95)

Reference: Schwingshackl L, Schwedhelm C, Galbete C, Hoffmann G. Adherence to Mediterranean Diet and Risk of Cancer: An Updated Systematic Review and Meta-Analysis. Nutrients. 2017 Sep 26;9(10):1063. doi: 10.3390/nu9101063. PMID: 28954418; PMCID: PMC5691680.

- Mediterranean diet	risk x	0.88	(0.80–0.95)

Reference: Benetou V, Trichopoulou A, Orfanos P, Naska A, Lagiou P, Boffetta P, Trichopoulos D; Greek EPIC cohort. Conformity to traditional Mediterranean diet and cancer incidence: the Greek EPIC cohort. Br J Cancer. 2008 Jul 8;99(1):191-5. doi: 10.1038/sj.bjc.6604418. PMID: 18594542; PMCID: PMC2453039.

- Regular sugary drink intake:	risk x	1.19	(1.08-1.32)
- Regular fruit juice drink intake:	risk x	1.12	(1.03-1.23)

Reference: Chazelas Eloi, Srour Bernard, Desmetz Elisa, Kesse-Guyot Emmanuelle, Julia Chantal, Deschamps Valérie et al. Sugary drink consumption and risk of cancer: results from NutriNet-Santé prospective cohort BMJ 2019; 366 :l2408

- Eating Mushrooms:	risk x	0.66	(0.55-0.78)

Reference: Ba DM, Ssentongo P, Beelman RB, Muscat J, Gao X, Richie JP. Higher Mushroom Consumption Is Associated with Lower Risk of Cancer: A Systematic Review and Meta-Analysis of Observational Studies. Adv Nutr. 2021 Oct 1;12(5):1691-1704. doi: 10.1093/advances/nmab015. PMID: 33724299; PMCID: PMC8483951.

- Coffee:		risk x	0.87	(0.82-0.92)

Reference: Yu X, Bao Z, Zou J, Dong J. Coffee consumption and risk of cancers: a meta-analysis of cohort studies. BMC Cancer. 2011;11:96. Published 2011 Mar 15. doi:10.1186/1471-2407-11-96

- Medical History

- Neurofibromatosis Type 1	Male	risk x	2.21	(1.17–3.78)
	Female	risk x	3.07	(1.95–4.61)

Reference: Walker L, Thompson D, Easton D, Ponder B, Ponder M, Frayling I, Baralle D. A prospective study of neurofibromatosis type 1 cancer incidence in the UK. Br J Cancer. 2006 Jul 17;95(2):233-8. doi: 10.1038/sj.bjc.66 03227. Epub 2006 Jun 20. PMID: 16786042; PMCID: PMC2360616.

- HIV positivity:	- without treatment:	risk x	17.6	(16.1–19.1)
	- with treatment:	risk x	3.0	(2.6–3.6)

Reference: Franceschi S, Lise M, Clifford GM, et al. Changing patterns of cancer incidence in the early- and late-HAART periods: the Swiss HIV Cohort Study. Br J Cancer 2010; 103:416.

-Peutz-Jeghers syndrome (STK11):	risk x	15.2	(12-19)

Reference: Francis M. Giardiello, Jill D. Brensinger, Anne C. Tersmette, Steven N. Goodman, Gloria M. Petersen, Susan V. Booker, Marcia Cruz–Correa, Johan A. Offerhaus. Very high risk of cancer in familial Peutz–Jeghers syndrome. Gastroenterology, Volume 119, Issue 6, December 2000, Pages 1447-1453

- Hereditary polycystic kidney disease:	risk x	1·83	(1·57–2·15)

Reference: Yu TM, Chuang YW, Yu MC, Chen CH, Yang CK, Huang ST, Lin CL, Shu KH, Kao CH. Risk of cancer in patients with polycystic kidney disease: a propensity-score matched analysis of a nationwide, population-based cohort study. Lancet Oncol. 2016 Oct;17(10):1419-1425. doi: 10.1016/S1470-2045(16)30250-9. Epub 2016 Aug 20. PMID: 27550645.

- Familial Adenomatous Polyposis :	risk x	50	

Reference: Winawer SW, Fletcher RH, Mille L, et al. AGA guidelines: Colorectal cancer screening: Clinical guidelines and rationale. Gastroenterology 1997; 112:594.

- Diabetes: Men:		risk x	1.27	(1.14-1.42)
Women:		risk x	1.21	(0.99-1.47)

Reference: Inoue M, Iwasaki M, Otani T, et al. Diabetes Mellitus and the Risk of Cancer: Results From a Large-Scale Population-Based Cohort Study in Japan. Arch Intern Med. 2006;166(17):1871–1877.

- History of hemochromatosis:	risk x	1.7	(1.5–2.0)

Reference: Elmberg M, Hultcrantz R, Ekbom A, et al. Cancer risk in patients with hereditary hemochromatosis and in their first-degree relatives. Gastroenterology 2003; 125:1733.

-Hepatitis B:	risk x	2.18	(2.05-2.32)

Reference: Song C, Lv J, Liu Y, Chen JG, Ge Z, Zhu J, Dai J, Du LB, Yu C, Guo Y, Bian Z, Yang L, Chen Y, Chen Z, Liu J, Jiang J, Zhu L, Zhai X, Jiang Y, Ma H, Jin G, Shen H, Li L, Hu Z; China Kadoorie Biobank Collaborative Group. Associations Between Hepatitis B Virus Infection and Risk of All Cancer Types. JAMA Netw Open. 2019 Jun 5;2(6):e195718. doi: 10.1001/jamanetworkopen.2019.5718. PMID: 31199446; PMCID: PMC6575146.

-Genital Warts:	Men	risk x	1.5	(1.4–1.6)
	Women	risk x	1.2	(1.2–1.3)

Reference: Blomberg M, Friis S, Munk C, Bautz A, Kjaer SK. Genital warts and risk of cancer: a Danish study of nearly 50,000 patients with genital warts. J Infect Dis. 2012 May 15;205(10):1544-53. doi: 10.1093/infdis/jis228. Epub 2012 Mar 15. PMID: 22427679.

-History of cancer

- History of childhood cancer:	risk x	6.38	(5.69-7.13)

Reference: Neglia JP, Friedman DL, Yasui Y, Mertens AC, Hammond S, Stovall M, Donaldson SS, Meadows AT, Robison LL, Second malignant neoplasms in five-year survivors of childhood cancer: childhood cancer survivor study., J Natl Cancer Inst. 2001 Apr 18;93(8):618-29.

- History BCC:	1	risk x	1.61	(1.58–1.65)
	6+	risk x	3.12	(2.98–3.26)
	12+	risk x	4.15	(3.79–4.53)

Reference: Cho HG et al. Frequent basal cell cancer development is a clinical marker for inherited cancer susceptibility. JCI Insight. 2018; 3(15): e122744.

- Thyroid cancer treated with radioactive iodine (relative to thyroid cancer survivors) risk x 1.19 (1.04-1.36)
Reference: Sawka AM, Thabane L, Parlea L, Ibrahim-Zada I, Tsang RW, Brierley JD, Straus S, Ezzat S, Goldstein DP. Second primary malignancy risk after radioactive iodine treatment for thyroid cancer: a systematic review and meta-analysis. Thyroid. 2009 May;19(5):451-7. doi:10.1089/thy.2008.0392. PMID: 19281429.

-History of Multiple myeloma: risk x 1.26 (1.16-1.36)
-History of MGUS risk x 3.05 (2.90-3.21)
Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

- Exposure

- Cadmium: risk x 1.31 (0.81–2.12)
Reference: Nawrot T, Plusquin M, Hogervorst J, et al. Environmental exposure to cadmium and risk of cancer: a prospective population-based study. Lancet Oncol 2006; 7:119.
- Agent Orange: risk x 1.08 (1.03-1.13)
Reference: Sang‐Wook Yi, Heechoul Ohrr. Agent Orange exposure and cancer incidence in Korean Vietnam veterans: A prospective cohort study. Cancer. 2014 Dec 1;120(23):3699-706.

- Mutation

- BRCA1 gene IN WOMEN: risk x 2.30 (1.93-2.75)
Reference: Thompson D, Easton DF; Breast Cancer Linkage Consortium. Cancer Incidence in BRCA1 mutation carriers. J Natl Cancer Inst. 2002 Sep 18;94(18):1358-65. doi: 10.1093/jnci/94.18.1358. PMID: 12237281.

- HOBX13 gene: risk x 2,872 (2.121–3.888)
Reference: Cai Q, Wang Oncotarget 2015; 6:42312.

-Intake

- Aspirine intake: risk x 0.86 (0.74-0.99)
Reference: Whitlock EP, Williams SB, Burda BU, Feightner A, Beil T. Aspirin Use in Adults: Cancer, All-Cause Mortality, and Harms: A Systematic Evidence Review for the US Preventive Services Task Force [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2015 Sep. Report No.: 13-05193-EF-1. PMID: 26491756.

- Multivitamin intake: risk x 0.92 (0.86–0.998)
Reference: Gaziano JM, Sesso HD, Christen WG, Bubes V, Smith JP, MacFadyen J, Schvartz M, Manson JE, Glynn RJ, Buring JE. Multivitamins in the prevention of cancer in men: the Physicians' Health Study II randomized controlled trial. JAMA. 2012 Nov 14;308(18):1871-80. doi: 10.1001/jama.2012.14641. Erratum in: JAMA. 2014 Aug 6;312(5):560. PMID: 23162860; PMCID: PMC3517179.

Anal cancer

- Medical History

- HIV positivity:	- without treatment:	risk x	25 .7	(2.4–94.5)
	- with treatment:	risk x	49.9	(18.0–109)

Reference: Franceschi S, Lise M, Clifford GM, et al. Changing patterns of cancer incidence in the early- and late-HAART periods: the Swiss HIV Cohort Study. Br J Cancer 2010; 103:416.

- History of organ transplantation:	risk x	4.85	(1·36–17·3)

Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

- History of	Multiple myeloma:	risk x	1.30	(1.09-1.53)
	MGUS:	risk x	1.25	(1.05-1.48)

Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

- Genital Warts:	Men	risk x	21.5	(14.4–30.9)
	Women	risk x	7.8	(5.4–11.0)

Reference: Blomberg M, Friis S, Munk C, Bautz A, Kjaer SK. Genital warts and risk of cancer: a Danish study of nearly 50,000 patients with genital warts. J Infect Dis. 2012 May 15;205(10):1544-53. doi: 10.1093/infdis/jis228. Epub 2012 Mar 15. PMID: 22427679.

Basocellular skin cancer

-Ethnicity

- African:	risk x	0.004	
- Asian:	risk x	0.049	
- Hispanic, Pacific Islanders, Native American:	risk x	0.524	

Reference: Gloster HM Jr, Neal K. Skin cancer in skin of color. J Am Acad Dermatol 2006; 55:741.

- Physical attributes

- Hair color	Brown	risk x	1.13	(0.90- 1.51)
	Light/brown	risk x	1.19	(0.89- 1.59)
	Blonde	risk x	1.24	(0.90- 1.72)
	Light blonde	risk x	1.72	(1.16-2.57)
	Red	risk x	1.31	(0.57- 3.03)
- Light eye color		risk x	1.38	(1.16-1.63)
- Skin reaction to sun exposure	Tan, no burn	risk x	1	
	Burn, then tan	risk x	1.49	(1.26- 1.78)
	Burn, never tan	risk x	2.70	(2.10- 3.47)
- Age at first sunburn	15 years old or less	risk x	1.65	(1.16-2.36)

Reference: Zanetti R, Rosso S, Martinez C, et al. The multicentre south European study 'Helios'. I: Skin characteristics and sunburns in basal cell and squamous cell carcinomas of the skin. Br J Cancer. 1996;73(11):1440–1446. doi:10.1038/bjc.1996.274

- Solar exposure High or Medium Intermittent: risk x 2.46 (1.48-4.09)
Reference: Wu S, Han J, Li WQ, Li T, Qureshi AA. Basal-cell carcinoma incidence and associated risk factors in US women and men. Am J Epidemiol. 2013 Sep 15;178(6):890-7. doi: 10.1093/aje/kwt073. Epub 2013 Jul 4. PMID: 23828250; PMCID: PMC3775544.

- Ever used a sunbed: risk x 1.29 (1.08-1.53)
Reference: Wehner MR, Shive ML, Chren MM, et al. Indoor tanning and non-melanoma skin cancer: systematic review and meta-analysis. BMJ 2012; 345:e5909.

-Treatment with PUVA: risk x 3.09 (2.36-4.06)
Reference: Stern RS, PUVA Follow-Up Study. The risk of squamous cell and basal cell cancer associated with psoralen and ultraviolet A therapy: a 30-year prospective study. J Am Acad Dermatol 2012; 66:553.

-Intake of citrus fruits 2x/week or more: risk x 1.03 (0.99–1.08)
Reference: Wu S, Cho E, Feskanich D, et al. Citrus consumption and risk of basal cell carcinoma and squamous cell carcinoma of the skin. Carcinogenesis 2015; 36:1162.

- Radiotherapy in childhood: risk x 39.8 (8.6-185)
Reference: Watt TC, Inskip PD, Stratton K, et al. Radiation-related risk of basal cell carcinoma: a report from the Childhood Cancer Survivor Study. J Natl Cancer Inst 2012; 104:1240.

-Family history of skin cancer: risk x 2.49 (1.74–3.35)
Reference: Berlin NL, Cartmel B, Leffell DJ, et al. Family history of skin cancer is associated with early-onset basal cell carcinoma independent of MC1R genotype. Cancer Epidemiol 2015; 39:1078.

-Coffee intake: risk x 0.57 (0.34–0.95)
Reference: Ferrucci LM, Cartmel B, Molinaro AM, et al. Tea, coffee, and caffeine and early-onset basal cell carcinoma in a case-control study. Eur J Cancer Prev 2014; 23:296.

- Flight crew, women: risk x 4.09 (2.70–6.20)
Reference: McNeely E, Mordukhovich I, Staffa S, Tideman S, Gale S, Coull B. Cancer prevalence among flight attendants compared to the general population. Environ Health. 2018;17(1):49. Published 2018 Jun 26. doi:10.1186/s12940-018-0396-8

- Medical History

- HIV positivity with treatment: risk x 3.3 (2.1–4.9)
Reference: Franceschi S, Lise M, Clifford GM, et al. Changing patterns of cancer incidence in the early- and late-HAART periods: the Swiss HIV Cohort Study. Br J Cancer 2010; 103:416.

- History of organ transplantation: risk x 28.62 (9·39–87·2)
Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

- History of Parkinson's: risk x 1.25 (1.1–1.4)
Reference: Olsen JH, Friis S, Frederiksen K, et al. Atypical cancer pattern in patients with Parkinson's disease. Br J Cancer 2005; 92:201.

- Xeroderma pigmentosum: risk x 10000
Reference: Kraemer KH, DiGiovanna JJ. Forty years of research on xeroderma pigmentosum at the US National Institutes of Health. Photochem Photobiol. 2015;91(2):452-9.

-History of Multiple myeloma: risk x 2.22 (1.74-2.80)
-History of MGUS: risk x 3.30 (2.76-3.90)
Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

-Nevoid basal cell carcinoma syndrome: risk x 2500
Reference: Endo M, Fujii K, Sugita K, Saito K, Kohno Y, Miyashita T. 2012. Nationwide survey of nevoid basal cell carcinoma syndrome in Japan revealing the low frequency of basal cell carcinoma. Am J Med Genet Part A 158A:351–357.

- Genital Warts: Men risk x 1.4 (1.2–1.7)
Women risk x 1.2 (1.0–1.3)
Reference: Blomberg M, Friis S, Munk C, Bautz A, Kjaer SK. Genital warts and risk of cancer: a Danish study of nearly 50,000 patients with genital warts. J Infect Dis. 2012 May 15;205(10):1544-53. doi: 10.1093/infdis/jis228. Epub 2012 Mar 15. PMID: 22427679.

-Exposure to arsenic: risk x 1.18 (1.08-1.28)
Reference: G. Leonardi, M. Vahter, F. Clemens, W. Goessler, E. Gurzau, K. Hemminki, R. Hough, K.Koppova, R. Kumar, P. Rudnai, S. Surdu, T. Fletcher. Inorganic arsenic and basal cell carcinoma in areas of Hungary, Romania, and Slovakia: a case-control study. Environ. Health Perspect., 120 (2012), pp. 721-726

-(MC1R) gene 151Cys variant: risk x 1.56 (1.03-2.34)
Reference: Han J, Kraft P, Colditz GA, et al. Melanocortin 1 receptor variants and skin cancer risk. Int J Cancer 2006; 119:1976.

-Medication

-Tetracycline: risk x 1.8 (1.2–2.8)
Reference: Robinson SN, Zens MS, Perry AE, et al. Photosensitizing agents and the risk of non-melanoma skin cancer: a population-based case-control study. J Invest Dermatol 2013; 133:1950.

-Methotrexate: risk x 3.04 (2.39-3.80)
Reference: Lange E, Blizzard L, Venn A, et al. Disease-modifying anti-rheumatic drugs and non-melanoma skin cancer in inflammatory arthritis patients: a retrospective cohort study. Rheumatology (Oxford) 2016; 55:1594.

-Thiazide diuretics: risk x 1.17 (1.03–1.33)

Reference: Bendinelli B., Masala G., Garamella G., Palli D., Caini S. Do thiazide diuretics increase the risk of skin cancer? A critical review of the scientific evidence and updated meta-analysis. Curr. Cardiol. Rep. 2019;21:92. doi:10.1007/s11886-019-1183-z.

-Calcium channel blockers:	risk x	1.15	(1.09–1.21)
-Beta-Blockers:	risk x	1.09	(1.04–1.15)

Reference: Tang H., Fu S., Zhai S., Song Y., Asgari MM, Han J. Use of antihypertensive drugs and risk of keratinocyte carcinoma: A meta-analysis of observational studies. Pharmacoepidemiol. Drug Saf. 2018;27:279–288. doi:10.1002/pds.4384.

-NSAIDs:	risk x	0.94	(0.89–1.00)

Reference: Ma Y., Yu P., Lin S., Li Q., Fang Z., Huang Z. The association between nonsteroidal anti-inflammatory drugs and skin cancer: Different responses in American and European populations. Pharmacol. Res. 2019;152:104499. doi: 10.1016/j.phrs.2019.104499.

- Medications for long term daily use			
Diclofenac	risk x	1.1	(1.1-1.1)
Amiodarone	risk x	1.2	(1.0-1.3)
Methyldopa	risk x	1.3	(1.0-1.6)
Sotalol	risk x	1.2	(1.2-1.3)
Verapamil	risk x	1.2	(1.1-1.3)
Metformin	risk x	0.8	(0.7-0.8)
Tolbutamide	risk x	0.9	(0.8-1.0)
Carbamazepine	risk x	1.1	(1.0-1.2)
Valproate	risk x	1.3	(1.1-1.4)
- Medications for short term use			
Acyclovir	risk x	1.3	(1.3-1.4)
Ciprofloxacin	risk x	1.2	(1.1-1.2)
Doxycycline	risk x	1.3	(1.2-1.3)
Ketoconazole	risk x	1.5	(1.4-1.5)
Levofloxacin	risk x	1.5	(1.1-2.1)
Sulfamethazole with trimethoprim	risk x	1.1	(1.0-1.2)
Hydroxychloroquine	risk x	1.4	(1.3-1.4)
Isotretinoin	risk x	2.0	(1.7-2.4)

Reference: Kaae J, Boyd HA, Hansen AV, Wulf HC, Wohlfahrt J, Melbye M. Photosensitizing medication use and risk of skin cancer. Cancer Epidemiol Biomarkers Prev. 2010 Nov;19(11):2942-9. doi: 10.1158/1055-9965.EPI-10-0652. Epub 2010 Sep 22. PMID: 20861398.

Bladder cancer

- Treatments

- History of treatment with cyclophosphamide: risk x 4.5 (1.5-13.6)

Reference: Travis LB, Curtis RE, Glimelius B, et al. Bladder and kidney cancer following cyclophosphamide therapy for non-Hodgkin's lymphoma. J Natl Cancer Inst 1995; 87:524.

- Permanent catheter in place: risk x 4.9 (1.3–13.8)

Reference: Groah SL, Weitzenkamp DA, Lammertse DP, et al. Excess risk of bladder cancer in spinal cord injury: evidence for an association between indwelling catheter use and bladder cancer. Arch Phys Med Rehabil 2002; 83:346.

- Habits

- Smoking:

Cigarette smoking status - women	Former smoker	risk x	2.5	(2.0-3.1)
	Current smoker	risk x	4.7	(3.7-5.8)
Cigarette smoking status - men	Former smoker	risk x	2.2	(2.0-2.4)
	Current smoker	risk x	4.0	(3.5-4.5)

Reference: Freedman ND, Abnet CC, Caporaso NE, et al. Impact of changing US cigarette smoking patterns on incident cancer: risks of 20 smoking-related cancers among the women and men of the NIH-AARP cohort. Int J Epidemiol 2016; 45:846.

- Drinking chlorinated drinking water: risk x 1.3 (1.2-1.7)

Reference: Villanueva CM, Fernández F, Malats N, et al. Meta-analysis of studies on individual consumption of chlorinated drinking water and bladder cancer. J Epidemiol Community Health 2003; 57:166.

- Drinking more than 2.5l per day: risk x 0.51 (0.32-0.80)

Reference: Michaud DS, Spiegelman D, Clinton SK, et al. Fluid intake and the risk of bladder cancer in men. N Engl J Med 1999; 340:1390.

- Drinking coffee: risk x 1.18 (1.01-1.38)

Reference: Zeegers MP, Tan FE, Goldbohm RA, van den Brandt PA. Are coffee and tea consumption associated with urinary tract cancer risk? A systematic review and meta-analysis. Int J Epidemiol 2001; 30:353.

-Night work: risk x 1.74 (1.22-2.49)

Reference: Parent, M. -E.; El-Zein, M.; Rousseau, M. -C.; Pintos, J.; Siemiatycki, J. (2012). "Night Work and the Risk of Cancer Among Men". American Journal of Epidemiology. 176(9):751–759.

- Familial History

- Parent with bladder cancer:	Men	risk x	1.35	(0.97-1.79)
	Women	risk x	2.29	(1.46-3.29)

Reference: Plna K, Hemminki K. Familial bladder cancer in the National Swedish Family Cancer Database. J Urol 2001; 166:2129.

- Medical History

- History of organ transplantation: risk x 2.46 (1.82-3.34)

Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

- Necrotizing vasculopathies risk x 3.80 (1.22-11.8)

Reference: He MM, Lo CH, Wang K, Polychronidis G, Wang L, Zhong R, Knudsen MD, Fang Z, Song M. Immune-Mediated Diseases Associated With Cancer Risks. JAMA Oncol. 2021 Dec 2:e215680. doi: 10.1001/jamaoncol.2021.5680. Epub ahead of print. PMID: 34854871; PMCID: PMC8640951.

- Lynch syndrome (mismatch repair genes MLH1, MSH2, MSH6) risk x 9.51 (1.15-34.37)

Reference: Win AK, Young JP, Lindor NM, et al. Colorectal and other cancer risks for carriers and noncarriers from families with a DNA mismatch repair gene mutation: a prospective cohort study. J Clin Oncol 2012; 30:958.

- MGUS risk x 1.58 (1.21-2.03)

Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

- Genital warts: risk x 1.4 (1.1–1.8)

Reference: Blomberg M, Friis S, Munk C, Bautz A, Kjaer SK. Genital warts and risk of cancer: a Danish study of nearly 50,000 patients with genital warts. J Infect Dis. 2012 May 15;205(10):1544-53. doi: 10.1093/infdis/jis228. Epub 2012 Mar 15. PMID: 22427679.

- Medication

- Finasteride: risk x 0.64 (0.51–0.80)

Reference: Zhu D, Srivastava A, Agalliu I, Fram E, Kovac EZ, Aboumohamed A, Schoenberg MP, Sankin AI. Finasteride Use and Risk of Bladder Cancer in a Multiethnic Population. J Urol. 2021 Jul;206(1):15-21. doi: 10.1097/JU.0000000000001694. Epub 2021 Feb 22. PMID: 33617325.

- Exposure

- Aluminum risk x 2.85 (1.23–5.62)

Reference: Maltseva A, Serra C, Kogevinas M. Cancer risk among workers of a secondary aluminum smelter. Occup Med (London). 2016;66(5):412-414. doi:10.1093/occmed/kqw054

- Polycyclic aromatic hydrocarbons risk x 1.3 (1.03-1.6)
- Painters risk x 1.3 (1.2-1.4)
- Ever worked in rubber industry risk x 1.5 (1.4-1.6)
- Laundry or dry-cleaning worker risk x 1.4 (1.1-1.9)
- Hairdressers risk x 1.3 (1.2-1.4)

Reference: Marant Micallef C, Shield KD, Baldi I, Charbotel B, Fervers B, Gilg Soit Ilg A, Guénel P, Olsson A, Rushton L, Hutchings SJ, Straif K, Soerjomataram I. Occupational exposures and cancer: a review of agents and relative risk estimates. Occup Environ Med. 2018 Aug;75(8):604-614. doi: 10.1136/oemed-2017-104858. Epub 2018 May 7. PMID: 29735747.

- Arsenic: risk x 2.05 (1.22-3.24)

Reference: Chiou HY, Chiou ST, Hsu YH, et al. Incidence of transitional cell carcinoma and arsenic in drinking water: a follow-up study of 8,102 residents in an arseniasis-endemic area in northeastern Taiwan. Am J Epidemiol 2001; 153:411.

- Diesel: risk x 1.61 (1.08-2.40)

Reference: Koutros S, Kogevinas M, Friesen MC, Stewart PA, Baris D, Karagas MR, Schwenn M, Johnson A, Monawar Hosain GM, Serra C, Tardon A, Carrato A, Garcia-Closas R, Moore LE, Nickerson ML, Hewitt SM, Lenz P, Schned AR, Lloreta J, Allory Y, Zhang H, Chatterjee N, Garcia-Closas M, Rothman N, Malats N, Silverman DT. Diesel exhaust and bladder cancer risk by pathologic stage and grade subtypes. Environ Int. 2020 Feb;135:105346. doi: 10.1016/j.envint.2019.105346. Epub 2019 Dec 18. PMID: 31864026; PMCID: PMC8237313.

Bone & Joint Sarcoma

-Genetics

-TP53: risk x 35,000

Reference: Bougeard G, Renaux-Petel M, Flaman JM, Charbonnier C, Fermey P, Belotti M, Gauthier-Villars M, Stoppa-Lyonnet D, Consolino E, Brugières L, Caron O, Benusiglio PR, Bressac-de Paillerets B, Bonadona V, Bonaïti-Pellié C, Tinat J, Baert-Desurmont S, Frebourg T. Revisiting Li-Fraumeni Syndrome From TP53 Mutation Carriers. J Clin Oncol. 2015 Jul 20;33(21):2345-52. doi: 10.1200/JCO.2014.59.5728. Epub 2015 May 26. PMID: 26014290.

- CHEK2: risk x 3.45 (1.09-10.9)

Reference: Näslund-Koch C, Nordestgaard BG, Bojesen SE. Increased Risk for Other Cancers in Addition to Breast Cancer for CHEK2*1100delC Heterozygotes Estimated From the Copenhagen General Population Study. J Clin Oncol 2016; 34:1208.

- Medical History

- Rothmund-Thomson syndrome: risk x 3000

Reference: Wang LL, Levy ML, Lewis RA, Chintagumpala MM, Lev D, Rogers M, Plon SE. Clinical manifestations in a cohort of 41 Rothmund-Thomson syndrome patients. Am J Med Genet. 2001 Jul 22;102(1):11-7. doi: 10.1002/1096-8628(20010722)102:1<11::aid-ajmg1413>3.0.co;2-a. PMID: 11471165.

-Paget disease of the bone: risk x 147

Reference: Hadjipavlou A, Lander P, Srolovitz H, Enker IP. Malignant transformation in Paget disease of bone. Cancer. 1992 Dec 15;70(12):2802-8. doi: 10.1002/1097-0142(19921215)70:12<2802::aid-cncr2820701213>3.0.co;2-n. PMID: 1451058.

- History of cancer

- History of childhood cancer: risk x 19.14 (12.72-27.67)

Reference: Neglia JP, Friedman DL, Yasui Y, Mertens AC, Hammond S, Stovall M, Donaldson SS, Meadows AT, Robison LL, Second malignant neoplasms in five-year survivors of childhood cancer: childhood cancer survivor study., J Natl Cancer Inst. 2001 Apr 18;93(8):618-29.

Brain or nervous system tumors

- Environment

- Exposure to high doses of electromagnetic radiation: risk x 2.4 (1.0–5.4)

Reference:Wertheimer N, Leeper E. Electrical wiring configurations and childhood cancer. Am J Epidemiol 1979; 109:273.

- Living on a farm: risk x 1.96 (1.11-3.47)

Reference: Piel C, Pouchieu C, Tual S, et al. Central nervous system tumors and agricultural exposures in the prospective cohort AGRICAN. Int J Cancer 2017; 141:1771.

- Genetics

- Mutation: TP53 risk x 2000

Reference: Bougeard G, Renaux-Petel M, Flaman JM, Charbonnier C, Fermey P, Belotti M, Gauthier-Villars M, Stoppa-Lyonnet D, Consolino E, Brugières L, Caron O, Benusiglio PR, Bressac-de Paillerets B, Bonadona V, Bonaïti-Pellié C, Tinat J, Baert-Desurmont S, Frebourg T. Revisiting Li-Fraumeni Syndrome From TP53 Mutation Carriers. J Clin Oncol. 2015 Jul 20;33(21):2345-52. doi: 10.1200/JCO.2014.59.5728. Epub 2015 May 26. PMID: 26014290.

- Medical History

- HIV positivity: risk x 2.18 (1.29-3.68)

Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

-Nevoid basal cell carcinoma syndrome: risk x 400

Reference: Endo M, Fujii K, Sugita K, Saito K, Kohno Y, Miyashita T. 2012. Nationwide survey of nevoid basal cell carcinoma syndrome in Japan revealing the low frequency of basal cell carcinoma. Am J Med Genet Part A 158A:351–357.

- Neurofibromatosis Type 1: risk x 22.6 (9.06–46.5)

Reference: Walker L, Thompson D, Easton D, Ponder B, Ponder M, Frayling I, Baralle D. A prospective study of neurofibromatosis type 1 cancer incidence in the UK. Br J Cancer. 2006 Jul 17;95(2):233-8. doi: 10.1038/sj.bjc.6603227. Epub 2006 Jun 20. PMID: 16786042; PMCID: PMC2360616.

- Asthma: risk x 1.68 (1.18-2.39)
- Autoimmune hepatitis: risk x 10.8 (1.52-77.4)

Reference: He MM, Lo CH, Wang K, Polychronidis G, Wang L, Zhong R, Knudsen MD, Fang Z, Song M. Immune-Mediated Diseases Associated With Cancer Risks. JAMA Oncol. 2021 Dec 2:e215680. doi: 10.1001/jamaoncol.2021.5680. Epub ahead of print. PMID: 34854871; PMCID: PMC8640951.

- History of allergy: risk x 0.61 (0.55-0.67)
- History of eczema: risk x 0.69 (0.58-0.82)

Reference: Linos E, Raine T, Alonso A, Michaud D. Atopy and risk of brain tumors: a meta-analysis. J Natl Cancer Inst 2007; 99:1544.

- History of cancer

- History of childhood cancer: risk x 9.85 (6.90-13.63)

Reference: Neglia JP, Friedman DL, Yasui Y, Mertens AC, Hammond S, Stovall M, Donaldson SS, Meadows AT, Robison LL, Second malignant neoplasms in five-year survivors of childhood cancer: childhood cancer survivor study., J Natl Cancer Inst. 2001 Apr 18;93(8):618-29.

- History of Basocellular skin carcinoma:

Number of BCCs:	1	risk x	1.32	(1.14–1.52)
	6+	risk x	2.68	(2.04–3.53)
	12+	risk x	3.98	(2.46–6.42)

Reference: Cho HG et al. Frequent basal cell cancer development is a clinical marker for inherited cancer susceptibility. JCI Insight. 2018; 3(15): e122744.

- Cranial radiotherapy in childhood: risk x 6.8 (1.54-29.7)

Reference: Neglia JP, Robison LL, Stovall M, et al. New primary neoplasms of the central nervous system in survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. J Natl Cancer Inst 2006; 98:1528.

Breast cancer

- Physical attributes

- BMI:
  - Postmenopausal per 5 kg/m² increase in BMI (above 25): risk x 1.12 (1.08-1.16)
  - Premenopausal , per 5 kg/m² increase in BMI (above 25): risk x 0.92 (0.88-0.97)

Reference: Renehan AG, Tyson M, Egger M, et al. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 2008; 371:569.

- Height (m)
  - <1.60 risk x 1.0
  - ≥1.75 risk x 1.22 (0.90-1.65)

Reference: Van den Brandt PA, Spiegelman D, Yaun SS, et al. Pooled analysis of prospective cohort studies on height, weight, and breast cancer risk. Am J Epidemiol 2000; 152:514.

- High bone density : risk x 1.62 (1.17-2.06)

Reference: Qu Breast Cancer Res Treat 2013; 138:261.

- Breast Tissue:
  - Atypical hyperplasia of the mammary gland tissue: risk x 5.3 (3.1-8.8)

    Reference: Dupont WD, Page DL. Risk factors for breast cancer in women with proliferative breast disease. N Engl J Med 1985; 312:146.

  - Dense mammary tissue (dense glandular tissue 75% of the breast or more): risk x 4.7 (3.0-7.4)

    Reference: Boyd NF, Guo H, Martin LJ, et al. Mammographic density and the risk and detection of breast cancer. N Engl J Med 2007; 356:227.

  - Usual ductal hyperplasia: risk x 1.53 (1.10-2.13)

    Reference: Shaaban AM, Sloane JP, West CR, Foster CS. Breast cancer risk in usual ductal hyperplasia is defined by estrogen receptor-alpha and Ki-67 expression. Am J Pathol. 2002;160(2):597-604.

  - Papilloma:
    - Single risk x 2.04 (1.43-2.81)
    - Multiple risk x 3.01 (1.10-6.55)

    Reference: Lewis JT, Hartmann LC, Vierkant RA, et al. An analysis of breast cancer risk in women with single, multiple, and atypical papilloma. Am J Surg Pathol 2006; 30:665.

  - Sclerosing adenosis: risk x 2.10 (1.91–2.30)

    Reference: Visscher DW, Nassar A, Degnim AC, et al. Sclerosing adenosis and risk of breast cancer. Breast Cancer Res Treat. 2014;144(1):205-12.

  - Radial scars: risk x 1.6 (1.35-1.89)

    Reference: Lv M, Zhu X, Zhong S, et al. Radial scars and subsequent breast cancer risk: a meta-analysis. PLoS One. 2014;9(7):e102503. Published 2014 Jul 14. doi:10.1371/journal.pone.0102503

  - Fibroadenomas: risk x 1.49 (1.26–1.74)

    Reference: Nassar A, Visscher DW, Degnim AC, et al. Complex fibroadenoma and breast cancer risk: a Mayo Clinic Benign Breast Disease Cohort Study. Breast Cancer Res Treat. 2015;153(2):397-405.

  - Flat epithelial atypia: risk x 1.47 (1.0–2.15)

    Reference: Boulos FI, Dupont WD, Simpson JF, et al. Histologic associations and long-term cancer risk in columnar cell lesions of the breast: a retrospective cohort and a nested case-control study. Cancer 2008; 113:2415.

- Female history

- Age at start of menopause 55 or more: risk x 1.12 (1.07-1.17)

Reference: Collaborative Group on Hormonal Factors in Breast Cancer. Menarche, menopause, and breast cancer risk: individual participant meta-analysis, including 118 964 women with breast cancer from 117 epidemiological studies. Lancet Oncol. 2012;13(11):1141-1151. doi:10.1016/S1470-2045(12)70425-4

Age at menarche ≥15 risk x 0.87 (0.78–0.97)

Parity of 0 risk x 1.16 (1.04–1.26)

Age at first birth
- <20 risk x 0.96 (0.82–1.11)
- 20–24 risk x 0.96 (0.82–1.11)
- ≥30 risk x 1.20 (1.02–1.42)

Reference: Nelson HD, Zakher B, Cantor A, Fu R, Griffin J, O'Meara ES, Buist DS, Kerlikowske K, van Ravesteyn NT, Trentham-Dietz A, Mandelblatt JS, Miglioretti DL. Risk factors for breast cancer for women aged 40 to 49 years: a systematic

review and meta-analysis. Ann Intern Med. 2012 May 1;156(9):635-48. doi: 10.7326/0003-4819-156-9-201205010-00006. PMID: 22547473; PMCID: PMC3561467.

- Lifetime months of breastfeeding:

≤6	risk x	0·98	(0.963-0.997)
7–18	risk x	0·94	(0.924-0.956)
19–30	risk x	0·89	(0.865-0.915)
31–54	risk x	0·88	(0.847-0.913)
≥55	risk x	0·73	(0.681-0.779)

Reference: Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50302 women with breast cancer and 96973 women without the disease. Lancet 2002; 360:187.

- Use of Postmenopausal Hormones:

Current use of estrogen only, by duration of use			
<1 year	risk x	1.08	(0.86-1.35)
1-4 years	risk x	1.17	(1.09-1.25)
5-9 years	risk x	1.22	(1.16-1.28)
10-14 years	risk x	1.43	(1.37-1.50)
15+ years	risk x	1.58	(1.50-1.67)
Current use of estrogen-progestogen, by duration of use			
<1 year	risk x	1.20	(1.01-1.43)
1-4 years	risk x	1.60	(1.52-1.69)
5-9 years	risk x	1.97	(1.89-2.04)
10-14 years	risk x	2.26	(2.16-2.36)
15+ years	risk x	2.51	(2.34-2.68)

Reference: Collaborative Group on Hormonal Factors in Breast Cancer. Type and timing of menopausal hormone therapy and breast cancer risk: individual participant meta-analysis of the worldwide epidemiological evidence. Lancet. 2019;394(10204):1159-1168. doi:10.1016/S0140-6736(19)31709-X

- Family history

No. of relatives with breast cancer

1	risk x	1·80	(1·70–1·91)
2	risk x	2·93	(2·37–3·63)
3 or more	risk x	3·90	(2·03–7·49)

Reference: Collaborative Group on Hormonal Factors in Breast Cancer. Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies including 58,209 women with breast cancer and 101,986 women without the disease. Lancet 2001; 358:1389.

- Habits

- Alcohol : per glass/d:	risk x	1.10	(1.07-1.12)

Reference: Chen WY, Rosner B, Hankinson SE, et al. Moderate alcohol consumption during adult life, drinking patterns, and breast cancer risk. JAMA 2011; 306:1884.

-Smoking: Active smoker:	risk x	1.10	(1.09-1.12)
Living with a smoker:	risk x	1.07	(1.02-1.13)

Reference: Macacu, A., Autier, P., Boniol, M. et al. Breast Cancer Res Treat (2015) 154: 213. https://doi.org/10.1007/s10549-015-3628-4

- Night work:	risk x	1.51	(1.36–1.68)

Reference: Megdal SP, Kroenke CH, Laden F, et al. Night work and breast cancer risk: a systematic review and meta-analysis. Eur J Cancer 2005; 41:2023.

- Nutrition:

- Mediterranean diet:	risk x	0.32	(0.13-0.79)

Reference: Toledo E, Salas-Salvadó J, Donat-Vargas C, et al. Mediterranean Diet and Invasive Breast Cancer Risk Among Women at High Cardiovascular Risk in the PREDIMED Trial: A Randomized Clinical Trial. JAMA Intern Med 2015; 175:1752.

- Intake of high amounts of fruit/vegetables:	risk x	0.89	(0.82-0.99)

Reference: Brennan SF, Cantwell MM, Cardwell CR, et al. Dietary patterns and breast cancer risk: a systematic review and meta-analysis. Am J Clin Nutr 2010; 91:1294.

- Large soy intake:	risk x	0.71	(0.60-0.85)

Reference: Wu AH, Yu MC, Tseng CC, Pike MC. Epidemiology of soy exposures and breast cancer risk. Br J Cancer 2008; 98:9.

- Intake of more than 2 cups of milk per day: risk x 1.22 (1.05-1.40)
Reference: Fraser GE, Jaceldo-Siegl K, Orlich M, Mashchak A, Sirirat R, Knutsen S. Dairy, soy, and risk of breast cancer: those confounded milks. Int J Epidemiol. 2020 Oct 1;49(5):1526-1537. doi: 10.1093/ije/dyaa007. PMID: 32095830; PMCID: PMC8453418.

- Sugary drink intake 1 or more per day: risk x 1.23 (1.03-1.48)
Reference: Chazelas Eloi, Srour Bernard, Desmetz Elisa, Kesse-Guyot Emmanuelle, Julia Chantal, Deschamps Valérie et al. Sugary drink consumption and risk of cancer: results from NutriNet-Santé prospective cohort BMJ 2019; 366 :l2408

- Eating Mushrooms: risk x 0.65 (0.52-0.81)
Reference: Ba DM, Ssentongo P, Beelman RB, Muscat J, Gao X, Richie JP. Higher Mushroom Consumption Is Associated with Lower Risk of Cancer: A Systematic Review and Meta-Analysis of Observational Studies. Adv Nutr. 2021 Oct 1;12(5):1691-1704. doi: 10.1093/advances/nmab015. PMID: 33724299; PMCID: PMC8483951.

-Physical activity (hours per week):
- less than 7 hours: no difference
- between 7 and 10 hours: risk x 0.98 (0.77-1.25)
- between 10 and 13 hours: risk x 0.93 (0.72-1.20)
- between 13 hours and 18 hours: risk x 0.74 (0.56-0.97)
- more than 18 hours: risk x 0.77 (0.59-1.01)
Reference: Maruti SS, Willett WC, Feskanich D, Rosner B, Colditz GA. A prospective study of age-specific physical activity and premenopausal breast cancer. J Natl Cancer Inst. 2008;100(10):728-37.

- Flight crew aircraft: risk x 1.51 (1.02-2.24)
Reference: McNeely E, Mordukhovich I, Staffa S, Tideman S, Gale S, Coull B. Cancer prevalence among flight attendants compared to the general population. Environ Health. 2018;17(1):49. Published 2018 Jun 26. doi:10.1186/s12940-018-0396-8

- Medication

- NSAIDs : risk x 0.88 (0.84-0.93)
- Aspirin: risk x 0.87 (0.64-0.97)
Reference: Takkouche B, Regueira-Méndez C, Etminan M. Breast cancer and use of nonsteroidal anti-inflammatory drugs: a meta-analysis. J Natl Cancer Inst 2008; 100:1439.

- Aromatase inhibitors: risk x 0.468 (0.346-0.634)
- Arzoxifene: risk x 0.415 (0.253-0.682)
- Lasofoxifene: risk x 0.208 (0.079-0.544)
- Raloxifene: risk x 0.572 (0.372-0.881)
- Tamoxifen: risk x 0.70 8 (0.595-0.842)
- Tibolone: risk x 0.317 (0.127-0.792)
Reference: Simone Mocellin, Pierluigi Pilati, Marta Briarava, Donato Nitti; Breast Cancer Chemoprevention: A Network Meta-Analysis of Randomized Controlled Trials, JNCI: Journal of the National Cancer Institute, Volume 108, Issue 2, 1 February 2016, djv318

- Transgender hormonal therapy: Man -> Woman: risk x 46.7 (27.2-75.4)
Woman -> Man: risk x 0.2 (0.1-0.5)
Reference: de Blok Christel JM, Wiepjes Chantal M, Nota Nienke M, van Engelen Klaartje, Adank Muriel A, Dreijerink Koen MA et al. Breast cancer risk in transgender people receiving hormone treatment: nationwide cohort study in the Netherlands BMJ 2019; 365 :l1652

- Surgery

- Bilateral ovariectomy risk x 0.59 (0.50-0.69)
- Hysterectomy with ovarian conservation risk x 0.83 (0.72-0.96)
- Hysterectomy with partial ovary removal risk x 0.73 (0.59-0.91)
Reference: Press DJ, Sullivan-Halley J, Ursin G, Deapen D, McDonald JA, Strom BL, Norman SA, Simon MS, Marchbanks PA, Folger SG, Liff JM, Burkman RT, Malone KE, Weiss LK, Spirtas R, Bernstein L. Breast cancer risk and ovariectomy, hysterectomy, and tubal sterilization in the women's contraceptive and reproductive experiences study. Am J Epidemiol. 2011 Jan 1;173(1):38-47. doi: 10.1093/aje/kwq339. Epub 2010 Nov 25. PMID: 21109566; PMCID: PMC3025644.

-Genetics

Gene

- ATM	risk x	1.74	(1.46-2.07)
- BARD1	risk x	1.92	(1.36-2.72)
- BRCA1	risk x	5.91	(5.25-6.67)
- BRCA2	risk x	3.31	(2.95-3.71)
- CHEK2	risk x	1.99	(1.70-2.33)
- PALB2	risk x	3.39	(2.79-4.12)
- PTEN	risk x	5.83	(2.43-14.0)
- TP53	risk x	5.37	(2.78-10.4)
- CDH1	risk x	17.7	(7.68-40.1)

Reference: Allison W. Kurian, Elisha Hughes, Elizabeth A. Handorf, Alexander Gutin, Brian Allen, Anne-Renee Hartman, Michael J. Hall. Breast and Ovarian Cancer Penetrance Estimates Derived From Germline Multiple-Gene Sequencing Results in Women. JCO Precision Oncology 2017 :1, 1-12

- Medical History

- Klinefelter syndrome: risk x 19.2 (5.2-49.2)

Reference: Swerdlow AJ, Schoemaker MJ, Higgins CD, Wright AF, Jacobs PA; UK Clinical Cytogenetics Group. Cancer incidence and mortality in men with Klinefelter syndrome: a cohort study. J Natl Cancer Inst. 2005 Aug 17;97(16):1204-10. doi: 10.1093/jnci/dji240. PMID: 16106025.

- History of Parkinson's: risk x 1.24 (1.0–1.5)

Reference: Olsen JH, Friis S, Frederiksen K, et al. Atypical cancer pattern in patients with Parkinson's disease. Br J Cancer 2005; 92:201.

- Cowden syndrome: risk x 25.4 (19.8 – 32.0)

Reference: Tan MH, Mester JL, Ngeow J, et al. Lifetime cancer risks in individuals with germline PTEN mutations. Clin Cancer Res 2012; 18:400.

- Lynch syndrome (mismatch repair genes MLH1, MSH2, MSH6): risk x 3.95 (11.71-33.27)

Reference: Win AK, Young JP, Lindor NM, et al. Colorectal and other cancer risks for carriers and noncarriers from families with a DNA mismatch repair gene mutation: a prospective cohort study. J Clin Oncol 2012; 30:958.

- Peutz-Jeghers syndrome (STK11): risk x 15.2 (7.6-27)

Reference: Francis M. Giardiello, Jill D. Brensinger, Anne C. Tersmette, Steven N. Goodman, Gloria M. Petersen, Susan V. Booker, Marcia Cruz–Correa, Johan A. Offerhaus. Very high risk of cancer in familial Peutz–Jeghers syndrome. Gastroenterology, Volume 119, Issue 6, December 2000, Pages 1447-1453

- MGUS: risk x 1.32 (1.02-1.69)

Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

- Rheumatoid arthritis	risk x	0.64	(0.46-0.89)
- Rheumatic fever / rheumatic heart diseases	risk x	0.44	(0.20-0.97)
- Psoriatic/enteropathic arthropathies	risk x	0.14	(0.02-0.99)

Reference: He MM, Lo CH, Wang K, Polychronidis G, Wang L, Zhong R, Knudsen MD, Fang Z, Song M. Immune-Mediated Diseases Associated With Cancer Risks. JAMA Oncol. 2021 Dec 2:e215680. doi: 10.1001/jamaoncol.2021.5680. Epub ahead of print. PMID: 34854871; PMCID: PMC8640951.

- History of cancer

- History of childhood cancer: risk x 16.18 (12.35-20.83)

Reference: Neglia JP, Friedman DL, Yasui Y, Mertens AC, Hammond S, Stovall M, Donaldson SS, Meadows AT, Robison LL, Second malignant neoplasms in five-year survivors of childhood cancer: childhood cancer survivor study., J Natl Cancer Inst. 2001 Apr 18;93(8):618-29.

- History of Basocellular skin carcinoma:

Number of BCCs:	1	risk x	1.26	(1.21–1.31)
	6+	risk x	1.55	(1.39–1.74)
	12+	risk x	2.17	(1.74–2.72)

Reference: Cho HG et al. Frequent basal cell cancer development is a clinical marker for inherited cancer susceptibility. JCI Insight. 2018; 3(15): e122744.

-Contralateral breast cancer: risk x 2

Reference: Ingrid M.Sonia L.SuggM.D.Ronald J.WeigelM.D., Ph.D.Carol EHScott-ConnerM.D., Ph.D. Review of risk factors for the development of contralateral breast cancer. The American Journal of Surgery Volume 206, Issue 5, November 2013, Pages 704-708

- Exposure

Ethylene oxide: risk x 1.9 (1.1-3.1)

Reference: Marant Micallef C, Shield KD, Baldi I, Charbotel B, Fervers B, Gilg Soit Ilg A, Guénel P, Olsson A, Rushton L, Hutchings SJ, Straif K, Soerjomataram I. Occupational exposures and cancer: a review of agents and relative risk estimates. Occup Environ Med. 2018 Aug;75(8):604-614. doi: 10.1136/oemed-2017-104858. Epub 2018 May 7. PMID: 29735747.

Cervical cancer

- Female History

- Partner who has been circumcised: risk x 0.42 (0.23-0.79)

Reference: Castellsagué N Engl J Med 2002; 346:1105.

	[Squamous cell carcinoma]	[Adenocarcinoma]
Number of sexual partners		
1	/	/
2–5	2.00 (1.91–2.09)	1.63 (1.47–1.80)
6+	2.98 (2.62–3.40)	2.64 (2.07–3.36)
Age at first intercourse (years)		
21+	/	/
18–20	1.60 (1.51–1.68)	1.50 (1.35–1.67)
<18	2.24 (2.11–2.38)	2.06 (1.83–2.33)
Number of full-term pregnancies		
Nulliparous	0.69 (0.60–0.78)	
1–2	/	/
3–4	1.50 (1.43–1.59)	1.36 (1.22–1.52)
5+	2.08 (1.95–2.23)	1.61 (1.37–1.90)
Age at first birth (years)		
25+	/	/
20–24	1.66 (1.57–1.74)	1.44 (1.30–1.60)
17–19	2.16 (2.03–2.30)	2.10 (1.84–2.40)
<17	2.72 (2.42–3.05)	2.01 (1.53–2.65)

Reference: International Collaboration of Epidemiological Studies of Cervical Cancer. Comparison of risk factors for invasive squamous cell carcinoma and adenocarcinoma of the cervix: collaborative reanalysis of individual data on 8,097 women with squamous cell carcinoma and 1,374 women with adenocarcinoma from 12 epidemiological studies. Int J Cancer 2007; 120:885.

- Older than 30 years AND Pap smear in the last three years: risk x 0.35 (0.30-0.41)

Reference: Peirson L, Fitzpatrick-Lewis D, Ciliska D, Warren R. Screening for cervical cancer: a systematic review and meta-analysis. System Rev. 2013;2:35. Published 2013 May 24. doi:10.1186/2046-4053-2-35

- HPV positive on the cervix: risk x 158.2 (113.4-220.6)

Reference: Muñoz N, Bosch FX, de Sanjosé S, Herrero R, Castellsagué X, Shah KV, Snijders PJ, Meijer CJ; International Agency for Research on Cancer Multicenter Cervical Cancer Study Group. Epidemiologic classification of human papillomavirus types associated with cervical cancer. N Engl J Med. 2003 Feb 6;348(6):518-27. doi: 10.1056/NEJMoa021641. PMID: 12571259.

- HPV vaccine : risk x 0.37 (0.21-0.57)

Reference: Lei J, Ploner A, Elfström KM, Wang J, Roth A, Fang F, Sundström K, Dillner J, Sparén P. HPV Vaccination and the Risk of Invasive Cervical Cancer. N Engl J Med. 2020 Oct 1;383(14):1340-1348. doi: 10.1056/NEJMoa1917338. PMID: 32997908.

-Contraceptive intake: 5y-9y: risk x 2.82 (1·46–5·42)
10 years or more: risk x 4.03 (2·09–7·79)

Reference: Moreno V, Bosch FX, Muñoz N, Meijer CJ, Shah KV, Walboomers JM, Herrero R, Franceschi S; International Agency for Research on Cancer. Multicentric Cervical Cancer Study Group. Effect of oral contraceptives on risk of cervical cancer in women with human papillomavirus infection: the IARC multicentric case-control study. Lancet. 2002 Mar 30;359(9312):1085-92. doi: 10.1016/S0140-6736(02)08150-3. PMID: 11943255.

- Chronic Condition

- HIV positivity: - without treatment: risk x 8.4 (2.2–21.8)
- with treatment: risk x 1 (No difference)

Reference: Franceschi S, Lise M, Clifford GM, et al. Changing patterns of cancer incidence in the early- and late-HAART periods: the Swiss HIV Cohort Study. Br J Cancer 2010; 103:416.

- History of organ transplantation: risk x 2.13 (1·37–3·30)

Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

- Genital warts: risk x 1.5 (1.3–1.8)

Reference: Blomberg M, Friis S, Munk C, Bautz A, Kjaer SK. Genital warts and risk of cancer: a Danish study of nearly 50,000 patients with genital warts. J Infect Dis. 2012 May 15;205(10):1544-53. doi: 10.1093/infdis/jis228. Epub 2012 Mar 15. PMID: 22427679.

- Hysterectomy:	risk x	0 (risk falls to zero)
- Transgender surgery for women:	risk x	0 (risk falls to zero)

Reference: /

- BRCA1: risk x 3.72 (2.26-6.10)
Reference: Thompson D, Easton DF, Breast Cancer Linkage Consortium. Cancer Incidence in BRCA1 mutation carriers. J Natl Cancer Inst 2002; 94:1358.

- Current Smokers: risk x 1.50 (1.38–1.63)
Reference: International Collaboration of Epidemiological Studies of Cervical Cancer. Comparison of risk factors for invasive squamous cell carcinoma and adenocarcinoma of the cervix: collaborative reanalysis of individual data on 8,097 women with squamous cell carcinoma and 1,374 women with adenocarcinoma from 12 epidemiological studies. Int J Cancer 2007; 120:885.

Colorectal cancer

- Familial History

- 1 first-degree relative diagnosed with colorectal carcinoma: risk x 2.25 (2.00-2.53)
- Family member diagnosed with colorectal carcinoma before age 45: risk x 3.87 (2.40-6.22)
- Multiple family members diagnosed with colorectal carcinoma: risk x 4.25 (3.01-6.08)
- 1 first-degree relative with a diagnosis of colorectal polyp: risk x 1.99 (1.55-2.55)

Reference: Armelao F, de Pretis G. Familial colorectal cancer: a review. *World J Gastroenterol* . 2014;20(28):9292-8.

- Medical History

- Familial Adenomatous Polyposis: risk x 1000

Reference: Winawer SW, Fletcher RH, Mille L, et al. AGA guidelines: Colorectal cancer screening: Clinical guidelines and rationale. Gastroenterology 1997; 112:594.

- Lynch syndrome: risk x

Study and Age	Males		Females	
30-39 years	135	(112-165)	99	(79-125)
40-49 years	52	(41-67)	52	(40-67)
50-59 years	35	(27-45)	31	(23-41)
60-69 years	9.0	(6.7-12)	9.2	(6.8-13)
70-79 years	4.0	2.8-5.7)	3.8	(2.6-5.6)

Reference: Jenkins MA, Dowty JG, Ait Ouakrim D, Mathews JD, Hopper JL, Drouet Y, Lasset C, Bonadona V, Win AK. Short-term risk of colorectal cancer in individuals with Lynch syndrome: a meta-analysis. J Clin Oncol. 2015 Feb 1;33(4):326-31. doi: 10.1200/JCO.2014.55.8536. Epub 2014 Dec 22. PMID: 25534380.

- MUTYH-associated polyposis : Biallelic Males risk x 108 (25.9–454)
  Females risk x 129 (43.7–380)
  Monoallelic Males risk x 2.46 (1.54–3.93)
  Females risk x 2.67 (1.67–4.26)

Reference: Win AK, Dowty JG, Cleary SP, et al. Risk of colorectal cancer for carriers of mutations in MUTYH, with and without a family history of cancer. Gastroenterology. 2014;146(5):1208-11.e1-5.

- Ulcerative colitis:
  - generalized colitis : risk x 14.8 (11.4-18.9)
  - only left-sided: risk x 2.8 (1.6-4.4)
  - proctitis only: risk x 1.7 (0.8-3.2)

Reference: Ekbom A, Helmick C, Zack M, Adami HO. Ulcerative colitis and colorectal cancer. A population-based study. N Engl J Med 1990; 323:1228.

- Crohn's disease:
  - disease only in terminal ileum: risk x 1 (no change)
  - disease in terminal ileum and parts of colon: risk x 3.2 (0.7-9.2)
  - disease only in colon: risk x 5.6 (2.1-12.2)
  - if diagnosed at age <30 years with colon involvement: risk x 20.9 (6.8-48.7)

Reference: Ekbom A, Helmick C, Zack M, Adami HO. Increased risk of large-bowel cancer in Crohn's disease with colonic involvement. Lancet 1990; 336:357.

- Primary sclerosing cholangitis (+ ulcerative colitis OR Crohn's disease): risk x 3.41 (2.13-5.48)
  primary sclerosing cholangitis & ulcerative colitis risk x 3.01 (1.44-6.29)
  primary sclerosing cholangitis & Crohn's disease risk x 2.91 (0.84-10.16)

Reference: Zheng HH, Jiang XL. Increased risk of colorectal neoplasia in patients with primary sclerosing cholangitis and inflammatory bowel disease: a meta-analysis of 16 observational studies. Eur J Gastroenterol Hepatol 2016; 28:383.

- Diabetes Mellitus: risk x 1.29
  [Colon] risk x 1.38 (1.26-1.51)
  [Rectum] risk x 1.20 (1.09-1.31)

Reference: Yuhara H, Steinmaus C, Cohen SE, et al. Is diabetes mellitus an independent risk factor for colon cancer and rectal cancer? Am J Gastroenterol 2011; 106:1911.

-Peutz-Jeghers syndrome (STK11): risk x 84 (47-137)

Reference: Francis M. Giardiello, Jill D. Brensinger, Anne C. Tersmette, Steven N. Goodman, Gloria M. Petersen, Susan V. Booker, Marcia Cruz–Correa, Johan A. Offerhaus. Very high risk of cancer in familial Peutz–Jeghers syndrome. Gastroenterology, Volume 119, Issue 6, December 2000, Pages 1447-1453

- Cowden syndrome: risk x 10.3 (5.6–17.4)

Reference: Tan MH, Mester JL, Ngeow J, et al. Lifetime cancer risks in individuals with germline PTEN mutations. Clin Cancer Res 2012; 18:400.

-Cystic fibrosis: risk x 10.91 (8·42–14·11)

Reference: Yamada A, Komaki Y, Komaki F, et al. Risk of gastrointestinal cancers in patients with cystic fibrosis: a systematic review and meta-analysis. Lancet Oncol 2018; 19:758.

- Hereditary polycystic kidney disease: risk x 1·63 (1·15–2·30)

Reference: Yu TM, Chuang YW, Yu MC, Chen CH, Yang CK, Huang ST, Lin CL, Shu KH, Kao CH. Risk of cancer in patients with polycystic kidney disease: a propensity-score matched analysis of a nationwide, population-based cohort study. Lancet Oncol. 2016 Oct;17(10):1419-1425. doi: 10.1016/S1470-2045(16)30250-9. Epub 2016 Aug 20. PMID: 27550645.

- History of Multiple myeloma: risk x 1.30 (1.09-1.53)
- History of MGUS: risk x 1.25 (1.05-1.48)

Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

- Chronic Viral Hepatitis B: risk x 1.18 (1.09-1.27)
- Chronic Viral Hepatitis C: risk x 1.88 (1.78-1.97)

Reference: Hong SW, Choi WM, Hwang HW, Kim DS, Yoon J, Lee JW, Shim JH, Yang DH, Myung SJ, Yang SK, Byeon JS. Chronic Viral Hepatitis Is Associated with Colorectal Neoplasia: A Systematic Review and Meta-Analysis. Dig Dis Sci. 2021 Nov;66(11):3715-3724. doi:10.1007/s10620-020-06745-x. Epub 2021 Jan 12. PMID: 33433792.

- History of large (>1 cm) adenomatous colonic polyp or polyp with villous or tubulovillian histology or high-grade dysplasia:
  - Single: risk x 2.9 (1.8-4.5)
  - Multiple: risk x 6.6 (2.4-5.0)

Reference: Atkin WS, Morson BC, Cuzick J. Long-term risk of colorectal cancer after excision of rectosigmoid adenomas. N Engl J Med. 1992;326(10):658.

- History of coronary heart disease: risk x 2.51 (1.43-4.35)

Reference: Chan AO, Jim MH, Lam KF, et al. Prevalence of colorectal neoplasm among patients with newly diagnosed coronary artery disease. JAMA 2007; 298:1412.

-BMI

- Men, per 5 kg/m² increase in BMI (above 25): risk x 1.15
- Women, per 5 kg/m² increase in BMI (above 25): risk x 1.06
  - [Colon]:
  - Men per 5 kg/m² increase in BMI (above 25): risk x 1.24 (1.20-1.28)
  - Women, per 5 kg/m² increase in BMI (above 25): risk x 1.09 (1.05-1.13)
  - [Rectum]:
  - Men, per 5 kg/m² increase in BMI (above 25): risk x 1.09 (1.06-1.12)
  - Women, per 5 kg/m² increase in BMI (above 25): risk x 1.02 (1.00-1.05)

Reference: Renehan AG, Tyson M, Egger M, et al. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 2008; 371:569.

- Adolescent BMI per 5 kg/m² increase in BMI Men risk x 1·29 (1·170-1·42)
  Women risk x 1·17 (1·03-1·33)

Reference: Furer A, Afek A, Sommer A, Keinan-Boker L, Derazne E, Levi Z, Tzur D, Tiosano S, Shina A, Glick Y, Kark JD, Tirosh A, Twig G. Adolescent obesity and midlife cancer risk: a population-based cohort study of 2·3 million adolescents in Israel. Lancet Diabetes Endocrinol. 2020 Mar;8(3):216-225. doi: 10.1016/S2213-8587(20)30019-X. Epub 2020 Feb 3. PMID: 32027851.

-Nutrition

- Red meat intake: risk x 1.16 (1.001–1.34)
  [Colon] risk x 1.21 (1.03–1.43)
- -Processed meat: risk x 1.17 (1.02–1.35)
  [Colon] risk x 1.23 (1.03–1.47)
- High poultry consumption [Rectum] risk x 0.80 (0.67–0.96)

Reference: Pham NM, Mizoue T, Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Wakai K, Nagata C, Inoue M, Tsugane S, Sasazuki S; Research Group for the Development and Evaluation of Cancer Prevention Strategies in Japan. Meat consumption and

colorectal cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2014 Jul;44(7):641-50. doi: 10.1093/jjco/hyu061. Epub 2014 May 19. PMID: 24842864.

- High intake of fruit & vegetables: risk x 0.78 (0.64–0.95)
  [Colon] risk x 0.81 (0.65–1.00)
  [Rectum] risk x 0.71 (0.47–1.06)

Reference: Orlich MJ, Singh PN, Sabaté J, et al. Vegetarian dietary patterns and the risk of colorectal cancers. JAMA Intern Med 2015; 175:767.

- High fiber intake: risk x 0.88 (0.82-0.94)
- Large intake of whole grains : risk x 0.79 (0.72-0.86)

Reference: Aune D, Chan DS, Lau R, et al. Dietary fiber, whole grains, and risk of colorectal cancer: systematic review and dose-response meta-analysis of prospective studies. BMJ. 2011;343:d6617. Published 2011 Nov 10. doi:10.1136/bmj.d6617

- High fish consumption: risk x 0.88 (0.80-0.95)
  [Rectum] risk x 0.79 (0.65-0.97)

Reference: Wu S, Feng B, Li K, et al. Fish consumption and colorectal cancer risk in humans: a systematic review and meta-analysis. Am J Med 2012; 125:551.

- Drinking coffee: risk x 0.72 (0.61-0.84)

Reference: Giovannucci E. Meta-analysis of coffee consumption and risk of colorectal cancer. Am J Epidemiol 1998; 147:1043.

- Habits

- Ever smoker: risk x 1.18 (1.11-1.25)

Reference: Botteri E, Iodice S, Bagnardi V, et al. Smoking and colorectal cancer: a meta-analysis. JAMA 2008; 300:2765.

- Alcohol:
  0-1 glasses/day: no difference
  2-3 glasses/day: risk x 1.21 (1.13-1.28)
  4 or more drinks/day: risk x 1.52 (1.27-1.81)

Reference: Fedirko V, Tramacere I, Bagnardi V, et al. Alcohol drinking and colorectal cancer risk: an overall and dose-response meta-analysis of published studies. Ann Oncol 2011; 22:1958.

- Physical activity (hours per week):
  - less than 3 hours: No change
  - between 3 hours and 10 hours: risk x 0.903 (0.851-0.952)
  - between 10pm and 44 p.m.: risk x 0.833 (0.771-0.896)
  - between 44 hours or more: risk x 0.789 (0.735-0.850)

Reference: Kyu HH, Bachman VF, Alexander LT, et al. Physical activity and risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events: systematic review and dose-response meta-analysis for the Global Burden of Disease Study 2013. The BMJ. 2016;354:i3857. doi:10.1136/bmj.i3857.

- Surgery

- History of cholecystectomy: risk x 2.08 (1.28–3.17)

Reference: Kim SB, Kim KO, Kim TN. Prevalence and Risk Factors of Gastric and Colorectal Cancer after Cholecystectomy. J Korean Med Sci. 2020 Nov 2;35(42):e354. doi: 10.3346/jkms.2020.35.e354. PMID: 33140590; PMCID: PMC7606888.

- Kidney transplant: risk x 12 (1.45-99.7)

Reference: Park JM, Choi MG, Kim SW, et al. Increased incidence of colorectal malignancies in renal transplant recipients: a case control study. Am J Transplant 2010; 10:2043.

- History of organ transplantation except kidney transplantation: risk x 1.69 (1·34–2·13)

Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

- Male History

- Treatment with GnRH agonist: risk x 1.31 (1.12-1.53)
- Orchiectomy: risk x 1.37 (1.14-1.66)

Reference: Gillessen S, Templeton A, Marra G, et al. Risk of colorectal cancer in men on long-term androgen deprivation therapy for prostate cancer. J Natl Cancer Inst 2010; 102:1760.

- Female History

- Intake of postmenopausal hormone therapy: risk x 0.56 (0.38-0.81)

Reference: Chlebowski RT, Wactawski-Wende J, Ritenbaugh C, et al. Estrogen plus progestin and colorectal cancer in postmenopausal women. N Engl J Med 2004; 350:991.

- Contraceptive intake: risk x 0.81 (0.66–0.99)

Reference: Iversen L, Sivasubramaniam S, Lee AJ, et al. Lifetime cancer risk and combined oral contraceptives: the Royal College of General Practitioners' Oral Contraception Study. Am J Obstet Gynecol 2017; 216:580.e1.

- Genetics

- Presence of ATM gene variant: risk x 1.97 (1.20–3.23)

Reference: Helgason H, Rafnar T, Olafsdottir HS, et al. Loss-of-function variants in ATM confer risk of gastric cancer. Nat Genet 2015; 47:906.

- Intake

- Vitamin B6 intake: risk x 0.80 (0.69-0.92)

Reference: Larsson SC, Orsini N, Wolk A. Vitamin B6 and risk of colorectal cancer: a meta-analysis of prospective studies. JAMA 2010; 303:1077.

- Vitamin D intake: risk x 0.73 (0.59-0.91)

Reference: McCullough ML, Zoltick ES, Weinstein SJ, et al. Circulating vitamin D and colorectal cancer risk. J Natl Cancer Inst 2018.

- Calcium intake: risk x 0.80 (0.68-0.93)

Reference: Shaukat A, Scouras N, Schünemann HJ. Role of supplemental calcium in the recurrence of colorectal adenomas: a metaanalysis of randomized controlled trials. Am J Gastroenterol 2005; 100:390.

- Magnesium intake: risk x 0.59 (0.40-0.87)
  - [Colon] risk x 0.66 (0.41-1.07)
  - [Rectum] risk x 0.45 (0.22-0.89)

Reference: Larsson SC, Bergkvist L, Wolk A. Magnesium intake in relation to risk of colorectal cancer in women. JAMA 2005; 293:86.

- Zinc intake: risk x 0.80 (0.70–0.92)

Reference: Li P, Xu J, Shi Y, Ye Y, Chen K, Yang J, Wu Y. Association between zinc intake and risk of digestive tract cancers: a systematic review and meta-analysis. Clin Nutr. 2014 Jun;33(3):415-20. doi: 10.1016/j.clnu.2013.10.001. Epub 2013 Oct 10. PMID: 24148607.

- Medication

- Long-term (= daily, 5 years or more) Aspirin: risk x 0.76 (0·63–0·94)

Reference: Rothwell PM, Wilson M, Elwin CE, et al. Long-term effect of aspirin on colorectal cancer incidence and mortality: 20-year follow-up of five randomized trials. Lancet 2010; 376:1741.

- Statin intake: risk x 0.53 (0.38-0.74)
  - [Colon] risk x 0.55 (0.38-0.80)
  - [Rectum] risk x 0.38 (0.19-0.73)

Reference: Poynter JN, Gruber SB, Higgins PD, et al. Statins and the risk of colorectal cancer. N Engl J Med 2005; 352:2184.

- Examinations

- Colon cancer screening: risk x 0.80 (0.70-0.92)

Reference: Holme Ø, Løberg M, Kalager M, et al. Effect of Flexible Sigmoidoscopy Screening on Colorectal Cancer Incidence and Mortality: A Randomized Clinical Trial. JAMA. 2014;312(6):606–615. doi:10.1001/jama.2014.8266

- History of cancer

-Childhood:

- History of childhood cancer:

Colorectal risk x 3.0 (2.6-3.4)
- [Colon] risk x 3.4 (2.9-4.1)
- [Rectum] risk x 2.3 (1.8-2.9)

Reference: Reulen RC, Wong KF, Bright CJ, Winter DL, Alessi D, Allodji RM, Bagnasco F, Bárdi E, Bautz A, Byrne J, Feijen EA, Fidler-Benaoudia MM, Diallo I, Garwicz S, Grabow D, Gudmundsdottir T, Guha J, Haddy N, Høgsholt S, Jankovic M, Kaatsch P, Kaiser M, Kuonen R, Linge H, Øfstaas H, Ronckers CM, Hau EM, Skinner R, van

Leeuwen FE, Teepen JC, Veres C, Zrafi W , Debiche G, Llanas D, Terenziani M, Vu-Bezin G, Wesenberg F, Wiebe T, Sacerdote C, Jakab Z, Haupt R, Lähteenmäki PM, Zadravec Zaletel L, Kuehni CE, Winther JF, de Vathaire F, Kremer LC, Hjorth L, Hawkins MM. Risk of digestive cancers in a cohort of 69 460 five-year survivors of childhood cancer in Europe: the PanCareSurFup study. Gut. 2020 Nov 2:gutjnl-2020-322237. doi: 10.1136/gutjnl-2020-322237. Epub ahead of print. PMID: 33139271.

- Abdominal radiotherapy: risk x 7.7 (2.0-44.3)
- High doses of alkylating drugs: risk x 8.8 (1.2-405.4)

Reference: Nottage K, McFarlane J, Krasin MJ, et al. Secondary colorectal carcinoma after childhood cancer. J Clin Oncol 2012; 30:2552.

- History of Basocellular skin carcinoma:

Number of BCCs: 6+ risk x 1.43 (1.18–1.73)
12+ risk x 1.77 (1.23–2.54)

Reference: Cho HG et al. Frequent basal cell cancer development is a clinical marker for inherited cancer susceptibility. JCI Insight. 2018; 3(15): e122744.

- History of endometrial cancer before 50 years: risk x 4.41 (1.47-13.26)

Reference: Singh H, Nugent Z, Demers A, et al. Risk of colorectal cancer after diagnosis of endometrial cancer: a population-based study. J Clin Oncol 2013; 31:2010.

- History diagnosis of prostate carcinoma: risk x 1.14 (1.02-1.27)
[Rectum] risk x 1.36 (1.09-1.71)

Treatment with radiotherapy: risk x 1.76 (CUMULATIVE WITH ABOVE)

[Rectum] risk x 2.06 (1.42-2.99)
[Colon] risk x 1.46 1.07-1.99)

Reference: Desautels D, Czaykowski P, Nugent Z, et al. Risk of colorectal cancer after the diagnosis of prostate cancer: A population-based study. Cancer 2016; 122:1254.

-History of Hodgkin lymphoma with Chemotherapy Plus Radiotherapy risk x 2.0 (1.2-3.2)

Reference: Swerdlow AJ, Higgins CD, Smith P, Cunningham D, Hancock BW, Horwich A, Hoskin PJ, Lister TA, Radford JA, Rohatiner AZ, Linch DC. Second cancer risk after chemotherapy for Hodgkin's lymphoma: a collaborative British cohort study. J Clin Oncol. 2011 Nov 1;29(31):4096-104. doi: 10.1200/JCO.2011.34.8268. Epub 2011 Oct 3. PMID: 21969511.

- History of seminoma testicular cancer: risk x 1.54 (1.31–1.79)

Reference: Richiardi L, Scélo G, Boffetta P, Hemminki K, Pukkala E, Olsen JH, Weiderpass E, Tracey E, Brewster DH, McBride ML, Kliewer EV, Tonita JM, Pompe-Kirn V, Kee-Seng C, Jonasson JG , Martos C, Brennan P. Second malignancies among survivors of germ-cell testicular cancer: a pooled analysis between 13 cancer registries. Int J Cancer. 2007 Feb 1;120(3):623-31. doi: 10.1002/ijc.22345. PMID: 17096341.

- History of Ovarian cancer: risk x 1.38
[Colon] risk x 1.33 (1.15-1.54)
[Rectum] risk x 1.43 (1.13-1.79)

Reference: Travis LB, Curtis RE, Boice JD Jr, Platz CE, Hankey BF, Fraumeni JF Jr. Second malignant neoplasms among long-term survivors of ovarian cancer. Cancer Res. 1996 Apr 1;56(7):1564-70. PMID: 8603403.

- History of thyroid carcinoma: risk x 1.27 (1.13-1.41)

Reference: Subramanian S, Goldstein DP, Parlea L, Thabane L, Ezzat S, Ibrahim-Zada I, Straus S, Brierley JD, Tsang RW, Gafni A, Rotstein L, Sawka AM. Second primary malignancy risk in thyroid cancer survivors: a systematic review and meta-analysis. Thyroid. 2007 Dec;17(12):1277-88. doi:10.1089/thy.2007.0171. PMID: 18020916.

- History of cancer of the colon or rectum: risk x

	Previous Colon Cancer	Previous Rectum Cancer
[Colon]	1.87 (1.80–1.94)	1.38 (1.29–1.48)
[Rectum]	1.80 (1.69–1.92)	2.88 (2.66–3.12)

Reference: Guan X, Jin Y, Chen Y, Jiang Z, Liu Z, Zhao Z, Yan P, Wang G, Wang PLoS One. 2015 Nov 16;10(11):e0143067. doi: 10.1371/journal.pone.0143067. PMID: 26571301; PMCID: PMC4646682.

- History of cancer of the uterus:

Age (years) at diagnosis	risk x	
<50	3.72	(2.60-5.15)
≥50	1.91	(1.52-2.37)

Reference: Lee KD, Chen CY, Huang HJ, Wang TY, Teng D, Huang SH, Lai CH, Chen MC. Increased risk of second primary malignancies following uterine cancer: a population-based study in Taiwan over a 30-year period. BMC Cancer. 2015 May 11;15:393. doi:10.1186/s12885-015-1426-3. PMID: 25957789; PMCID: PMC4469104.

- History of cervical cancer:

[Colon]	risk x	1.13	(0.99-1.28)
[Rectum]	risk x	1.31	(1.14-1.50)

Reference: Chen CY, Lai CH, Lee KD, Huang SH, Dai YM, Chen MC. Risk of second primary malignancies in women with cervical cancer: a population-based study in Taiwan over a 30-year period. Gynecol Oncol. 2012 Dec;127(3):625-30. doi: 10.1016/j.ygyno.2012.09.004. Epub 2012 Sep 10. PMID: 22975362.

- History of bladder cancer: risk x 0.88

Reference: Kwon WA, Joung JY, Lim J, Oh CM, Jung KW, Kim SH, Seo HK, Park WS, Chung J, Lee KH, Won YJ. Risk of second primary Cancer among bladder Cancer patients: a population-based cohort study in Korea. BMC Cancer. 2018 May 31;18(1):617. doi:10.1186/s12885-018-4530-3. PMID: 29855390; PMCID: PMC5984459.

- History of cancers of Stomach for men:

[Colon]	risk x	1.61	(1.31-1.95)
[Rectum]	risk x	1.28	(1.01-1.61)

Reference: Hiyama T, Hanai A, Fujimoto I. Second primary cancer after diagnosis of stomach cancer in Osaka, Japan. Jpn J Cancer Res. 1991 Jul;82(7):762-70. doi: 10.1111/j.1349-7006.1991.tb02700.x. PMID: 1908843; PMCID: PMC5918547.

- History of anal cancer:

Male	risk x	2.44	(1.91-3.08)
Female	risk x	1.57	(1.23-1.97)

Reference: Jani KS, Lu SE, Murphy JD, Romesser PB, Jethwa KR, Li D, Chundury A, Wu AJ, Hathout L, Hallemeier CL, Jabbour SK. Malignancies diagnosed before and after anal squamous cell carcinomas: A SEER registry analysis. Cancer Med. 2021 Jun;10(11):3575-3583. doi:10.1002/cam4.3909. Epub 2021 May 7. PMID: 33960690.

-History of Non-Hodgkin lymphoma with treatment without radiation: risk x 1.14 (1.04–1.26)

Reference: Tward JD, Wendland MM, Shrieve DC, Szabo A, Gaffney DK. The risk of secondary malignancies over 30 years after the treatment of non-Hodgkin lymphoma. Cancer. 2006 Jul 1;107(1):108-15. doi:10.1002/cncr.21971. PMID: 16708354.

- History of prostate cancer treated with radiotherapy: risk x 1.79 (1.34-2.38)

Reference: Wallis CJ, Mahar AL, Choo R, Herschorn S, Kodama RT, Shah PS, Danjoux C, Narod SA, Nam RK. Second malignancies after radiotherapy for prostate cancer: systematic review and meta-analysis. BMJ. 2016 Mar 2;352:i851. doi: 10.1136/bmj.i851. PMID: 26936410; PMCID: PMC4775870.

-Exposure

- Exposure to asbestos: risk x 1.2 (1.0-1.3)

Reference: Marant Micallef C, Shield KD, Baldi I, Charbotel B, Fervers B, Gilg Soit Ilg A, Guénel P, Olsson A, Rushton L, Hutchings SJ, Straif K, Soerjomataram I. Occupational exposures and cancer: a review of agents and relative risk estimates. Occup Environ Med. 2018 Aug;75(8):604-614. doi: 10.1136/oemed-2017-104858. Epub 2018 May 7. PMID: 29735747.

- Exposure to diesel: risk x 1.65 (0.98–2.80)

Reference: Kachuri L, Villeneuve PJ, Parent MÉ, Johnson KC, Canadian Cancer Registries Epidemiology Research Group, Harris SA. Workplace exposure to diesel and gasoline engine exhausts and the risk of colorectal cancer in Canadian men. Environ Health. 2016;15:4. Published 2016 Jan 14. doi:10.1186/s12940-016-0088-1

- Night work: risk x 2.06

[Colon]	risk x	2.03	(1.43-2.89)
[Rectum]	risk x	2.09	(1.40-3.14)

Reference: Parent, M. -E.; El-Zein, M.; Rousseau, M. -C.; Pintos, J.; Siemiatycki, J. (2012). "Night Work and the Risk of Cancer Among Men". American Journal of Epidemiology. 176(9):751–759.

Esophageal cancer

- Medical History:

- Peutz-Jeghers syndrome (STK11): risk x 57 (2.5-557)

Reference: Francis M. Giardiello, Jill D. Brensinger, Ann e C. Tersmette, Steven N. Goodman, Gloria M. Petersen, Susan V. Booker, Marcia Cruz–Correa, Johan A. Offerhaus. Very high risk of cancer in familial Peutz–Jeghers syndrome. Gastroenterology, Volume 119, Issue 6, December 2000, Pages 1447-1453

- HIV positivity: risk x 1.62 (1·20–2·19)
- History of organ transplantation: risk x 3.05 (1·87–4·98)

Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

- Celiac disease: risk x 12 (6.5–21)

Reference: Green PH, Fleischauer AT, Bhagat G, et al. Risk of malignancy in patients with celiac disease. Am J Med 2003; 115:191.

- History of Multiple myeloma: risk x 1.30 (1.09-1.53)
- History of MGUS: risk x 1.25 (1.05-1.48)

Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

- Diabetes (Type 1): risk x 2.13 (1.13-4.02)
- Autoimmune hepatitis: risk x 9.28 (1.31-65.9)

Reference: He MM, Lo CH, Wang K, Polychronidis G, Wang L, Zhong R, Knudsen MD, Fang Z, Song M. Immune-Mediated Diseases Associated With Cancer Risks. JAMA Oncol. 2021 Dec 2:e215680. doi: 10.1001/jamaoncol.2021.5680. Epub ahead of print. PMID: 34854871; PMCID: PMC8640951.

- Exposure

-Working in the rubber industry (Men only) risk x 1.2 (1.0-1.5)

Reference: Marant Micallef C, Shield KD, Baldi I, Charbotel B, Fervers B, Gilg Soit Ilg A, Guénel P, Olsson A, Rushton L, Hutchings SJ, Straif K, Soerjomataram I. Occupational exposures and cancer: a review of agents and relative risk estimates. Occup Environ Med. 2018 Aug;75(8):604-614. doi: 10.1136/oemed-2017-104858. Epub 2018 May 7. PMID: 29735747.

- Exposure to Agent Orange: risk x 1.36 (1.00-1.85)

Reference: Sang‐Wook Yi, Heechoul Ohrr. Agent Orange exposure and cancer incidence in Korean Vietnam veterans: A prospective cohort study. Cancer. 2014 Dec 1;120(23):3699-706.

-Intake

- Statins: risk x 0.72 (0.60-0.86)

Reference: Singh S, Singh AG, Singh PP, Murad MH, Iyer PG. Statins are associated with reduced risk of esophageal cancer, particularly in patients with Barrett's esophagus: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013 Jun;11(6):620-9. doi: 10.1016/j.cgh.2012.12.036. Epub 2013 Jan 26. PMID: 23357487; PMCID: PMC3660516.

- Selenium: risk x 0.56 (0.44–0.71)

Reference: Mark SD, Qiao YL, Dawsey SM, et al. Prospective study of serum selenium levels and incident esophageal and gastric cancers. J Natl Cancer Inst 2000; 92:1753.

*Adenocarcinoma Esophagus

- Medical History

- Gastroesophageal reflux: weekly complaints: risk x 4.92 (3.90-6.22)
  daily complaints: risk x 7.40 (4.94-11.1)

Reference: Rubenstein JH, Taylor JB. Meta-analysis: the association of oesophageal adenocarcinoma with symptoms of gastroesophageal reflux. Aliment Pharmacol Ther 2010; 32:1222.

- History of achalasia: risk x 6.63

Reference: Tustumi F, Bernardo WM, da Rocha JRM, Szachnowicz S, Seguro FC, Bianchi ET, Sallum RAA, Cecconello I. Esophageal achalasia: a risk factor for carcinoma. A systematic review and meta-analysis. Dis Esophagus. 2017 Oct 1;30(10):1-8. doi: 10.1093/dote/dox072. PMID: 28859394.

- History of Barrett's esophagus: risk x 11.3 (8.8-14.4)

Reference: Hvid-Jensen F, Pedersen L, Drewes AM, Sørensen HT, Funch-Jensen P. Incidence of adenocarcinoma among patients with Barrett's esophagus. N Engl J Med. 2011 Oct 13;365(15):1375-83. doi: 10.1056/NEJMoa1103042. PMID: 21995385.

-Smoking

Ex-smokers:		risk x	1.62	(1.40–1.87)
Current smokers:	Cigarette consumption (cigarettes/day)			
	Less than 20:	risk x	2.13	(1.64–2.77)
	More than 20:	risk x	3.27	(2.40–4.45)
	Duration of smoking habit (years)			
	Less than 20:	risk x	1.08	(0.43–2.68)
	20–39.9:	risk x	2.05	(1.12–3.73)
	40 or more:	risk x	2.23	(0.98–5.06)

Reference: Tramacere I, La Vecchia C, Negri E. Tobacco smoking and esophageal and gastric cardia adenocarcinoma: a meta-analysis. Epidemiology 2011; 22:344.

-BMI

- Men, per 5 kg/m² increase in BMI (above 25):	risk x	1.52	(1.33-1.74)
- Women, per 5 kg/m² increase in BMI (above 25):	risk x	1.51	(1.31-1.74)

Reference: Renehan AG, Tyson M, Egger M, et al. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 2008; 371:569.

- Interventions

- History of infection with Helicobacter Pylori:	risk x	0.52	(0.37–0.73)

Reference: Rokkas T, Pistiolas D, Sechopoulos P, et al. Relationship between Helicobacter pylori infection and esophageal neoplasia: a meta-analysis. Clin Gastroenterol Hepatol 2007; 5:1413.

- History of cholecystectomy:	risk x	1.3	(1.0–1.8)

Reference: Freedman J, Ye W, Näslund E, Lagergren J. Association between cholecystectomy and adenocarcinoma of the esophagus. Gastroenterology 2001; 121:548.

- Medication

- Nitroglycerin intake:	risk x	1.5	(0.9–2.6)
- Aminophylline intake:	risk x	1.4	(0.8–2.8)
- Intake b-Receptor agonists:	risk x	1.6	(0.8–3.1)
- Taking Anticholinergics:	risk x	2.7	(1.6–4.7)
- Intake of benzodiazepines:	risk x	1.5	(0.7–2.9)

Reference: Lagergren J, Bergström R, Adami HO, Nyrén O. Association between medications that relax the lower esophageal sphincter and risk for esophageal adenocarcinoma. Ann Intern Med 2000; 133:165.

- Aspirin intake:	risk x	0.61	(0.49–0.77)

Reference: Bosetti C, Santucci C, Gallus S, Martinetti M, La Vecchia C. Aspirin and the risk of colorectal and other digestive tract cancers: an updated meta-analysis through 2019. Ann Oncol. 2020 May;31(5):558-568. doi: 10.1016/j.annonc.2020.02.012. Epub 2020 Apr 1. PMID: 32272209.

- NSAIDs :	risk x	0.68	(0.56–0.82)
- Taking NSAIDs for more than 10 years	risk x	0.56	(0.43–0.73)

Reference: Liao LM, Vaughan TL, Corley DA, et al. Nonsteroidal anti-inflammatory drug use reduces risk of adenocarcinomas of the esophagus and esophagogastric junction in a pooled analysis. Gastroenterology 2012; 142:442.

-Nutrition

- Fiber intake:	risk x	0.28	(0.19–0.40)

Reference: Mayne ST, Risch HA, Dubrow R, et al. Nutrient intake and risk of subtypes of esophageal and gastric cancer. Cancer Epidemiol Biomarkers Prev 2001; 10:1055.

- Coffee:	risk x	1.18	(0.81–1.71)

Reference: Turati F, Galeone C, La Vecchia C, et al. Coffee and cancers of the upper digestive and respiratory tracts: meta-analyses of observational studies. Ann Oncol 2011; 22:536.

- Red meat :	risk x	1.42	(1.02-1.98)
- Processed meat:	risk x	1.38	(1.07-1.78)

Reference: Keszei AP, Schouten LJ, Goldbohm RA, van den Brandt PA. Red and processed meat consumption and the risk of esophageal and gastric cancer subtypes in The Netherlands Cohort Study. Ann Oncol 2012; 23:2319.

- Folic acid intake: risk x 0.50 (0.39–0.65)

Reference: Larsson SC, Giovannucci E, Wolk A. Folate intake, MTHFR polymorphisms, and risk of esophageal, gastric, and pancreatic cancer: a meta-analysis. Gastroenterology 2006; 131:1271.

*Squamous carcinoma Esophagus

- Habits

- Alcohol consumption: 1 glass/d or less: risk x 1.38 (1.14–1.67)
  1-4 glasses/d: risk x 2.62 (2.07–3.31)
  5 or more drinks/d: risk x 5.54 (3.92–7.28)

Reference: Islami F, Fedirko V, Tramacere I, et al. Alcohol drinking and esophageal squamous cell carcinoma with focus on light-drinkers and never-smokers: a systematic review and meta-analysis. Int J Cancer 2011; 129:2473.

- Smoking:

Current smoker Women risk x 7.3 (3.5-15.5)
Men risk x 6.2 (2.8-13.7)

Reference: Freedman ND, Abnet CC, Caporaso NE, et al. Impact of changing US cigarette smoking patterns on incident cancer: risks of 20 smoking-related cancers among the women and men of the NIH-AARP cohort. Int J Epidemiol 2016; 45:846.

- Betel nut chewing: risk x 3.7 (1.6–8.5)
- Chewing tobacco: risk x 4.3 (1.6–11.7)

Reference: Akhtar S, Sheikh AA, Qureshi HU. Chewing areca nut, betel quid, oral snuff, cigarette smoking and the risk of esophageal squamous-cell carcinoma in South Asians: a multicenter case-control study. Eur J Cancer 2012; 48:655.

-Nutrition

- Red meat: risk x 1.55 (1.10-2.17)
- Processed meat: risk x 1.08 (0.80-1.44)

Reference: Keszei AP, Schouten LJ, Goldbohm RA, van den Brandt PA. Red and processed meat consumption and the risk of esophageal and gastric cancer subtypes in The Netherlands Cohort Study. Ann Oncol 2012; 23:2319.

- Vegetables: risk x 0.57 (0.43–0.75)
- Fruit: risk x 0.53 (0.40–0.64)

Reference: Liu J, Wang J, Leng Y, Lv C. Intake of fruit and vegetables and risk of esophageal squamous cell carcinoma: a meta-analysis of observational studies. Int J Cancer 2013; 133:473.

- Drinks at a temperature of 60-64 degrees Celsius: risk x 2.07 (1.28-3.35)
- Drinks at a temperature of 65 or more degrees Celsius: risk x 8.16 (3.93-16.91)

Reference: Islami F, Pourshams A, Nasrollahzadeh D, et al. Tea drinking habits and oesophageal cancer in a high risk area in northern Iran: population based case-control study. BMJ 2009; 338:b929.

- Coffee: risk x 0.87 (0.65–1.17)

Reference: Turati F, Galeone C, La Vecchia C, et al. Coffee and cancers of the upper digestive and respiratory tracts: meta-analyses of observational studies. Ann Oncol 2011; 22:536.

- Intake

- Zinc intake: risk x 0.77 (0.45-1.33)

Reference: Ma J, Li Q, Fang A dose-response meta-analysis. Nutr Res. 2018 Nov;59:16-28. doi: 10.1016/j.nutres.2018.07.007. Epub 2018 Aug 3. PMID: 30442229.

- Folic acid intake: risk x 0.66 (0.53–0.83)

Reference: Larsson SC, Giovannucci E, Wolk A. Folate intake, MTHFR polymorphisms, and risk of esophageal, gastric, and pancreatic cancer: a meta-analysis. Gastroenterology 2006; 131:1271.

- Aspirin intake: risk x 0.67 (0.57–0.79)

Reference: Bosetti C, Santucci C, Gallus S, Martinetti M, La Vecchia C. Aspirin and the risk of colorectal and other digestive tract cancers: an updated meta-analysis through 2019. Ann Oncol. 2020 May;31(5):558-568. doi: 10.1016/j.annonc.2020.02.012. Epub 2020 Apr 1. PMID: 32272209.

- Medical History

- History of achalasia: risk x 72.65

Reference: Tustumi F, Bernardo WM, da Rocha JRM, Szachnowicz S, Seguro FC, Bianchi ET, Sallum RAA, Cecconello I. Esophageal achalasia: a risk factor for carcinoma. A systematic review and meta-analysis. Dis Esophagus. 2017 Oct 1;30(10):1-8. doi: 10.1093/dote/dox072. PMID: 28859394.

- History of caustic damage to the esophagus: risk x 1000
Reference: Kochhar R, Sethy PK, Kochhar S, et al. Corrosive induced carcinoma of esophagus: report of three patients and review of literature. J Gastroenterol Hepatol 2006; 21:777.

- History of chronic atrophic gastritis: risk x 2.10 (1.19–3.70)
Reference: Islami F, Sheikhattari P, Ren JS, Kamangar F. Gastric atrophy and risk of oesophageal cancer and gastric cardia adenocarcinoma--a systematic review and meta-analysis. Ann Oncol 2011; 22:754.

- History of Tylosis: risk x 6.2 (2.9–13.3)
Reference: Ilhan M, Erbaydar T, Akdeniz N, Arslan S. Palmoplantar keratoderma is associated with esophagus squamous cell cancer in Van region of Turkey: a case control study. BMC Cancer. 2005 Jul 28;5:90. doi: 10.1186/1471-2407-5-90. PMID: 16048655; PMCID: PMC1187881.

- HPV positivity in esophagus: risk x 3.32 (2.26-4.87)
Reference: Li Aliment Pharmacol Ther 2014; 39:270.

- BMI

- Men: per 5 kg/m² increase in BMI (above 25): risk x 0.71 (0.60-0.85)
- Women: per 5 kg/m² increase in BMI (above 25): risk x 0.57 (0.47-0.69)

Reference: Renehan AG, Tyson M, Egger M, et al. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 2008; 371:569.

Eye cancer:
(No generalized risk factors)

Gallbladder cancer

- Medical History

- History of primary sclerosing cholangitis: risk x 13.33

Reference:Bowlus CL, Lim JK, Lindor KD. AGA Clinical Practice Update on Surveillance for Hepatobiliary Cancers in Patients With Primary Sclerosing Cholangitis: Expert Review. Clin Gastroenterol Hepatol 2019; 17:2416.

-Gallstones: -smaller than 3 cm: risk x 2.4
-greater than 3 cm: risk x 10

Reference: Diehl AK. Gallstone Size and the Risk of Gallbladder Cancer. JAMA. 1983;250(17):2323–2326.

-Chronic Salmonella infection: risk x 4.28 (1.84–9.96)

Reference: Nagaraja V, Eslick GD. Systematic review with meta-analysis: the relationship between chronic Salmonella typhi carrier status and gallbladder cancer. Aliment Pharmacol Ther 2014; 39:745.

- Cystic fibrosis: risk x 17.87 (8·55–37·36)

Reference: Yamada A, Komaki Y, Komaki F, et al. Risk of gastrointestinal cancers in patients with cystic fibrosis: a systematic review and meta-analysis. Lancet Oncol 2018; 19:758.

- History of Multiple myeloma: risk x 1.30 (1.09-1.53)
MGUS: risk x 1.25 (1.05-1.48)

Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

- Rheumatism, unspecified risk x 4.72 (1.15-19.3)
- Ankylosing spondylitis risk x 8.69 (2.14-35.3)
- Primary biliary cholangitis risk x 12.3 (1.70-88.4)
- Myositis risk x 13.1 (1.82-93.9)

Reference: He MM, Lo CH, Wang K, Polychronidis G, Wang L, Zhong R, Knudsen MD, Fang Z, Song M. Immune-Mediated Diseases Associated With Cancer Risks. JAMA Oncol. 2021 Dec 2:e215680. doi: 10.1001/jamaoncol.2021.5680. Epub ahead of print. PMID: 34854871; PMCID: PMC8640951.

- Genital warts: risk x 2.4 (1.2–4.1)

Reference: Blomberg M, Friis S, Munk C, Bautz A, Kjaer SK. Genital warts and risk of cancer: a Danish study of nearly 50,000 patients with genital warts. J Infect Dis. 2012 May 15;205(10):1544-53. doi: 10.1093/infdis/jis228. Epub 2012 Mar 15. PMID: 22427679.

- Diabetes: risk x 1.43 (0.81–2.52)

Reference: Grainge MJ, West J, Solaymani-Dodaran M, Aithal GP, Card TR. The antecedents of biliary cancer: a primary care case-control study in the United Kingdom. Br J Cancer. 2009;100(1):178–180. doi:10.1038/sj.bjc.6604765

- Female History

- Higher age at menarche (>13 years): risk x 2.48 (1.16-5.3)
- Higher number of pregnancies (>3 pregnancies): risk x 6.66 (1.8-23.4)
- Higher age at last childbirth (>25 years): risk x 2.97 (1.04-8.5)

Reference: Pandey M, Shukla VK. Lifestyle, parity, menstrual and reproductive factors and risk of gallbladder cancer. Eur J Cancer Prev 2003; 12:269.

- Habits

- NOT brushing teeth daily: risk x 1.29 (0.77–2.19)

Reference: Jordão HW, McKenna G, McMenamin ÚC, Kunzmann AT, Murray LJ, Coleman HG. The association between self-reported poor oral health and gastrointestinal cancer risk in the UK Biobank: A large prospective cohort study. United European Gastroenterol J. 2019;7(9):1241–1249. doi:10.1177/2050640619858043

-Smoking: risk x 1.61 (1.00–2.62)

Reference: Grainge MJ, West J, Solaymani-Dodaran M, Aithal GP, Card TR. The antecedents of biliary cancer: a primary care case-control study in the United Kingdom. Br J Cancer. 2009;100(1):178–180. doi:10.1038/sj.bjc.6604765

- Genetics

- BRCA2: risk x 4.97 (1.50-16.52)

Reference: Breast Cancer Linkage Consortium. Cancer risks in BRCA2 mutation carriers. J Natl Cancer Inst 1999; 91:1310.

-Exposure

- Aflatoxins: risk x 2.71 (1.70-4.33)

Reference: Koshiol J, Gao YT, Dean M, et al. Association of Aflatoxin and Gallbladder Cancer. Gastroenterology. 2017;153(2):488–494.e1.

-BMI

-Women: Per 5 kg/m² increase in BMI (above 25): risk x 1.59 (1.02-2.47)

Reference: Renehan AG, Tyson M, Egger M, et al. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 2008; 371:569.

- Treatments

- Cholecystectomy: risk x 0 (risk falls to zero)

Reference: /

Hodgkin lymphoma

- Medication

- Aspirin intake: risk x 0.60 (0.42-0.85)

Reference: Chang ET, Zheng T, Weir EG, et al. Aspirin and the risk of Hodgkin's lymphoma in a population-based case-control study. J Natl Cancer Inst 2004; 96:305.

- Smoking

- Active smoker: risk x 1.35 (1.17-1.56)

Reference: Castillo JJ, Dalia S, Shum H. Meta-analysis of the association between cigarette smoking and incidence of Hodgkin's Lymphoma. J Clin Oncol 2011; 29:3900.

- Medical History

- HIV positivity:
  - without treatment: risk x 9.2 (3.6–19.0)
  - with treatment: risk x 28.1 (14.9–48.2)

Reference: Franceschi S, Lise M, Clifford GM, et al. Changing patterns of cancer incidence in the early- and late-HAART periods: the Swiss HIV Cohort Study. Br J Cancer 2010; 103:416.

- History of organ transplantation: risk x 3.89 (2·42–6·26)

Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

- History of rheumatoid arthritis: risk x 2.7 (1.9-4.0)
- History of systemic lupus erythematosus: risk x 5.8 (2.2-15.1)
- History of sarcoidosis: risk x 14.1 (5.4-36.8)
- Family history of sarcoidosis: risk x 1.8 (1.01-3.1)
- Family history of ulcerative colitis: risk x 1.6 (1.02-2.6)

Reference: Landgren O, Engels EA, Pfeiffer RM, et al. Autoimmunity and susceptibility to Hodgkin lymphoma: a population-based case-control study in Scandinavia. J Natl Cancer Inst 2006; 98:1321.

- Celiac disease risk x 2.23 (1.19-4.15)
- Allergic rhinitis risk x 2.70 (1.21-6.03)
- Rheumatism, unspecified risk x 2.38 (1.07-5.33)
- Graves'/autoimmune thyroiditis risk x 2.87 (1.08-7.65)
- Idiopathic thrombocytopenic purpura risk x 7.72 (3.67-16.2)

Reference: He MM, Lo CH, Wang K, Polychronidis G, Wang L, Zhong R, Knudsen MD, Fang Z, Song M. Immune-Mediated Diseases Associated With Cancer Risks. JAMA Oncol. 2021 Dec 2:e215680. doi: 10.1001/jamaoncol.2021.5680. Epub ahead of print. PMID: 34854871; PMCID: PMC8640951.

- Hepatitis B: risk x 2.10 (1.34-3.31)

Reference: Song C, Lv J, Liu Y, Chen JG, Ge Z, Zhu J, Dai J, Du LB, Yu C, Guo Y, Bian Z, Yang L, Chen Y, Chen Z, Liu J, Jiang J, Zhu L, Zhai X, Jiang Y, Ma H, Jin G, Shen H, Li L, Hu Z; China Kadoorie Biobank Collaborative Group. Associations Between Hepatitis B Virus Infection and Risk of All Cancer Types. JAMA Netw Open. 2019 Jun 5;2(6):e195718. doi: 10.1001/jamanetworkopen.2019.5718. PMID: 31199446; PMCID: PMC6575146.

- Genital warts risk x 1.8 (1.2–2.5)

Reference: Blomberg M, Friis S, Munk C, Bautz A, Kjaer SK. Genital warts and risk of cancer: a Danish study of nearly 50,000 patients with genital warts. J Infect Dis. 2012 May 15;205(10):1544-53. doi: 10.1093/infdis/jis228. Epub 2012 Mar 15. PMID: 22427679.

- History of Epstein-Barr infection: risk x 4.0 (1.4-11.4)

Reference: Mueller N, Evans A, Harris NL, et al. Hodgkin's disease and Epstein-Barr virus. Altered antibody pattern before diagnosis. N Engl J Med 1989; 320:689.

- History of infectious diseases in childhood: risk x 0.45 (0.25–0.83)

Reference: Alexander FE, Jarrett RF, Lawrence D, et al. Risk factors for Hodgkin's disease by Epstein-Barr virus (EBV) status: prior infection by EBV and other agents. Br J Cancer 2000; 82:1117.

- Family history of Hodgkin lymphoma

- for parent or child: risk x 2.1 (1.6-2.6)
- with sister: risk x 9.4 (5.9-14)

○	with brother:	risk x	4.5	(2.9-6.7)
○	Multiple first-degree relatives:	risk x	13	(2.8-39)

Reference: Kharazmi E, Fallah M, Pukkala E, et al. Risk of familial classical Hodgkin lymphoma by relationship, histology, age, and sex: a joint study from five Nordic countries. Blood 2015; 126:1990.

Identical twins with Hodgkin lymphoma:	risk x	99	(48–182)

Reference: Mack TM, Cozen W, Shibata DK, et al. Concordance for Hodgkin's disease in identical twins suggesting genetic susceptibility to the young-adult form of the disease. N Engl J Med 1995; 332:413.

- History of cancer

- History of Basocellular skin carcinoma:

Number of BCCs:	1	risk x	2.27	(1.99–2.59)
	6+	risk x	8.94	(7.45–10.72)
	12+	risk x	15.41	(11.57–20.52)

Reference: Cho HG et al. Frequent basal cell cancer development is a clinical marker for inherited cancer susceptibility. JCI Insight. 2018; 3(15): e122744.

Kaposi's sarcoma

- Habits

- Local corticosteroid use:	risk x	2.73	(1.35-5.51)
- Infrequent bathing:	risk x	1.85	(1.04-3.33)
- Smoking (per 10 pack years):	risk x	0.81	(0.74-0.89)

Reference: Goedert JJ, Vitale F, Lauria C, et al. Risk factors for classical Kaposi's sarcoma. J Natl Cancer Inst 2002; 94:1712.

- Medical History

- HIV positivity:	- without treatment:	risk x	246	(218–277)
	- with treatment:	risk x	22.9	(12.5–38.5)

Reference: Franceschi S, Lise M, Clifford GM, et al. Changing patterns of cancer incidence in the early- and late-HAART periods: the Swiss HIV Cohort Study. Br J Cancer 2010; 103:416.

- History of organ transplantation :	risk x	208	(114–349)

Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

- Chronic edema of the lower limbs:	risk x	3.65	(1.62-8.23)
- Diabetes mellitus:	risk x	4.73	(2.02-11.1)
- Oral corticosteroid medications:	risk x	2.34	(1.23-4.45)

Reference: Anderson LA, Lauria C, Romano N, et al. Risk factors for classical Kaposi sarcoma in a population-based case-control study in Sicily. Cancer Epidemiol Biomarkers Prev 2008; 17:3435.

- History of asthma:	risk x	2.18	(0.95-4.97)
- History of allergy in men:	risk x	2.59	(1.15-5.83)

Reference: Goedert JJ, Vitale F, Lauria C, et al. Risk factors for classical Kaposi's sarcoma. J Natl Cancer Inst 2002; 94:1712.

- History of cancer

- History of Hodgkin lymphoma:	risk x	7.5	(1.6–37)
- History of leukemia:	risk x	5.3	(2.5–12)
- History of breast carcinoma:	risk x	2.2	(1.0–4.8)

Reference: Iscovich J, Boffetta P, Winkelmann R, Brennan P. Classic Kaposi's sarcoma as a second primary neoplasm. Int J Cancer 1999; 80:178.

- History of Non-Hodgkin lymphoma with treatment:

No Radiation	risk x	13.24	(10.54–16.41)
Radiation	risk x	11.09	(7.48–15.83)

Reference: Tward JD, Wendland MM, Shrieve DC, Szabo A, Gaffney DK. The risk of secondary malignancies over 30 years after the treatment of non-Hodgkin lymphoma. Cancer. 2006 Jul 1;107(1):108-15. doi:10.1002/cncr.21971. PMID: 16708354.

Kidney cancer

-BMI

	Baseline BMI (kg/m2)						
	<18.5	18.5–<22.5	22.5–<25	25–<27.5	27.5–<30	30–<35	≥35
Men							
HR	1.37	1.0	1.15	1.43	1.64	1.87	2.47
95% CI	(0.49-3.77)	Referent	(0.85-1.57)	(1.07-1.92)	(1.22-2.22)	(1.38-2.53)	(1.72-3.53)
Women							
HR	1.70	1.0	1.11	1.57	1.60	2.16	2.59
95% CI	(0.67-4.30)	Referent	(0.74-1.65)	(1.07-2.29)	(1.05-2.44)	(1.47-3.17)	(1.70-3.96)

Reference: Adams KF, Leitzmann MF, Albanes D, et al. Body size and renal cell cancer incidence in a large US cohort study. Am J Epidemiol 2008; 168:268.

- Use of NSAIDS risk x 1.51 (1.12-2.04)
Reference: Cho E, Curhan G, Hankinson SE, et al. Prospective evaluation of analgesic use and risk of renal cell cancer. Arch Intern Med 2011; 171:1487.

- History of kidney stones risk x 1.39 (1.05–1.84)
Reference: van de Pol JAA, van den Brandt PA, Schouten LJ. Kidney stones and the risk of renal cell carcinoma and upper tract urothelial carcinoma: the Netherlands Cohort Study. Br J Cancer. 2019 Feb;120(3):368-374. doi:10.1038/s41416-018-0356-7. Epub 2018 Dec 19. PMID: 30563989; PMCID: PMC6353869.

- Habits

- Smoking: current smoker: risk x 1.36 (1.19–1.56)
ex-smoker: risk x 1.16 (1.08–1.25)
Reference: Cumberbatch MG, Rota M, Catto JW, La Vecchia C. The Role of Tobacco Smoke in Bladder and Kidney Carcinogenesis: A Comparison of Exposures and Meta-analysis of Incidence and Mortality Risks. Euro Urol 2016; 70:458.

- Active alcohol use: risk x 0.85 (0.80–0.92)
Reference: Bellocco R, Pasquali E, Rota M, et al. Alcohol drinking and risk of renal cell carcinoma: results of a meta-analysis. Ann Oncol 2012; 23:2235.

- Eating red meat: risk x 1.36 (1.16–1.58)
- Eating processed meat: risk x 1.13 (1.03–1.24)
Reference: Zhang S, Wang Q, He J. Intake of red and processed meat and risk of renal cell carcinoma: a meta-analysis of observational studies. Oncotarget. 2017 Jun 16;8(44):77942-77956. doi: 10.18632/oncotarget.18549. Erratum in: Oncotarget. 2018 Jun 22;9(48):29018. PMID: 29100437; PMCID: PMC5652826.

- Female History

- Use Oral contraceptives: risk x 0.8 (0.58–1.09)
- Pregnancy:
  - 1 or 2 pregnancies: risk x 1.62 (0.90–2.92)
  - 3 or 4 pregnancies: risk x 1.77 (0.99–3.16)
  - 5 or more pregnancies: risk x 2.41 (1.27–4.59)

Reference: Kabat GC, Silvera SA, Miller AB, Rohan TE. A cohort study of reproductive and hormonal factors and renal cell cancer risk in women. Br J Cancer 2007; 96:845.

- Hysterectomy: risk x 1.29 (1.16-1.43)
Reference: Karami S, Daugherty SE, Purdue MP. Hysterectomy and kidney cancer risk: a meta-analysis. Int J Cancer. 2014 Jan 15;134(2):405-10. doi: 10.1002/ijc.28352. Epub 2013 Jul 30. PMID: 23818138; PMCID: PMC3834077.

- Medical History

- Lynch syndrome (mismatch repair genes MLH1, MSH2, MSH6): risk x 11.22 (2.31-32.79)
Reference: Win AK, Young JP, Lindor NM, et al. Colorectal and other cancer risks for carriers and noncarriers from families with a DNA mismatch repair gene mutation: a prospective cohort study. J Clin Oncol 2012; 30:958.

- HIV positivity: risk x 1.50 (1·23–1·83)

- History of organ transplantation: risk x 6.78 (5·69–8·08)
Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

- Cowden syndrome: risk x 30.6 (17.8 – 49.4)
Reference: Tan MH, Mester JL, Ngeow J, et al. Lifetime cancer risks in individuals with germline PTEN mutations. Clin Cancer Res 2012; 18:400.

- Diabetes (for men): risk x 1.92 (1.06-3.46)
Reference: Inoue M, Iwasaki M, Otani T, et al. Diabetes Mellitus and the Risk of Cancer: Results From a Large-Scale Population-Based Cohort Study in Japan. Arch Intern Med. 2006;166(17):1871–1877.

- Hereditary polycystic kidney disease: risk x 2·45 (1·29–4·65)
Reference: Yu TM, Chuang YW, Yu MC, Chen CH, Yang CK, Huang ST, Lin CL, Shu KH, Kao CH. Risk of cancer in patients with polycystic kidney disease: a propensity-score matched analysis of a nationwide, population-based cohort study. Lancet Oncol. 2016 Oct;17(10):1419-1425. doi: 10.1016/S1470-2045(16)30250-9. Epub 2016 Aug 20. PMID: 27550645.

- Chronic hepatitis C infection: risk x 1.77 (1.05-2.98)
Reference: Gordon SC, Moonka D, Brown KA, et al. Risk for renal cell carcinoma in chronic hepatitis C infection. Cancer Epidemiol Biomarkers Prev 2010; 19:1066.

- Hypertension: risk x 1.12 (1.06–1.17)
Reference: Kim CS, Han KD, Choi HS, Bae EH, Ma SK, Kim SW. Association of Hypertension and Blood Pressure With Kidney Cancer Risk: A Nationwide Population-Based Cohort Study. Hypertension. 2020 Jun;75(6):1439-1446. doi: 10.1161/HYPERTENSIONAHA.120.14820. Epub 2020 Apr 27. PMID: 32336229; PMCID: PMC7682799.

- Development of polycystic kidney disease after dialysis: risk x 30
Reference: Brennan JF, Stilmant MM, Babayan RK, Siroky MB. Acquired renal cystic disease: implications for the urologist. Br J Urol 1991; 67:342.

- History of MGUS: risk x 1.58 (1.21-2.03)
Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

- Rheumatism, unspecified risk x 2.94 (1.21-7.11)
- Necrotizing vasculopathies risk x 3.89 (1.45-10.4)
Reference: He MM, Lo CH, Wang K, Polychronidis G, Wang L, Zhong R, Knudsen MD, Fang Z, Song M. Immune-Mediated Diseases Associated With Cancer Risks. JAMA Oncol. 2021 Dec 2:e215680. doi: 10.1001/jamaoncol.2021.5680. Epub ahead of print. PMID: 34854871; PMCID: PMC8640951.

- History of cancer

- History of childhood cancer: risk x 8.0 (5.2-11.7)
Reference: Wilson CL, Ness KK, Neglia JP, et al. Renal carcinoma after childhood cancer: a report from the childhood cancer survivor study. J Natl Cancer Inst. 2013;105(7):504-8.

- History of Basocellular skin carcinoma:
Number of BCCs: 1 risk x 1.15 (1.04–1.28)
6+ risk x 1.48 (1.17–1.86)
Reference: Cho HG et al. Frequent basal cell cancer development is a clinical marker for inherited cancer susceptibility. JCI Insight. 2018; 3(15): e122744.

-Exposure

- Exposure to asbestos: risk x 1.4 (1.1-1.8)
- Exposure to cadmium: risk x 2.0 (1.0-3.9)
- Exposure to gasoline: risk x 1.6 (1.2-2.0)
- Working in the blast furnace or the coke oven industry: risk x 1.7 (1.1-2.7)
- Working in the iron and steel industry: risk x 1.6 (1.2-2.2)
- Exposure to dry‐cleaning solvents: risk x 1.4 (1.1-1.7)
- Exposure to other petroleum products: risk x 1.6 (1.3-2.1)
Reference: Mandel JS, McLaughlin JK, Schlehofer B, et al. International renal-cell cancer study. IV. Occupation. Int J Cancer 1995; 61:601.

- Exposure to trichloroethylene: risk x 1.25 (1.05-1.46)

Reference: Li N, Zhai Z, Zheng Y, Lin S, Deng Y, Xiang G, Yao J, Xiang D, Wang S, Yang P, Yang S, Xu P, Wu Y, Hu J, Dai Z, Wang M. Association of 13 Occupational Carcinogens in Patients With Cancer, Individually and Collectively, 1990-2017. JAMA Netw Open. 2021 Feb 1;4(2):e2037530. doi: 10.1001/jamanetworkopen.2020.37530. PMID: 33599775; PMCID: PMC7893501.

- Presence of CHEK2 mutation: risk x 3.61 (1.33-9.79)
Reference: Näslund-Koch C, Nordestgaard BG, Bojesen SE. Increased Risk for Other Cancers in Addition to Breast Cancer for CHEK2*1100delC Heterozygotes Estimated From the Copenhagen General Population Study. J Clin Oncol 2016; 34:1208.

Laryngeal cancer

- Habits

- Alcohol:

Frequency, drinks/day	
Never drinker	1.00 (referent)
<1	0.92 (0.5-1.69)
1–2	1.26 (0.77-2.07)
3–4	1.24 (0.62-2.45)
≥5	2.98 (1.72-5.17)
Duration, y	
Never drinker	1.00 (referent)
1–10	2.61 (1.14-5.98)
11–20	1.63 (0.78-3.43)
21–30	1.40 (0.79-2.48)
31–40	1.10 (0.64-1.89)
>40	1.00 (0.58-1.73)

- Smoking:

Frequency, cigarettes/day	
Never smokers	1.00 (referent)
1–10	5.72 (3.41-9.60)
11–20	8.36 (5.18-13.51)
21–30	14.38 (8.47-24.43)
31–40	18.38 (7.14-47.31)
>40	11.02 (4.92-24.72)
Duration, y	
Never smokers	1.00 (referent)
1–10	4.33 (1.13-16.62)
11–20	3.48 (1.61-7.50)
21–30	5.75 (2.94-11.23)
31–40	9.30 (5.40-16.02)
>40	16.32 (9.58-27.79)

Reference: Hashibe M, Brennan P, Benhamou S, et al. Alcohol drinking in never users of tobacco, cigarette smoking in never drinkers, and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. J Natl Cancer Inst 2007; 99:777.

- Stop drinking & smoking (only to be implemented if people have already drunk/smoked):

Cessation of alcohol drinking		
Current drinkers	1.00	Ref.
>1–4 years	1.16	(0.82–1.63)
5–9 years	0.88	(0.65–1.19)
10–19 years	0.93	(0.64–1.36)
≥20 years	0.69	(0.52–0.91)
Cessation of tobacco smoking		
Current smokers	1.00	Ref.
>1–4 years	0.70	(0.56–0.87)
5–9 years	0.57	(0.46–0.71)
10–19 years	0.36	(0.27–0.47)
≥20 years	0.19	(0.15–0.25)

Reference: Marron M, Boffetta P, Zhang ZF, et al. Cessation of alcohol drinking, tobacco smoking and the reversal of head and neck cancer risk. International Journal of Epidemiology. 2010;39(1):182-196. doi:10.1093/ije/dyp291.

- Nutrition

- High intakes of vegetables risk x 0.77 (0.49–1.22)
- High intakes of fruits risk x 0.80 (0.51–1.23)

Reference: Freedman ND, Park Y, Subar AF, et al. Fruit and vegetable intake and head and neck cancer risk in a large United States prospective cohort study. Int J Cancer 2008; 122:2330.

- Coffee: risk x 1.56 (0.60–4.02)

Reference: Turati F, Galeone C, La Vecchia C, et al. Coffee and cancers of the upper digestive and respiratory tracts: meta-analyses of observational studies. Ann Oncol 2011; 22:536.

- HIV positivity: risk x 2.72 (2·29–3·22)

- History of organ transplantation: risk x 1.99 (1·23–3·23)

Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

-Exposure

Occupational exposure to asbestos	Males	risk x	1.38	(1.19-1.61)
	Females	risk x	1.39	(1.19-1.60)
Occupational exposure to sulfuric acid	High exposure	risk x	4.57	(2.12-8.33)
	Low exposure	risk x	2.02	(0.94-3.78)

Reference: Li N, Zhai Z, Zheng Y, Lin S, Deng Y, Xiang G, Yao J, Xiang D, Wang S, Yang P, Yang S, Xu P, Wu Y, Hu J, Dai Z, Wang M. Association of 13 Occupational Carcinogens in Patients With Cancer, Individually and Collectively, 1990-2017. JAMA Netw Open. 2021 Feb 1;4(2):e2037530. doi: 10.1001/jamanetworkopen.2020.37530. PMID: 33599775; PMCID: PMC7893501.

- Chronic Condition

Psoriasis	risk x	4.86	(1.53-15.4)
Psoriatic/enteropathic arthropathies	risk x	7.76	(1.07-56.2)
Necrotizing vasculopathies	risk x	9.18	(1.27-66.5)
Bullous disorders	risk x	26.2	(3.62-190)

Reference: He MM, Lo CH, Wang K, Polychronidis G, Wang L, Zhong R, Knudsen MD, Fang Z, Song M. Immune-Mediated Diseases Associated With Cancer Risks. JAMA Oncol. 2021 Dec 2:e215680. doi: 10.1001/jamaoncol.2021.5680. Epub ahead of print. PMID: 34854871; PMCID: PMC8640951.

- Genital Warts:	Men	risk x	2.4	(1.4–3.8)
	Women	risk x	2.9	(1.3–5.7)

Reference: Blomberg M, Friis S, Munk C, Bautz A, Kjaer SK. Genital warts and risk of cancer: a Danish study of nearly 50,000 patients with genital warts. J Infect Dis. 2012 May 15;205(10):1544-53. doi: 10.1093/infdis/jis228. Epub 2012 Mar 15. PMID: 22427679.

- Tooth brushing (≥once/day vs <once/day): risk x 0.78 (0.72-0.85)
Reference: Hashim D, Sartori S, Brennan P, et al. The role of oral hygiene in head and neck cancer: results from International Head and Neck Cancer Epidemiology (INHANCE) consortium. Ann Oncol 2016; 27:1619.

Liver cancer

- Medical History

- History of chronic Hepatitis B infection: risk x 6.92 (2.92-16.39)
- History of chronic Hepatitis C infection: risk x 4.09 (1.30-12.85)

Reference: Tsukuma H, Hiyama T, Tanaka S, et al. Risk factors for hepatocellular carcinoma among patients with chronic liver disease. N Engl J Med 1993; 328:1797.

- History of chronic Hepatitis infection (B & C) & aspirin intake: risk x 0.69 (0.62-0.76)

Reference: Simon TG, Duberg, AS, Aleman S, et al. Association of aspirin with hepatocellular carcinoma and liver-related mortality. N Engl J Med 2020;382:1018-28.

- Cirrhosis: risk x 1.43 (1.04–1.97)

Reference: Flemming JA, Yang JD, Vittinghoff E, Kim WR, Terrault NA. Risk prediction of hepatocellular carcinoma in patients with cirrhosis: the ADRESS-HCC risk model. Cancer. 2014;120(22):3485-93.

- Diabetes: risk x 2.31 (1.87–2.84)

Reference: Wang P, Kang D, Cao W, et al. Diabetes mellitus and risk of hepatocellular carcinoma: a systematic review and meta-analysis. Diabetes Metab Res Rev 2012; 28:109.

- History of hemochromatosis: risk x 21 (16–22)

Reference: Elmberg M, Hultcrantz R, Ekbom A, et al. Cancer risk in patients with hereditary hemochromatosis and in their first-degree relatives. Gastroenterology 2003; 125:1733.

- Alpha-1 antitrypsin deficiency: risk x 20 (3.5-114.3)

Reference: Eriksson S, Carlson J, Velez R. Risk of cirrhosis and primary liver cancer in alpha 1-antitrypsin deficiency. N Engl J Med. 1986 Mar 20;314(12):736-9. doi: 10.1056/NEJM198603203141202. PMID: 3485248.

- HIV positivity:
  - without treatment: risk x 5.5 (0.5–20.2)
  - with treatment: risk x 6.1 (1.9–14.3)

Reference: Franceschi S, Lise M, Clifford GM, et al. Changing patterns of cancer incidence in the early- and late-HAART periods: the Swiss HIV Cohort Study. Br J Cancer 2010; 103:416.

- History of organ transplantation: risk x 2.13 (1·16–3·91)

Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

- Hereditary polycystic kidney disease: risk x 1·49 (1·04–2·13)

Reference: Yu TM, Chuang YW, Yu MC, Chen CH, Yang CK, Huang ST, Lin CL, Shu KH, Kao CH. Risk of cancer in patients with polycystic kidney disease: a propensity-score matched analysis of a nationwide, population-based cohort study. Lancet Oncol. 2016 Oct;17(10):1419-1425. doi: 10.1016/S1470-2045(16)30250-9. Epub 2016 Aug 20. PMID: 27550645.

- Genital warts: risk x 1.8 (1.0–2.9)

Reference: Blomberg M, Friis S, Munk C, Bautz A, Kjaer SK. Genital warts and risk of cancer: a Danish study of nearly 50,000 patients with genital warts. J Infect Dis. 2012 May 15;205(10):1544-53. doi: 10.1093/infdis/jis228. Epub 2012 Mar 15. PMID: 22427679.

- History of Multiple myeloma: risk x 1.30 (1.09-1.53)
- History of MGUS: risk x 1.25 (1.05-1.48)

Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

- Ulcerative colitis risk x 2.59 (1.15-5.81)
- Diabetes (Type 1) risk x 2.82 (1.43-5.56)
- Psoriasis risk x 2.85 (1.17-6.92)
- Crohn's disease risk x 4.01 (1.65-9.72)
- Idiopathic thrombocytopenic purpura risk x 12.0 (3.82-37.4)
- Primary biliary cholangitis risk x 62.4 (29.1-134)
- Autoimmune hepatitis risk x 35.1 (11.1-111)

Reference: He MM, Lo CH, Wang K, Polychronidis G, Wang L, Zhong R, Knudsen MD, Fang Z, Song M. Immune-Mediated Diseases Associated With Cancer Risks. JAMA Oncol. 2021 Dec 2:e215680. doi: 10.1001/jamaoncol.2021.5680. Epub ahead of print. PMID: 34854871; PMCID: PMC8640951.

- Habits

- Betel nut chewing: risk x 3.49 (1.74–6.96)
Reference: Tsai JF, Chuang LY, Jeng JE, et al. Betel quid chewing as a risk factor for hepatocellular carcinoma: a case-control study. Br J Cancer 2001; 84:709.

- Former smokers risk x 1.98 (0.90-4.39)
- Current smokers risk x 4.55 (1.90-10.91)
Reference: Trichopoulos D, Bamia C, Lagiou P, et al. Hepatocellular carcinoma risk factors and disease burden in a European cohort: a nested case-control study. J Natl Cancer Inst 2011; 103:1686.

- Alcohol:

2 cons/day	5 cons/day	10 cons/day
1.19 (1.12–1.27)	1.40 (1.25–1.56)	1.81 (1.50–2.19)

Reference: Corrao G, Bagnardi V, Zambon A, La Vecchia C. A meta-analysis of alcohol consumption and the risk of 15 diseases. Prev Med. 2004;38:613–619

- History of gallstones WITHOUT cholecystectomy: risk x 2.54 (1.71–3.79)
- History of gallstones WITH cholecystectomy: risk x 1.62 (1.29–2.02)
Reference: Liu Y, He Y, Li T, et al. Risk of primary liver cancer associated with gallstones and cholecystectomy: a meta-analysis. PLoS One 2014; 9:e109733.

- Statin intake: risk x 0.63 (0.52–0.76)
Reference: Singh S, Singh PP, Singh AG, et al. Statins are associated with a reduced risk of hepatocellular cancer: a systematic review and meta-analysis. Gastroenterology 2013; 144:323.

- Nutrition
- Red meat intake: risk x 1.10 (0.85–1.42)
- White meat intake: risk x 0.69 (0.58–0.81)
- Fish intake: risk x 0.78 (0.67–0.90)
Reference: Luo J, Yang Y, Liu J, et al. Systematic review with meta-analysis: meat consumption and the risk of hepatocellular carcinoma. Aliment Pharmacol Ther 2014; 39:913.

- Vegetables: risk x 0.72 (0.63–0.83)
Reference: Yang Y, Zhang D, Feng N, et al. Increased intake of vegetables, but not fruit, reduces risk for hepatocellular carcinoma: a meta-analysis. Gastroenterology 2014; 147:1031.

- Coffee, 2 or more per day: risk x 0.57 (0.49–0.67)
Reference: Larsson SC, Wolk A. Coffee consumption and risk of liver cancer: a meta-analysis. Gastroenterology 2007; 132:1740.

- Intake of omega-3 fatty acids: risk x 0.64 (0.42-0.96)
Reference: Sawada N, Inoue M, Iwasaki M, et al. Consumption of n-3 fatty acids and fish reduces risk of hepatocellular carcinoma. Gastroenterology 2012; 142:1468.

- Vitamin E intake: risk x 0.52 (0.30-0.90)
Reference: Zhang W, Shu XO, Li H, et al. Vitamin intake and liver cancer risk: a report from two cohort studies in China. J Natl Cancer Inst 2012; 104:1173.

- DO NOT brush teeth daily: risk x 1.75 (1.04–2.92)
Reference: Jordão HW, McKenna G, McMenamin ÚC, Kunzmann AT, Murray LJ, Coleman HG. The association between self-reported poor oral health and gastrointestinal cancer risk in the UK Biobank: A large prospective cohort study. United European Gastroenterol J. 2019;7(9):1241–1249. doi:10.1177/2050640619858043

- History of cancer
- History of Basocellular skin carcinoma (6+): risk x 1.59 (1.11–2.29)
Reference: Cho HG et al. Frequent basal cell cancer development is a clinical marker for inherited cancer susceptibility. JCI Insight. 2018; 3(15): e122744.

- Exposure
    - Trichlorethylene: risk x 1.3 (1.1-1.6)
    Reference: Marant Micallef C, Shield KD, Baldi I, Charbotel B, Fervers B, Gilg Soit Ilg A, Guénel P, Olsson A, Rushton L, Hutchings SJ, Straif K, Soerjomataram I. Occupational exposures and cancer: a review of agents and relative risk estimates. Occup Environ Med. 2018 Aug;75(8):604-614. doi: 10.1136/oemed-2017-104858. Epub 2018 May 7. PMID: 29735747.
    - Aflatoxins: risk x 5.39 (1.11–26.18)
    Reference: Chu YJ, Yang HI, Wu HC, et al. Aflatoxin B1 exposure increases the risk of cirrhosis and hepatocellular carcinoma in chronic hepatitis B virus carriers. Int J Cancer 2017; 141:711.

Lung cancer

- Habits

Pack-years smoked	risk x	1,039	(1,031-1,048)
Smoking duration, per 1 y	risk x	1.013	(0.996-1.030)
Smoking quit-time, per 1 y	risk x	0.941	(0.912-0.972)
Current smoker	risk x	1,339	(1,067-1,682)

Reference: Tammemagi CM, Pinsky PF, Caporaso NE, et al. Lung cancer risk prediction: Prostate, Lung, Colorectal And Ovarian Cancer Screening Trial models and validation. J Natl Cancer Inst. 2011;103(13):1058-68.

- Alcohol: Never:	risk x	0.89	(0.82-0.96)
With ≥7 glasses per day:	risk x	1.11	(1.00-1.24)

Reference: Troche JR, Mayne ST, Freedman ND, et al. The Association Between Alcohol Consumption and Lung Carcinoma by Histological Subtype. Am J Epidemiol 2016; 183:110.

- Medical History

- COPD	risk x	1,370	(1,142-1,644)

Reference: Tammemagi CM, Pinsky PF, Caporaso NE, et al. Lung cancer risk prediction: Prostate, Lung, Colorectal And Ovarian Cancer Screening Trial models and validation. J Natl Cancer Inst. 2011;103(13):1058-68.

- Pulmonary fibrosis:	risk x	7.31	(4.47-11.93)

Reference: Hubbard R, Venn A, Lewis S, Britton J. Lung cancer and cryptogenic fibrosing alveolitis. A population-based cohort study. Am J Respir Crit Care Med 2000; 161:5.

- HIV positivity:	- without treatment:	risk x	3.3	(1.4–6.6)
	- with treatment:	risk x	2.6	(1.3–4.6)

Reference: Franceschi S, Lise M, Clifford GM, et al. Changing patterns of cancer incidence in the early- and late-HAART periods: the Swiss HIV Cohort Study. Br J Cancer 2010; 103:416.

- History of organ transplantation:	risk x	2.18	(1·85–2·57)

Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

-Peutz-Jeghers syndrome (STK11):	risk x	17	(5.4-39)

Reference: Francis M. Giardiello, Jill D. Brensinger, Anne C. Tersmette, Steven N. Goodman, Gloria M. Petersen, Susan V. Booker, Marcia Cruz–Correa, Johan A. Offerhaus. Very high risk of cancer in familial Peutz–Jeghers syndrome. Gastroenterology, Volume 119, Issue 6, December 2000, Pages 1447-1453

- Alpha-1 antitrypsin deficiency:	risk x	1.7	(1.2-2.4)

Reference: Yang P, Sun Z, Krowka MJ, et al. Alpha1-antitrypsin deficiency carriers, tobacco smoke, chronic obstructive pulmonary disease, and lung cancer risk. Arch Intern Med 2008; 168:1097.

- History of MGUS:	risk x	1.42	(1.05-1.89)

Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

- Genital Warts:	Men	risk x	1.8	(1.4–2.1)
	Women	risk x	2.3	(2.0–2.7)

Reference: Blomberg M, Friis S, Munk C, Bautz A, Kjaer SK. Genital warts and risk of cancer: a Danish study of nearly 50,000 patients with genital warts. J Infect Dis. 2012 May 15;205(10):1544-53. doi: 10.1093/infdis/jis228. Epub 2012 Mar 15. PMID: 22427679.

- Asthma	risk x	1.34	(1.14-1.57)
- Rheumatoid arthritis	risk x	1.71	(1.28-2.28)
- Psoriasis	risk x	1.60	(1.04-2.47)

Reference: He MM, Lo CH, Wang K, Polychronidis G, Wang L, Zhong R, Knudsen MD, Fang Z, Song M. Immune-Mediated Diseases Associated With Cancer Risks. JAMA Oncol. 2021 Dec 2:e215680. doi: 10.1001/jamaoncol.2021.5680. Epub ahead of print. PMID: 34854871; PMCID: PMC8640951.

- History of Tuberculosis:	risk x	1.48	(1.17-1.87)
- History of Pneumonia:	risk x	1.57	(1.22-2.01)

Reference: Brenner DR, Boffetta P, Duell EJ, et al. Previous lung diseases and lung cancer risk: a pooled analysis from the International Lung Cancer Consortium. Am J Epidemiol 2012; 176:573.

- Beta-carotene intake: risk x 1.19 (1.03-1.36)
Reference: Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group. The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. N Engl J Med 1994; 330:1029.

-Night work: risk x 1.76 (1.25-2.47)
Reference: Parent, M. -E.; El-Zein, M.; Rousseau, M. -C.; Pintos, J.; Siemiatycki, J. (2012). "Night Work and the Risk of Cancer Among Men". American Journal of Epidemiology. 176(9):751–759.

- Education (every 3 years after age 6) risk x 0.927 (0.885-0.970)
- Family history of lung cancer risk x 1,560 (1,311-1,855)
- Chest x-ray in last 3 years risk x 1,122 (1,023-1,230)
Reference: Tammemagi CM, Pinsky PF, Caporaso NE, et al. Lung cancer risk prediction: Prostate, Lung, Colorectal And Ovarian Cancer Screening Trial models and validation. J Natl Cancer Inst. 2011;103(13):1058-68.

- History of cancer:

- History of Basocellular skin carcinoma:

Number of BCCs:	6+	risk x	1.67	(1.34–2.08)
	12+	risk x	2.65	(1.82–3.85)

Reference: Cho HG et al. Frequent basal cell cancer development is a clinical marker for inherited cancer susceptibility. JCI Insight. 2018; 3(15): e122744.

-Exposure

- Occupational exposure to beryllium	Males	risk x	1.17	(1.09-1.30)
	Females	risk x	1.17	(1.08-1.27)
- Occupational exposure to chromium	Males	risk x	1.18	(1.11-1.25)
	Females	risk x	1.18	(1.12-1.25)
- Occupational exposure to nickel	High vs. No exposure	risk x	2.15	(1.30-3.30)
	Low vs. No exposure	risk x	1.54	(0.61-3.36)
- Occupational exposure to polycyclic aromatic hydrocarbons	Males	risk x	1.31	(1.17-1.47)
	Females	risk x	1.31	(1.15-1.49)
- Occupational exposure to silica	High vs. No exposure	risk x	1.70	(1.16-2.26)
	Low vs. No exposure	risk x	1.54	(1.06-1.99)

Reference: Li N, Zhai Z, Zheng Y, Lin S, Deng Y, Xiang G, Yao J, Xiang D, Wang S, Yang P, Yang S, Xu P, Wu Y, Hu J, Dai Z, Wang M. Association of 13 Occupational Carcinogens in Patients With Cancer, Individually and Collectively, 1990-2017. JAMA Netw Open. 2021 Feb 1;4(2):e2037530. doi: 10.1001/jamanetworkopen.2020.37530. PMID: 33599775; PMCID: PMC7893501.

- Men ever worked in rubber industry	risk x	1.2	(1.1-1.4)
- Women ever worked in rubber industry	risk x	1.8	(1.1-2.8)
- Iron and steel foundry work	risk x	1.4	(1.3-1.5)
- Bis(chloromethyl) ether exposure	risk x	7.6	(4.3-13.5)
- Acid mists exposure	risk x	1.4	(1.0-1.9)
- Cobalt metal with tungsten carbide	risk x	1.9	(1.03-3.6)
- Diazinon exposure	risk x	1.6	(1.1-2.3)
- Art glass exposure	risk x	1.3	(1.0-1.6)

Reference: Marant Micallef C, Shield KD, Baldi I, Charbotel B, Fervers B, Gilg Soit Ilg A, Guénel P, Olsson A, Rushton L, Hutchings SJ, Straif K, Soerjomataram I. Occupational exposures and cancer: a review of agents and relative risk estimates. Occup Environ Med. 2018 Aug;75(8):604-614. doi: 10.1136/oemed-2017-104858. Epub 2018 May 7. PMID: 29735747.

- Working as a welder: risk x 1.29 (1.20-1.39)
Reference: Honaryar MK, Lunn RM, Luce D, Ahrens W, 't Mannetje A, Hansen J, Bouaoun L, Loomis D, Byrnes G, Vilahur N, Stayner L, Guha N. Welding fumes and lung cancer: a meta-analysis or case-control and cohort studies. Occup Environ Med. 2019 Jun;76(6):422-431. doi: 10.1136/oemed-2018-105447. Epub 2019 Apr 4. PMID: 30948521.

- Exposure to arsenic risk x 2.44 (1.57-3.80)
Reference: Gamboa-Loira B, Cebrián ME, Franco-Marina F, López-Carrillo L. Arsenic metabolism and cancer risk: A meta-analysis. Environ Res. 2017 Jul;156:551-558. doi: 10.1016/j.envres.2017.04.016.

- Exposure to cadmium: risk x 4.17 (1·21–14·4)
Reference: Nawrot T, Plusquin M, Hogervorst J, et al. Environmental exposure to cadmium and risk of cancer: a prospective population-based study. Lancet Oncol 2006; 7:119.
- Daily exposure to burning bituminous coal: risk x 2.66 (1.39-5.07)
Reference: Zhao Y, Wang S, Aunan K, Seip HM, Hao J. Air pollution and lung cancer risks in China--a meta-analysis. Sci Total Environ. 2006 Aug 1;366(2-3):500-13. doi: 10.1016/j.scitotenv.2005.10.010. Epub 2006 Jan 10. PMID: 16406110.

- Exposure to diesel: risk x 1.31 (1.19-1.43)
Reference: Olsson AC, Gustavsson P, Kromhout H, et al. Exposure to diesel engine exhaust and lung cancer risk in a pooled analysis from case-control studies in Europe and Canada. Am J Respir Crit Care Med 2011; 183:941.

- Exposure to heavy air pollution: risk x 1.22 (1·03–1·45)
Reference: Raaschou-Nielsen O, Andersen ZJ, Beelen R, et al. Air pollution and lung cancer incidence in 17 European cohorts: prospective analyzes from the European Study of Cohorts for Air Pollution Effects (ESCAPE). Lancet Oncol 2013; 14:813.

- Living with a smoker: risk x 1.21
Reference: US Department of Health and Human Services (USDHHS). The health consequences of involuntary exposure to tobacco smoke. Centers for Disease Control and Prevention, Rockville, MD, 2006.

- Exposure to paint dust: risk x 2.48 (0.88-6.97)
Reference: van Loon AJ, Kant IJ, Swaen GM, et al. Occupational exposure to carcinogens and risk of lung cancer: results from The Netherlands cohort study. Occup Environ Med 1997; 54:817.

-Working in a uranium mine:

Duration of exposure (years)	
<5	1.0
5–14	1.38 (0.63–3.06)
15–24	2.04 (0.92–4.0)
25–34	1.58 (0.70–3.53)
35+	1.16 (0.46–2.93)

Reference: Grosche B, Kreuzer M, Kreisheimer M, Schnelzer M, Tschense A. Lung cancer risk among German male uranium miners: a cohort study, 1946-1998. Br J Cancer. 2006;95(9):1280-7.

- Exposure to asbestos: risk x 3.49
Reference: van Loon AJ, Kant IJ, Swaen GM, et al. Occupational exposure to carcinogens and risk of lung cancer: results from The Netherlands cohort study. Occup Environ Med 1997; 54:817.

- Taking Aspirin risk x 0.95
Reference: Cuzick J, Thorat MA, Bosetti C, Brown PH, Burn J, Cook NR, Ford LG, Jacobs EJ, Jankowski JA, La Vecchia C, Law M, Meyskens F, Rothwell PM, Senn HJ, Umar A. Estimates of benefits and harms of prophylactic use of aspirin in the general population. Ann Oncol. 2015 Jan;26(1):47-57. doi: 10.1093/annonc/mdu225. Epub 2014 Aug 5. PMID: 25096604; PMCID: PMC4269341.

-Genetic:

SNP panel:
α5-nAChR (rs 16969968) AA: risk x 1.8 (1.2-2.7)
CYP 2E1 (rs 2031920) TT/TC: risk x 2.1 (1.0-4.3)
Interleukin-18 (rs 360721) CC: risk x 1.4 (1.1-1.9)
Interleukin-8 (rs 4073) TT: risk x 1.5 (1.1-2.1)
Interleukin 1B (rs 16944) GG: risk x 1.2 (0.9-1.6)
ITGA11 (rs 2306022) AA: risk x 2.6 (0.9-7.6)
N-Acetylcysteine transferase 2 (rs 1799930) GG: risk x 1.4 (1.1-1.9)
α1-Antichymotrypsin (rs 4934) GG: risk x 1.6 (1.2-2.2)
Cerberus 1 (rs 10115703) AA/AG: risk x 1.4 (0.9-2.0)
DAT1 (rs 6413429) GT/TT: risk x 1.5 (1.0-2.3)
TNFR1 (TNFRSF1A) (rs 1139417) AA: risk x 1.3 (1.0-1.8)
TLR9 (rs 5743836) CC: risk x 2.2 (0.8-6.6)

P73 (TP73) (rs 2273953) CC:	risk x	0.65	(0.49-0.85)
SOD3 (rs 1799895) GG/GC:	risk x	0.28	(0.10-0.90)
ITGB3 (rs 2317676) GG/GA:	risk x	0.59	(0.39-0.89)
DRD2 (rs 1799732) CDel/Del.Del:	risk x	0.68	(0.48-0.96)
BCL2 (rs 2279115) AA:	risk x	0.71	(0.53-0.97)
XPD (ERCC2) (rs 13181) GG:	risk x	0.74	(0.51-1.10)
REV1 (REV1L) (rs 3087386) CC:	risk x	0.79	(0.59-1.10)
FasL (TNFSF6) (rs 763110) TT:	risk x	0.72	(0.49-1.10)

Reference: Young RP, Hopkins RJ, Hay BA, Epton MJ, Mills GD, Black PN, Gardner HD, Sullivan R, Gamble GD. A gene-based risk score for lung cancer susceptibility in smokers and ex-smokers. Postgrad Med J. 2009 Oct;85(1008):515-24. doi: 10.1136/pgmj.2008.077107. PMID: 19789190.

SNP panels

Rs2736100:	risk x	1.18	(1.09-1.27)
Rs402710:	risk x	1.10	(1.01-1.19)
Rs4083914:	risk x	1.15	(1.03-1.28)
Rs4488809:	risk x	1.21	(1.11-1.30)

Reference: Li H, Yang L, Zhao BMC Med Genet. 2012 Dec 10;13:118. doi: 10.1186/1471-2350-13-118. PMID: 23228068; PMCID: PMC3573944.

Merkel cell skin cancer

- Medical History

-Organ transplantation: risk x 23.8 (19.6-28.7)

Reference: Becker JC, Stang A, DeCaprio JA, et al. Merkel cell carcinoma. Nat Rev Dis Primers. 2017;3:17077. Published 2017 Oct 26. doi:10.1038/nrdp.2017.77

-HIV/AIDS+: risk x 13·4 (4·9–29·1)

Reference: Engels EA, Frisch M, Goedert JJ, Biggar RJ, Miller RW. Merkel cell carcinoma and HIV infection. Lancet. 2002 Feb 9;359(9305):497-8. doi: 10.1016/S0140-6736(02)07668-7. PMID: 11853800.

-History of Multiple myeloma: risk x 2.22 (1.74-2.80)
-History of MGUS: risk x 3.30 (2.76-3.90)

Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

-Medication

- Medications for long term daily use
  - Furosemide risk x 2.0 (1.3-2.8)
  - Indomethacin risk x 2.8 (1.3-5.9)
  - Simvastatin risk x 3.6 (2.0-6.4)
- Medications for short term use
  - Acitretin risk x 7.8 (1.1-56)
  - Isotretinoin risk x 22.6 (3.1-166)

Reference: Kaae J, Boyd HA, Hansen AV, Wulf HC, Wohlfahrt J, Melbye M. Photosensitizing medication use and risk of skin cancer. Cancer Epidemiol Biomarkers Prev. 2010 Nov;19(11):2942-9. doi: 10.1158/1055-9965.EPI-10-0652. Epub 2010 Sep 22. PMID: 20861398.

Mesothelioma

- Exposure to asbestos:
  - certain: risk x 17.7 (3.4-253)
  - probable: risk x 3.0 (0.9-10.6)

Reference: Tuomi T, Huuskonen MS, Virtamo M, Tossavainen A, Tammilehto L, Mattson K, Lahdensuo A, Mattila J, Karhunen P, Liippo K, et al. Relative risk of mesothelioma associated with different levels of exposure to asbestos. Scand J Work Environ Health 1991;17(6):404-408

- Family member with mesothelioma:
  -Parent: risk x 3.88 (1.01–10.04)
  -Sibling: risk x 12.37 (5.89–22.84)
  -Sibling with kidney cancer: risk x 2.13 (1.16-3.59)
  -Sibling with bladder cancer: risk x 2.09 (1.32-3.14)

Reference: Ji J, Sundquist J, Sundquist K. Incidence and familial risk of pleural mesothelioma in Sweden: a national cohort study. Eur Respir J 2016; 48:873.

- History of radiotherapy: risk x 1.34 (1.04-1.77)

Reference: Farioli A, Ottone M, Morganti AG, et al. Radiation-induced mesothelioma among long-term solid cancer survivors: a longitudinal analysis of SEER database. Cancer Med. 2016;5(5):950-9.

- Chronic Condition
  - History of MGUS: risk x 1.42 (1.05-1.89)

  Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

  - Rheumatic fever / rheumatic heart diseases: risk x 3.07 (1.14-8.27)
  - Multiple sclerosis: risk x 5.02 (1.24-20.3)

  Reference: He MM, Lo CH, Wang K, Polychronidis G, Wang L, Zhong R, Knudsen MD, Fang Z, Song M. Immune-Mediated Diseases Associated With Cancer Risks. JAMA Oncol. 2021 Dec 2:e215680. doi: 10.1001/jamaoncol.2021.5680. Epub ahead of print. PMID: 34854871; PMCID: PMC8640951.

Myeloma

- Relative with any cancer : risk x 1.4 (1.1-1.8)
Reference: Multiple myeloma and family history of cancer. A case-control study. CC Bourguet, S. Grufferman, E. Delzell, ER DeLong, HJ Cohen. Cancer. 1985 Oct 15; 56(8):2133–2139.

- per 5 kg/m² increase in BMI (above 25): risk x 1.11 (1.07-1.15)
Reference: Renehan AG, Tyson M, Egger M, et al. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 2008; 371:569.

- Large intake of fish: risk x 0.64 (0.45-0.90)
Reference: Dietary Fish Intake and Risk of Leukemia, Multiple Myeloma, and Non-Hodgkin Lymphoma. Lin Fritschi, Gina L. Ambrosini, Erich V. Kliewer, Kenneth C. Johnson and Canadian Cancer Registries Epidemiologic Research Group. Cancer Epidemiol Biomarkers Prev April 1 2004 (13) (4) 532-537;

- Chronic Condition

- HIV positivity: - without treatment: risk x 14.8 (2.8–43.9)
- with treatment: risk x 5.1 (0.5–18.9)
Reference: Franceschi S, Lise M, Clifford GM, et al. Changing patterns of cancer incidence in the early- and late-HAART periods: the Swiss HIV Cohort Study. Br J Cancer 2010; 103:416.

- History of organ transplantation: risk x 3.12 (2·13–4·57)
Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

- History of MGUS risk x 79.86 (73.21-86.94)
Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

- Rheumatism, unspecified risk x 3.57 (1.14-11.2)
- Necrotizing vasculopathies risk x 7.98 (2.97-21.4)
Reference: He MM, Lo CH, Wang K, Polychronidis G, Wang L, Zhong R, Knudsen MD, Fang Z, Song M. Immune-Mediated Diseases Associated With Cancer Risks. JAMA Oncol. 2021 Dec 2:e215680. doi: 10.1001/jamaoncol.2021.5680. Epub ahead of print. PMID: 34854871; PMCID: PMC8640951.

Non-Hodgkin lymphoma

- For men, per 5 kg/m² increase in BMI (above 25): risk x 1.06 (1.03-1.09)
- For women, per 5 kg/m² increase in BMI (above 25): risk x 1.07 (1.00-1.14)

Reference: Renehan AG, Tyson M, Egger M, et al. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 2008; 371:569.

- Large intake of fish: risk x 0.71 (0.60-0.85)

Reference: Dietary Fish Intake and Risk of Leukemia, Multiple Myeloma, and Non-Hodgkin Lymphoma. Lin Fritschi, Gina L. Ambrosini, Erich V. Kliewer, Kenneth C. Johnson and Canadian Cancer Registries Epidemiologic Research Group. Cancer Epidemiol Biomarkers Prev April 1 2004 (13) (4) 532-537;

-Chronic

- History of primary Sjögren syndrome: risk x 18.8 (9.5-37.3)

Reference: Zintzaras E, Voulgarelis M, Moutsopoulos HM. The risk of lymphoma development in autoimmune diseases: a meta-analysis. Arch Intern Med 2005; 165:2337.

- HIV positivity: - without treatment: risk x 103 (88.8–119)
  - with treatment: risk x 16.2 (11.1–22.9)

Reference: Franceschi S, Lise M, Clifford GM, et al. Changing patterns of cancer incidence in the early- and late-HAART periods: the Swiss HIV Cohort Study. Br J Cancer 2010; 103:416.

- History of organ transplantation: risk x 8.07 (6·40–10·2)

Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

- Rheumatoid arthritis risk x 2.01 (1.34-3.01)
- Celiac disease risk x 2.23 (1.19-4.15)
- Allergic rhinitis risk x 2.70 (1.21-6.03)
- Rheumatism, unspecified risk x 2.38 (1.07-5.33)
- Graves'/autoimmune thyroiditis risk x 2.87 (1.08-7.65)
- Systemic lupus erythematosus risk x 4.46 (1.85-10.8)
- Idiopathic thrombocytopenic purpura risk x 7.72 (3.67-16.2)

Reference: He MM, Lo CH, Wang K, Polychronidis G, Wang L, Zhong R, Knudsen MD, Fang Z, Song M. Immune-Mediated Diseases Associated With Cancer Risks. JAMA Oncol. 2021 Dec 2:e215680. doi: 10.1001/jamaoncol.2021.5680. Epub ahead of print. PMID: 34854871; PMCID: PMC8640951.

- Hepatitis B: risk x 2.10 (1.34-3.31)

Reference: Song C, Lv J, Liu Y, Chen JG, Ge Z, Zhu J, Dai J, Du LB, Yu C, Guo Y, Bian Z, Yang L, Chen Y, Chen Z, Liu J, Jiang J, Zhu L, Zhai X, Jiang Y, Ma H, Jin G, Shen H, Li L, Hu Z; China Kadoorie Biobank Collaborative Group. Associations Between Hepatitis B Virus Infection and Risk of All Cancer Types. JAMA Netw Open. 2019 Jun 5;2(6):e195718. doi: 10.1001/jamanetworkopen.2019.5718. PMID: 31199446; PMCID: PMC6575146.

- Genital warts: risk x 2.0 (1.6–2.5)

Reference: Blomberg M, Friis S, Munk C, Bautz A, Kjaer SK. Genital warts and risk of cancer: a Danish study of nearly 50,000 patients with genital warts. J Infect Dis. 2012 May 15;205(10):1544-53. doi: 10.1093/infdis/jis228. Epub 2012 Mar 15. PMID: 22427679.

-Night work: risk x 2.31 (1.48-3.61)

Reference: Parent, M. -E.; El-Zein, M.; Rousseau, M. -C.; Pintos, J.; Siemiatycki, J. (2012). "Night Work and the Risk of Cancer Among Men". American Journal of Epidemiology. 176(9):751–759.

-History of cancer

- History of Basocellular skin carcinoma:

Number of BCCs:	1	risk x	1.40	(1.24–1.58)
	6+	risk x	2.59	(2.05–3.29)
	12+	risk x	3.10	(1.97–4.89)

Reference: Cho HG et al. Frequent basal cell cancer development is a clinical marker for inherited cancer susceptibility. JCI Insight. 2018; 3(15): e122744.

- Exposure

- Lindane	risk x	1.6	(1.2- 2.2)
- Diazinon	risk x	1.4	(1.0-1.9)
- Dichloromethane	risk x	1.5	(1.0-2.3)
- Trichloroethylene	risk x	1.2	(1.0-1.4)
- Ethylene oxide	risk x	1.3	(1.0-1.9)

Reference: Marant Micallef C, Shield KD, Baldi I, Charbotel B, Fervers B, Gilg Soit Ilg A, Guénel P, Olsson A, Rushton L, Hutchings SJ, Straif K, Soerjomataram I. Occupational exposures and cancer: a review of agents and relative risk estimates. Occup Environ Med. 2018 Aug;75(8):604-614. doi: 10.1136/oemed-2017-104858. Epub 2018 May 7. PMID: 29735747.

Leukemia

- Men, per 5 kg/m² increase in BMI (above 25): risk x 1.08 (1.02-1.14)
- Women, per 5 kg/m² increase in BMI (above 25): risk x 1.17 (1.04-1.32)

Reference: Renehan AG, Tyson M, Egger M, et al. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 2008; 371:569.

- Nutrition

- Large intake of fish: risk x 0.72 (0.58-0.89)

Reference: Dietary Fish Intake and Risk of Leukemia, Multiple Myeloma, and Non-Hodgkin Lymphoma. Lin Fritschi, Gina L. Ambrosini, Erich V. Kliewer, Kenneth C. Johnson and Canadian Cancer Registries Epidemiologic Research Group. Cancer Epidemiol Biomarkers Prev April 1 2004 (13) (4) 532-537;

- Coffee: risk x 0.64 (0.51-0.77)

Reference: Yu X, Bao Z, Zou J, Dong J. Coffee consumption and risk of cancers: a meta-analysis of cohort studies. BMC Cancer. 2011;11:96. Published 2011 Mar 15. doi:10.1186/1471-2407-11-96

- History of cancer

- History of childhood cancer:	All Leukemia	risk x	6.86	(4.39-10.21)
	[ALL]	risk x	3.49	(1.27-7.59)
	[AML]	risk x	7.92	(3.61-15.04)
	[Other leukemia]	risk x	9.36	(3.42-20.38)

Reference: Neglia JP, Friedman DL, Yasui Y, Mertens AC, Hammond S, Stovall M, Donaldson SS, Meadows AT, Robison LL, Second malignant neoplasms in five-year survivors of childhood cancer: childhood cancer survivor study., J Natl Cancer Inst. 2001 Apr 18;93(8):618-29.

- Thyroid cancer treated with radioactive iodine risk x 2.5 (1.13-5.53)

Reference: Sawka AM, Thabane L, Parlea L, Ibrahim-Zada I, Tsang RW, Brierley JD, Straus S, Ezzat S, Goldstein DP. Second primary malignancy risk after radioactive iodine treatment for thyroid cancer: a systematic review and meta-analysis. Thyroid. 2009 May;19(5):451-7. doi:10.1089/thy.2008.0392. PMID: 19281429.

- History of Basocellular skin carcinoma:

Number of BCCs:	1	risk x	1.76	(1.60–1.95)
	6+	risk x	3.23	(2.68–3.89)
	12+	risk x	5.78	(4.31–7.76)

Reference: Cho HG et al. Frequent basal cell cancer development is a clinical marker for inherited cancer susceptibility. JCI Insight. 2018; 3(15): e122744.

-Exposure

- Occupational exposure to benzene	High exposure	risk x	2.62	(1.22-3.98)
	Low exposure	risk x	1.63	(1.00- 2.26)
- Occupational exposure to formaldehyde				
	Males	risk x	1.48	(1.19-1.82)
	Females	risk x	1.49	(1.20-1.85)

Reference: Li N, Zhai Z, Zheng Y, Lin S, Deng Y, Xiang G, Yao J, Xiang D, Wang S, Yang P, Yang S, Xu P, Wu Y, Hu J, Dai Z, Wang M. Association of 13 Occupational Carcinogens in Patients With Cancer, Individually and Collectively, 1990-2017. JAMA Netw Open. 2021 Feb 1;4(2):e2037530. doi: 10.1001/jamanetworkopen.2020.37530. PMID: 33599775; PMCID: PMC7893501.

- Exposure to 1,3-Butadiene risk x 3.8 (1.6-8.9)

Reference: Marant Micallef C, Shield KD, Baldi I, Charbotel B, Fervers B, Gilg Soit Ilg A, Guénel P, Olsson A, Rushton L, Hutchings SJ, Straif K, Soerjomataram I. Occupational exposures and cancer: a review of agents and relative risk estimates. Occup Environ Med. 2018 Aug;75(8):604-614. doi: 10.1136/oemed-2017-104858. Epub 2018 May 7. PMID: 29735747.

- Chronic Condition

- HIV positivity:		risk x	3.20	(2·51–4·09)
- History of organ transplantation:		risk x	2.38	(1·77–3·79)

Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

- History of Multiple myeloma:	[AML]	risk x	11.51	(8.19-15.74)
- History of MGUS:	[AML]	risk x	8.01	(5.40-11.43)

Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

- Rheumatism, unspecified	risk x	3.20	(1.19-8.59)
- Idiopathic thrombocytopenic purpura	risk x	7.47	(2.79-20.0)

Reference: He MM, Lo CH, Wang K, Polychronidis G, Wang L, Zhong R, Knudsen MD, Fang Z, Song M. Immune-Mediated Diseases Associated With Cancer Risks. JAMA Oncol. 2021 Dec 2:e215680. doi: 10.1001/jamaoncol.2021.5680. Epub ahead of print. PMID: 34854871; PMCID: PMC8640951.

Oral Cavity and Pharynx cancer

- Habits

- Alcohol

Frequency, drinks/day	
Never drinker	1.00 (referent)
<1	1.39 (0.99-1.96)
1–2	1.66 (1.18-2.34)
3–4	2.33 (1.37-3.98)
≥5	5.50 (2.26-13.36)
Duration, y	
Never drinker	1.00 (referent)
1–10	1.76 (0.99-3.14)
11–20	1.34 (0.81-2.11)
21–30	1.95 (1.37-2.77)
31–40	1.44 (0.78-2.66)
>40	1.51 (0.68-3.37)

-Smoking

Frequency, cigarettes/day	
Never smokers	1.00 (referent)
1–10	2.55 (1.59-4.10)
11–20	2.15 (1.38-3.34)
21–30	3.86 (1.80-8.25)
31–40	4.82 (2.42-9.60)
>40	3.10 (1.43-6.69)
Duration, y	
Never smokers	1.00 (referent)
1–10	1.69 (1.00-2.88)
11–20	1.18 (0.61-2.28)
21–30	1.47 (0.94-2.31)
31–40	3.74 (2.61-5.38)
>40	4.84 (2.22-10.54)

Reference: Hashibe M, Brennan P, Benhamou S, et al. Alcohol drinking in never users of tobacco, cigarette smoking in never drinkers, and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. J Natl Cancer Inst 2007; 99:777.

- Stop drinking & smoking (only to be implemented if people have already drunk/smoked):

Cessation of alcohol drinking		
Current drinkers	1.00	Ref.
>1–4 years	0.99	(0.69–1.43)
5–9 years	0.90	(0.62–1.30)
10–19 years	0.94	(0.75–1.18)
≥20 years	0.60	(0.40–0.89)
Cessation of tobacco smoking		
Current smokers	1.00	Ref.
>1–4 years	0.70	(0.61–0.81)
5–9 years	0.48	(0.40–0.58)
10–19 years	0.34	(0.28–0.40)
≥20 years	0.23	(0.18–0.31)

Reference: Marron M, Boffetta P, Zhang ZF, et al. Cessation of alcohol drinking, tobacco smoking and the reversal of head and neck cancer risk. *International Journal of Epidemiology* . 2010;39(1):182-196. doi:10.1093/ije/dyp291.

- Chewing tobacco: risk x 1.20 (0.81-1.77)

Reference: Wyss AB, Hashibe M, Lee YA, et al. Smokeless Tobacco Use and the Risk of Head and Neck Cancer: Pooled Analysis of US Studies in the INHANCE Consortium. Am J Epidemiol 2016.

- Chewing Betel nuts: risk x 2.56 (2.00–3.28)

	Betel quid+Tobacco		Betel quid-Tobacco	
[Oral cavity]	8.47	6.49–11.05	2.41	1.82–3.19
[Oropharynx]	4.36	2.23–8.53	2.61	1.74–3.92
[Tongue]	4.10	2.61–6.45	1.61	1.12–2.31

Reference: Guha N, Warnakulasuriya S, Vlaanderen J, Straif K. Betel quid chewing and the risk of oral and oropharyngeal cancers: a meta-analysis with implications for cancer control. Int J Cancer 2014; 135:1433.

- Nutrition

- Vegetables : risk x 0.56 (0.31–1.01)

Reference: Freedman ND, Park Y, Subar AF, et al. Fruit and vegetable intake and head and neck cancer risk in a large United States prospective cohort study. Int J Cancer 2008; 122:2330.

- Coffee: risk x 0.64 (0.51–0.80)

Reference: Turati F, Galeone C, La Vecchia C, et al. Coffee and cancers of the upper digestive and respiratory tracts: meta-analyses of observational studies. Ann Oncol 2011; 22:536.

- Exposure

- Occupational exposure to formaldehyde

[Nasopharynx cancer]	Males	risk x	2.22	(1.03-4.23)
[Nasopharynx cancer]	Females	risk x	2.20	(1.04-4.06)

Reference: Li N, Zhai Z, Zheng Y, Lin S, Deng Y, Xiang G, Yao J, Xiang D, Wang S, Yang P, Yang S, Xu P, Wu Y, Hu J, Dai Z, Wang M. Association of 13 Occupational Carcinogens in Patients With Cancer, Individually and Collectively, 1990-2017. JAMA Netw Open. 2021 Feb 1;4(2):e2037530. doi: 10.1001/jamanetworkopen.2020.37530. PMID: 33599775; PMCID: PMC7893501.

- Exposure to wood dust: [Nasopharynx] risk x 2.4 (1.1-4.5)
- Exposure to asbestos: risk x 1.4 (1.04-2.0)

Reference: Marant Micallef C, Shield KD, Baldi I, Charbotel B, Fervers B, Gilg Soit Ilg A, Guénel P, Olsson A, Rushton L, Hutchings SJ, Straif K, Soerjomataram I. Occupational exposures and cancer: a review of agents and relative risk estimates. Occup Environ Med. 2018 Aug;75(8):604-614. doi: 10.1136/oemed-2017-104858. Epub 2018 May 7. PMID: 29735747.

- Exposure to Agent Orange: risk x 2.54 (1.13-5.70)

Reference: Sang‐Wook Yi, Heechoul Ohrr. Agent Orange exposure and cancer incidence in Korean Vietnam veterans: A prospective cohort study. Cancer. 2014 Dec 1;120(23):3699-706.

- BRCA2: risk x 2.26 (1.09-4.68)

Reference: Breast Cancer Linkage Consortium. Cancer risks in BRCA2 mutation carriers. J Natl Cancer Inst 1999; 91:1310.

- Chronic Condition

- Ulcerative colitis	[Tongue cancer]	risk x	3.49	(1.29-9.43)
- Diabetes (Type 1)	[Tonsil cancer]	risk x	3.57	(1.11-11.5)
- Rheumatic fever / rheumatic heart diseases	[Tongue cancer]	risk x	4.84	(1.53-15.3)
- Lichen planus	[Tongue cancer]	risk x	24.3	(8.96-65.8)
	[Mouth cancer]	risk x	9.31	(1.29-67.0)
- Sjögren syndrome	[Mouth cancer]	risk x	13.6	(1.86-99.1)
- Systemic lupus erythematosus	[Tonsil cancer]	risk x	11.54	(1.60- 83.4)
	[Mouth cancer]	risk x	10.9	(1.50-78.9)
- Idiopathic thrombocytopenic purpura	[Tongue cancer]	risk x	9.25	(1.29-66.2)
- Autoimmune hepatitis	[Tongue cancer]	risk x	27.7	(3.82-200)

Reference: He MM, Lo CH, Wang K, Polychronidis G, Wang L, Zhong R, Knudsen MD, Fang Z, Song M. Immune-Mediated Diseases Associated With Cancer Risks. JAMA Oncol. 2021 Dec 2:e215680. doi: 10.1001/jamaoncol.2021.5680. Epub ahead of print. PMID: 34854871; PMCID: PMC8640951.

- Hepatitis B: [Mouth cancer] risk x 1.58 (1.01-2.49)

Reference: Song C, Lv J, Liu Y, Chen JG, Ge Z, Zhu J, Dai J, Du LB, Yu C, Guo Y, Bian Z, Yang L, Chen Y, Chen Z, Liu J, Jiang J, Zhu L, Zhai X, Jiang Y, Ma H, Jin G, Shen H, Li L, Hu Z; China Kadoorie Biobank Collaborative Group. Associations Between Hepatitis B Virus Infection and Risk of All Cancer Types. JAMA Netw Open. 2019 Jun 5;2(6):e195718. doi: 10.1001/jamanetworkopen.2019.5718. PMID: 31199446; PMCID: PMC6575146.

- Genital Warts:		risk x	2.4	(1.4–3.8)
[Mouth]	Men	risk x	2.61.	(4–4.3)
	Women	risk x	2.9	(1.5–4.9)

Reference: Blomberg M, Friis S, Munk C, Bautz A, Kjaer SK. Genital warts and risk of cancer: a Danish study of nearly 50,000 patients with genital warts. J Infect Dis. 2012 May 15;205(10):1544-53. doi: 10.1093/infdis/jis228. Epub 2012 Mar 15. PMID: 22427679.

- HIV positivity: risk x 2.32 (1·65–3·25)
- History of organ transplantation: risk x 3.23 (2·40–4·35)

Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

- Xeroderma pigmentosum:		risk x	2000	

Reference: Kraemer KH, DiGiovanna JJ. Forty years of research on xeroderma pigmentosum at the US National Institutes of Health. Photochem Photobiol 2015; 91:452.

- Tooth brushing (≥once/day vs <once/day)		risk x	0.83	(0.79-0.88)
	[Oral cavity]	risk x	0.81	(0.75-0.88)
	[Oropharynx]	risk x	0.87	(0.80-0.95)
	[Hypopharynx]	risk x	0.80	(0.70-0.92)

Reference: Hashim D, Sartori S, Brennan P, et al. The role of oral hygiene in head and neck cancer: results from International Head and Neck Cancer Epidemiology (INHANCE) consortium. Ann Oncol 2016; 27:1619.

Ovarian cancer

- Current smoker risk x 1.11 (0.92-1.35)

Reference: Gates MA, Rosner BA, Hecht JL, Tworoger SS. Risk factors for epithelial ovarian cancer by histologic subtype. Am J Epidemiol. 2009;171(1):45-53.

- Family History
  - Family history of breast cancer risk x 1.29 (1.07-1.56)
  - Family history of ovarian cancer risk x 1.75 (1.19-2.57)

  Reference: Gates MA, Rosner BA, Hecht JL, Tworoger SS. Risk factors for epithelial ovarian cancer by histologic subtype. Am J Epidemiol. 2009;171(1):45-53.

- Female History:
  - IVF: risk x 1.36 (0.71–2.62)
  - Endometriosis: risk x 2.33 (1.02–5.35)
  - Tubal ligation: risk x 0.66 (0.26–1.68)
  - Hysterectomy: risk x 0.55 (0.13–2.32)
  - Hysterectomy with USO: risk x 0.72 (0.10–5.27)
  - Unilateral salpingo-oophorectomy (USO): risk x 4.23 (1.30–13.77)

  Reference: Stewart LM, Holman CD, Aboagye-Sarfo P, et al. In vitro fertilization, endometriosis, nulliparity and ovarian cancer risk. Gynecol Oncol 2013; 128:260.

  - Ovulatory years (per 1-year increase): risk x 1.07 (1.05-1.08)

  Reference: Gates MA, Rosner BA, Hecht JL, Tworoger SS. Risk factors for epithelial ovarian cancer by histologic subtype. Am J Epidemiol. 2009;171(1):45-53.

  - Pregnancies:
    - Never risk x 1.00
    - 1 risk x 0.80 (0.63–1.02)
    - 2 risk x 0.74 (0.61–0.91)
    - 3 risk x 0.64 (0.50–0.81)
    - ⩾4 risk x 0.62 (0.46–0.83)

  Reference: Tsilidis KK, Allen NE, Key TJ, et al. Oral contraceptive use and reproductive factors and risk of ovarian cancer in the European Prospective Investigation into Cancer and Nutrition. Br J Cancer. 2011;105(9):1436-1442. doi:10.1038/bjc.2011.371

  - Age at last birth
    - <25 risk x 1.0
    - 25–29 risk x 0.75 (0.52–1.10)
    - 30–34 risk x 0.56 (0.37–0.84)
    - 35+ risk x 0.57 (0.36–0.90)

  Reference: Whiteman DC, Siskind V, Purdie DM, Green AC. Timing of pregnancy and the risk of epithelial ovarian cancer. Cancer Epidemiol Biomarkers Prev 2003; 12:42.

  - Breastfeeding:
    - <6 months vs. Never risk x 0.83 (0.78-0.89)
    - 6–12 months vs. Never risk x 0.72 (0.66-0.78)
    - >12 months vs. Never risk x 0.63 (0.56-0.71)

  Reference: Chowdhury R, Sinha B, Sankar MJ, et al. Breastfeeding and maternal health outcomes: a systematic review and meta-analysis. Acta Paediatr 2015; 104:96.

  - Oral contraceptives:

	<5 years	5–9 years	10+ years
Current use or use less than 10 years previously	0·88 (0·75–1·04)	0·52 (0·43–0·64)	0·39 (0·33–0·47)
Last use 10–19 years previously	0·85 (0·75–0·97)	0·62 (0·53–0·73)	0·51 (0·44–0·59)
More than 20 years earlier	0·81 (0·74–0·89)	0·69 (0·60–0·78)	0·60 (0·51–0·72)

  Reference: Collaborative Group on Epidemiological Studies of Ovarian Cancer, Beral V, Doll R, et al. Ovarian cancer and oral contraceptives: collaborative reanalysis of data from 45 epidemiological studies including 23,257 women with ovarian cancer and 87,303 controls. Lancet 2008; 371:303.

  - Double oophorectomy: risk x 0 (risk falls to zero)
  - Transgender surgery for women: risk x 0 (risk falls to zero)

  Reference: /

- Intrauterine contraceptive : risk x 1.76 (1.08-2.85)
- Infertility: risk x 1.36 (1.07-1.75)
Reference: Tworoger SS, Fairfield KM, Colditz GA, et al. Association of oral contraceptive use, other contraceptive methods, and infertility with ovarian cancer risk. Am J Epidemiol 2007; 166:894.

- Ever use of genital talc: risk x 1.22 (1.13-1.30)
Reference: Berge W, Mundt K, Luu H, Boffetta P. Genital use of talc and risk of ovarian cancer: a meta-analysis. Eur J Cancer Prev. 2018 May;27(3):248-257. doi: 10.1097/CEJ.0000000000000340. PMID: 28079603.

- Medical History

- HIV positivity: risk x 1.63 (0·95–2·80)
- History of organ transplantation: risk x 1.55 (0·99–2·43)
Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

- Diabetes: risk x 2.42 (0.96-6.09)
Reference: Inoue M, Iwasaki M, Otani T, et al. Diabetes Mellitus and the Risk of Cancer: Results From a Large-Scale Population-Based Cohort Study in Japan. Arch Intern Med. 2006;166(17):1871–1877.

- Polycystic ovary syndrome: risk x 2.52 (1.08–5.89)
Reference: Chittenden BG, Fullerton G, Maheshwari A, Bhattacharya S. Polycystic ovary syndrome and the risk of gynecological cancer: a systematic review. Reprod Biomed Online 2009; 19:398.

-Peutz-Jeghers syndrome (STK11): risk x 27 (7.3-68)
Reference: Francis M. Giardiello, Jill D. Brensinger, Anne C. Tersmette, Steven N. Goodman, Gloria M. Petersen, Susan V. Booker, Marcia Cruz–Correa, Johan A. Offerhaus. Very high risk of cancer in familial Peutz–Jeghers syndrome. Gastroenterology, Volume 119, Issue 6, December 2000, Pages 1447-1453

- Lynch syndrome (mismatch repair genes MLH1, MSH2, MSH6): risk x 18.81 (3.88-54.95)
Reference: Win AK, Young JP, Lindor NM, et al. Colorectal and other cancer risks for carriers and noncarriers from families with a DNA mismatch repair gene mutation: a prospective cohort study. J Clin Oncol 2012; 30:958.

- Pelvic inflammatory disease: risk x 1.92 (1·27–2·92)
Reference: Lin HW, Tu YY, Lin SY, Su WJ, Lin WL, Lin WZ, Wu SC, Lai YL. Risk of ovarian cancer in women with pelvic inflammatory disease: a population-based study. Lancet Oncol. 2011 Sep;12(9):900-4.

- BMI 25-29.9: risk x 1.2 (1.0-1.3)
30 or more: risk x 1.3 (1.1-1.5)
Reference: Olsen CM, Green AC, Whiteman DC, et al. Obesity and the risk of epithelial ovarian cancer: a systematic review and meta-analysis. Eur J Cancer 2007; 43:690.

- Nutrition

- High soy intake: risk x 0.52 (0.42–0.66)
Reference: Myung SK, Ju W, Choi HJ, et al. Soy intake and risk of endocrine-related gynecological cancer: a meta-analysis. BJOG 2009; 116:1697.

- Regularly drink green tea: risk x 0.66 (0.54-0.80)
Reference: Butler LM, Wu AH. Green and black tea in relation to gynecologic cancers. Mol Nutr Food Res 2011; 55:931.

- Exposure to asbestos: risk x 1.77 (1.37-2.28)
Reference: Camargo MC, Stayner LT, Straif K, et al. Occupational exposure to asbestos and ovarian cancer: a meta-analysis. Environ Health Perspective. 2011;119(9):1211-7.

-Mutation

ATM risk x 1.69 (1.19-2.40)
BRCA1 risk x 11.8 (9.99-14.0)
BRCA2 risk x 5.26 (4.38-6.31)
BRIP1 risk x 2.62 (1.72-3.98)
MLH1 risk x 3.11 (1.47-6.59)
MSH2 risk x 2.04 (1.08-3.84)

MSH6			risk x	1.92 (1.19-3.10)
NBN			risk x	1.85 (1.05-3.24)
RAD51C			risk x	4.98 (3.09-8.04)
RAD51D			risk x	4.78 (2.13-10.7)

Reference: Allison W. Kurian, Elisha Hughes, Elizabeth A. Handorf, Alexander Gutin, Brian Allen, Anne-Renee Hartman, Michael J. Hall. Breast and Ovarian Cancer Penetrance Estimates Derived From Germline Multiple-Gene Sequencing Results in Women. JCO Precision Oncology 2017 :1, 1-12

- Medication

- Aspirin intake:		risk x	0.90 (0.82-1.00)
- Paracetamol intake (daily):		risk x	1.28 (1.00-1.65)

Reference: Trabert B., Poole EM, White E., Visvanathan K., Adami HO, Anderson GL, Brasky TM, Brinton LA, Fortner RT, Gaudet M., et al. Analgesic Use and Ovarian Cancer Risk: An Analysis in the Ovarian Cancer Cohort Consortium. J. Natl. Cancer Inst. 2018 doi: 10.1093/jnci/djy100.

- History of cancer

- History of Basocellular skin carcinoma:

Number of BCCs:	12+	risk x	2.01 (1.07–3.74)

Reference: Cho HG et al. Frequent basal cell cancer development is a clinical marker for inherited cancer susceptibility. JCI Insight. 2018; 3(15): e122744.

Pancreatic cancer

-Mutation

- BRCA1: risk x 2.26 (1.26-4.06)
Reference: Thompson D, Easton DF, Breast Cancer Linkage Consortium. Cancer Incidence in BRCA1 mutation carriers. J Natl Cancer Inst 2002; 94:1358.

- BRCA2: risk x 3.51 (1.87-6.58)
Reference: Breast Cancer Linkage Consortium. Cancer risks in BRCA2 mutation carriers. J Natl Cancer Inst 1999; 91:1310.

- FAMMM (CDKN2A): risk x 21.8 (8.7-44.8)
Reference: Goldstein AM, Fraser MC, Struewing JP, et al. Increased risk of pancreatic cancer in melanoma-prone kindreds with p16INK4 mutations. N Engl J Med 1995; 333:970.

- Presence of ATM gene variant: risk x 3.81 (1.98–7.34)
Reference: Helgason H, Rafnar T, Olafsdottir HS, et al. Loss-of-function variants in ATM confer risk of gastric cancer. Nat Genet 2015; 47:906.

-Family history

- 1 first-degree relative affected: risk x 4.6 (0.5–16.4)
- 2 first-degree relative affected : risk x 6.4 (1.8–16.4)
- 3 first-degree relative affected : risk x 32.0 (10.2–74.7)
Reference: Klein AP, Brune KA, Petersen GM, et al. Prospective risk of pancreatic cancer in familial pancreatic cancer kindreds. Cancer Res 2004; 64:2634.

- Medical History

- Lynch syndrome (mismatch repair genes MLH1, MSH2, MSH6): risk x 10.68 (2.68-47.70)
Reference: Win AK, Young JP, Lindor NM, et al. Colorectal and other cancer risks for carriers and noncarriers from families with a DNA mismatch repair gene mutation: a prospective cohort study. J Clin Oncol 2012; 30:958.

- Hereditary pancreatitis (PRSS1, SPINK1): risk x 53 (23-105)
Reference: Lowenfels AB, Maisonneuve P, DiMagno EP, Elitsur Y, Gates LK Jr, Perrault J, Whitcomb DC. Hereditary pancreatitis and the risk of pancreatic cancer. International Hereditary Pancreatitis Study Group. J Natl Cancer Inst. 1997 Mar 19;89(6):442-6. doi: 10.1093/jnci/89.6.442. PMID: 9091646.

- Peutz-Jeghers syndrome (STK11): risk x 132 (44-261)
Reference: Francis M. Giardiello, Jill D. Brensinger, Anne C. Tersmette, Steven N. Goodman, Gloria M. Petersen, Susan V. Booker, Marcia Cruz–Correa, Johan A. Offerhaus. Very high risk of cancer in familial Peutz–Jeghers syndrome. Gastroenterology, Volume 119, Issue 6, December 2000, Pages 1447-1453

- Chronic pancreatitis: risk x 11.8 (5.8–24.1)
Reference: Raimondi S, Lowenfels AB, Morselli-Labate AM, Maisonneuve P, Pezzilli R. Pancreatic cancer in chronic pancreatitis; aetiology, incidence, and early detection. Best Practice Res Clin Gastroenterol. 2010 Jun;24(3):349-58. doi: 10.1016/j.bpg.2010.02.007. PMID: 20510834.

- Diabetes: risk x 1.97 (1.78–2.18)
Reference: Batabyal P, Vander Hoorn S, Christophi C, Nikfarjam M. Association of diabetes mellitus and pancreatic adenocarcinoma: a meta-analysis of 88 studies. Ann Surg Oncol 2014; 21:2453.

-Cystic fibrosis : risk x 6.18 (1·31–29·27)
Reference: Yamada A, Komaki Y, Komaki F, et al. Risk of gastrointestinal cancers in patients with cystic fibrosis: a systematic review and meta-analysis. Lancet Oncol 2018; 19:758.

- History of Hepatitis C infection: risk x 2.1 (1.4-2.9)
Reference: Huang J, Magnusson M, Törner A, et al. Risk of pancreatic cancer among individuals with hepatitis C or hepatitis B virus infection: a nationwide study in Sweden. Br J Cancer 2013; 109:2917.

- Diagnosed pancreatic cysts : risk x 15.6 (7.5−28.7)
Reference: Pergolini I, Sahora K, Ferrone CR, et al. Long-term Risk of Pancreatic Malignancy in Patients With Branch Duct Intraductal Papillary Mucinous Neoplasm in a Referral Center. Gastroenterology 2017; 153:1284.

-History of Multiple myeloma: risk x 1.30 (1.09-1.53)
-History of MGUS: risk x 1.25 (1.05-1.48)

Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

- Hepatitis B: risk x 1.65 (1.03-2.65)
Reference: Song C, Lv J, Liu Y, Chen JG, Ge Z, Zhu J, Dai J, Du LB, Yu C, Guo Y, Bian Z, Yang L, Chen Y, Chen Z, Liu J, Jiang J, Zhu L, Zhai X, Jiang Y, Ma H, Jin G, Shen H, Li L, Hu Z; China Kadoorie Biobank Collaborative Group. Associations Between Hepatitis B Virus Infection and Risk of All Cancer Types. JAMA Netw Open. 2019 Jun 5;2(6):e195718. doi: 10.1001/jamanetworkopen.2019.5718. PMID: 31199446; PMCID: PMC6575146.

- Blood type
  - A: risk x 1.32 (1.02-1.72)
  - AB: risk x 1.51 (1.02-2.23)
  - B: risk x 1.72 (1.25-2.38)

Reference: Wolpin BM, Chan AT, Hartge P, et al. ABO blood group and the risk of pancreatic cancer. J Natl Cancer Inst 2009; 101:424.

- Smoking:

Intensity (cigarettes per day)	Risk x
<15	1.60 (1.24–2.06)
15 to <25	2.30 (1.76–3.01)
25 to <35	2.76 (1.92–3.97)
≥35	3.38 (2.36–4.86)
Duration (years)	
<20	1.46 (0.89–2.40)
20 to <30	1.85 (1.44–2.37)
30 to <40	2.43 (1.91–3.09)
≥40	2.10 (1.58–2.78)
Years since quitting	
1 to <10	0.73 (0.56–0.95)
10 to <15	0.62 (0.49–0.80)
15 to <20	0.46 (0.35–0.60)
20 to <30	0.41 (0.30–0.56)
≥30	0.42 (0.29–0.60)

Reference: Bosetti C, Lucenteforte E, Silverman DT, et al. Cigarette smoking and pancreatic cancer: an analysis from the International Pancreatic Cancer Case-Control Consortium (Panc4). Ann Oncol. 2011;23(7):1880-8.

- BMI: For women, per 5 kg/m² increase in BMI (above 25): risk x 1.12 (1.03-1.23)
Reference: Renehan AG, Tyson M, Egger M, et al. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 2008; 371:569.

- Length (per 2.5 cm, from 160 cm) : risk x 1.06 (0.99-1.12)
Reference: Michaud DS, Giovannucci E, Willett WC, et al. Physical activity, obesity, height, and the risk of pancreatic cancer. JAMA 2001; 286:921.

- History of infection with Helicobacter pylori: risk x 1.47 (1.22-1.77)
Reference: Xiao M, Wang Y, Gao Y. Association between Helicobacter pylori infection and pancreatic cancer development: a meta-analysis. PLoS One 2013; 8:e75559.

- Physical activity (hours per week):
  - less than 1 hour: no difference

- between 1 and 3 hours: risk x 1.06 (0.73-1.54)
- between 3 and 6 hours: risk x 0.91 (0.61-1.34)
- between 6 and 11 hours: risk x 0.88 (0.59-1.32)
- more than 11 hours: risk x 0.74 (0.49-1.14)

Reference: Michaud DS, Giovannucci E, Willett WC, Colditz GA, Stampfer MJ, Fuchs CS. Physical Activity, Obesity, Height, and the Risk of Pancreatic Cancer. JAMA. 2001;286(8):921–929. doi:10.1001/jama.286.8.921

-Night work: risk x 2.27 (1.24-4.15)

Reference: Parent, M. -E.; El-Zein, M.; Rousseau, M. -C.; Pintos, J.; Siemiatycki, J. (2012). "Night Work and the Risk of Cancer Among Men". American Journal of Epidemiology. 176(9):751–759.

- Coffee: risk x 0.82 (0.69-0.95)

Reference: Yu X, Bao Z, Zou J, Dong J. Coffee consumption and risk of cancers: a meta-analysis of cohort studies. BMC Cancer. 2011;11:96. Published 2011 Mar 15. doi:10.1186/1471-2407-11-96

- Aspirin intake: risk x 0.78 (0.68–0.89)

Reference: Bosetti C, Santucci C, Gallus S, Martinetti M, La Vecchia C. Aspirin and the risk of colorectal and other digestive tract cancers: an updated meta-analysis through 2019. Ann Oncol. 2020 May;31(5):558-568. doi: 10.1016/j.annonc.2020.02.012. Epub 2020 Apr 1. PMID: 32272209.

Penile cancer

- Medical History

- HIV positivity:	risk x	4.42	(2·77–7·07)
- History of organ transplantation:	risk x	15.79	(5·79–34·4)

Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

-History of MGUS:	risk x	1.32	(1.11-1.57)

Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

-Genital warts:	risk x	8.2	(4.1–14.6)

Reference: Blomberg M, Friis S, Munk C, Bautz A, Kjaer SK. Genital warts and risk of cancer: a Danish study of nearly 50,000 patients with genital warts. J Infect Dis. 2012 May 15;205(10):1544-53. doi: 10.1093/infdis/jis228. Epub 2012 Mar 15. PMID: 22427679.

Education > 12 years after age 6:	risk x	0.7	(0.5–1.0)
Marital status			
Married/living as married/widowed	risk x	1.0	
Never married	risk x	2.5	(1.1–5.6)
Separated/divorced	risk x	1.3	(0.7–2.2)
Lifetime number of female sex partners			
2–4	risk x	2.1	(1.0–4.0)
5–14	risk x	1.8	(0.9–3.5)
15+	risk x	2.4	(1.3–4.7)
Cigarette smoking status			
Former	risk x	1.4	(0.8–2.3)
Current	risk x	2.3	(1.4–4.0)
Circumcised in childhood			
Yes	risk x	1.0	
Never circumcised	risk x	1.4	(0.9–2.1)
Genital warts	risk x	7.6	(4.3–13.5)
Genital Herpes	risk x	3.0	(1.9–4.7)
HPV 16 serology	risk x	1.9	(1.2–3.2)
Gonorrhea (Ever)	risk x	1.5	(0.9–2.7)
Urinary tract infections (Ever)	risk x	1.7	(1.1–2.7)
Phimosis	risk x	7.4	(3.7–15.0)
Smegma (Sometimes/usually)	risk x	1.9	(0.7–5.4)
Penile tear	risk x	5.2	(3.1–8.7)
Penile rash	risk x	14.9	(7.2–30.8)
Penile injury	risk x	3.2	(1.5–6.8)
Penile inflammation	risk x	3.5	(1.5–8.5)
Urethral stricture	risk x	2.0	(1.1–3.9)

Reference: Daling JR, Madeleine MM, Johnson LG, et al. Penile cancer: importance of circumcision, human papillomavirus and smoking in in situ and invasive disease. Int J Cancer 2005; 116:606.

- Habits

-Tobacco chewing:	risk x	4.082	(12.72-3.107)
-Chewing betel nut:	risk x	3.046	(2.086-4.449)
-Sniffing tobacco:	risk x	4.121	(1.589-11.260)

Reference: Harish K, Ravi R. The role of tobacco in penile carcinoma. Br J Urol 1995; 75:375.

-Treatment with PUVA: risk x 5 8.8 (26.9-111.7)
Reference: Stern RS. Genital tumors among men with psoriasis exposed to psoralens and ultraviolet A radiation (PUVA) and ultraviolet B radiation. The Photochemotherapy Follow-up Study. N Engl J Med 1990; 322:1093.

- Zoophilia: risk x 2.07 (1.21–3.52)
Reference: Zequi Sde C, Guimarães GC, da Fonseca FP, et al. Sex with animals (SWA): behavioral characteristics and possible association with penile cancer. A multicenter study. J Sex Med 2012; 9:1860.

- Transgender surgery for men: risk x 0 (risk falls to zero)
Reference: /

Prostate cancer

- Family history

-1 first-degree relative: risk x 2.5 (2.2–2.8)
-2 first-degree relative: risk x 3.5 (2.6–4.8)
Reference: Johns LE, Houlston RS. A systematic review and meta-analysis of familial prostate cancer risk. BJU Int. 2003 Jun;91(9):789-94. doi: 10.1046/j.1464-410x.2003.04232.x. PMID: 12780833.

- Mutations

- Presence of HOBX13 gene: risk x 3.23 (2,313–4,560)
Reference: Cai Q, Wang Oncotarget 2015; 6:42312.

- Presence of BRCA2 gene: risk x 2.64 (2.03-3.47)
- Presence of BRCA1 gene: risk x 1.35 (1.03-1.76)
Reference :Mok Oh, Rana Aljadeed, Nasser Mubarak Al Khushaym, Abdulhamid Althagafi, Saad Fallatah, Hani M. Babiker, Ali McBride, Ivo Abraham The association of BRCA1 and BRCA2 mutations on prostate cancer risk, frequency, and mortality: Systematic review and meta -analysis. Journal of Clinical Oncology 36, no. 15_suppl (May 2018) 5060-5060.

- Presence of ATM gene variant: risk x 2.18 (1.40–3.39)
Reference: Helgason H, Rafnar T, Olafsdottir HS, et al. Loss-of-function variants in ATM confer risk of gastric cancer. Nat Genet 2015; 47:906.

- Presence of CHEK2 mutation: risk x 1.60 (1.00-2.56)
Reference: Näslund-Koch C, Nordestgaard BG, Bojesen SE. Increased Risk for Other Cancers in Addition to Breast Cancer for CHEK2*1100delC Heterozygotes Estimated From the Copenhagen General Population Study. J Clin Oncol 2016; 34:1208.

- Presence of NBN (also called NBS1) mutation: risk x 4.5 (1.7–11.5)
Reference: Cybulski C, Górski B, Debniak T, et al. NBS1 is a prostate cancer susceptibility gene. Cancer Res 2004; 64:1215.

-Chronic Condition

- Diagnosis of Lynch syndrome: risk x 1.99 (1.31-3.03)
Reference: Raymond VM, Mukherjee B, Wang F, et al. Elevated risk of prostate cancer among men with Lynch syndrome. J Clin Oncol 2013; 31:1713.

- Klinefelter syndrome: risk x 0.2 (0.02-0.7)
Reference: Swerdlow AJ, Schoemaker MJ, Higgins CD, Wright AF, Jacobs PA; UK Clinical Cytogenetics Group. Cancer incidence and mortality in men with Klinefelter syndrome: a cohort study. J Natl Cancer Inst. 2005 Aug 17;97(16):1204-10. doi: 10.1093/jnci/dji240. PMID: 16106025.

- History of MGUS: risk x 1.32 (1.11-1.57)
Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

- Rheumatoid arthritis risk x 0.62 (0.41-0.94)
- Ulcerative colitis risk x 1.45 (1.13-1.85)
- Diabetes (Type 1) risk x 0.67 (0.46-0.97)
Reference: He MM, Lo CH, Wang K, Polychronidis G, Wang L, Zhong R, Knudsen MD, Fang Z, Song M. Immune-Mediated Diseases Associated With Cancer Risks. JAMA Oncol. 2021 Dec 2:e215680. doi: 10.1001/jamaoncol.2021.5680. Epub ahead of print. PMID: 34854871; PMCID: PMC8640951.

- Nutrition

- High intake of red meat: risk x 1.1 2 (1.04-1.21)
- Intake of processed meat: risk x 1.07 (1.00-1.14)
Reference: Sinha R, Park Y, Graubard BI, et al. Meat and meat-related compounds and risk of prostate cancer in a large prospective cohort study in the United States. Am J Epidemiol 2009; 170:1165.

- Tomatoes: risk x 0.91 (0.56-0.94)
Reference: Zu K, Mucci L, Rosner BA, et al. Dietary lycopene, angiogenesis, and prostate cancer: a prospective study in the prostate-specific antigen era. J Natl Cancer Inst 2014; 106:djt430.

- Soya intake: risk x 0.7 (0.59-0.83)
Reference: Yan L, Spitznagel EL. Meta-analysis of soy food and risk of prostate cancer in men. Int J Cancer 2005; 117:667

- Eating mushrooms: 1–2 times/week: risk x 0.92 (0.81-1.05)
≥3 times/week: risk x 0.83 (0.70-0.98)
Reference: Zhang, S., Sugawara, Y., Chen, S., Beelman, RB, Tsuduki, T., Tomata, Y., Matsuyama, S. and Tsuji, I. (2019), Mushroom consumption and incident risk of prostate cancer in Japan: A pooled analysis of the Miyagi Cohort Study and the Ohsaki Cohort Study. Int. J Cancer.

-Supplements

- High folic acid intake: risk x 2.63 (1.23-5.65)
Reference: Figueiredo JC, Grau MV, Haile RW, et al. Folic acid and risk of prostate cancer: results from a randomized clinical trial. J Natl Cancer Inst 2009; 101:432.

- Large intake of B12: risk x 1.12 (1.01–1.25)
Reference: Price AJ, Travis RC, Appleby PN, et al. Circulating Folate and Vitamin B12 and Risk of Prostate Cancer: A Collaborative Analysis of Individual Participant Data from Six Cohorts Including 6875 Cases and 8104 Controls. Euro Urol 2016; 70:941.

- Large selenium intake: risk x 0.86 (0.78-0.94)
Reference: Sayehmiri K, Azami M, Mohammadi Y, Soleymani A, Tardeh Z. The association between Selenium and Prostate Cancer: a Systematic Review and Meta-Analysis. Asian Pac J Cancer Prev. 2018 Jun 25;19(6):1431-1437. doi: 10.22034/APJCP.2018.19.6.1431. PMID: 29936712; PMCID: PMC6103565.

- High zinc intake: risk x 2.37 (1.42-3.95)
Reference: Leitzmann MF, Stampfer MJ, Wu K, et al. Zinc supplement use and risk of prostate cancer. J Natl Cancer Inst 2003; 95:1004.

- High calcium intake: risk x 1.39 (1.09-1.77)
- Large milk intake: risk x 1.11 (1.00-1.22)
Reference: Gao X, LaValley MP, Tucker KL. Prospective studies of dairy product and calcium intakes and prostate cancer risk: a meta-analysis. J Natl Cancer Inst 2005; 97:1768.

- Per 5 kg/m² increase in BMI (above 25): risk x 1.03 (1.00-1.07)
Reference: Renehan AG, Tyson M, Egger M, et al. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 2008; 371:569.

- History of prostatitis: risk x 2.12 (1.38-3.22)
Reference: Perletti G, Monti E, Magri V, et al. The association between prostatitis and prostate cancer. Systematic review and meta-analysis. Arch Ital Urol Androl 2017; 89:259.

- History of gonorrhea: risk x 5.66 (1.36-23.52)
Reference: Wang YC, Chung CH, Chen JH, et al. Gonorrhea infection increases the risk of prostate cancer in Asian population: a nationwide population-based cohort study. Eur J Clin Microbiol Infect Dis 2017; 36:813.

- Low sunlight exposure: risk x 3.03 (1·59–5·78)
Reference: Luscombe CJ, Fryer AA, French ME, et al. Exposure to ultraviolet radiation: association with susceptibility and age at presentation with prostate cancer. Lancet 2001; 358:641.

- History of barium enema: risk x 2.06 (1.01–4.20)
- History of pelvic X-ray photographs: risk x 2.23 (1.42–3.49)
Reference: Myles P, Evans S, Lophatananon A, et al. Diagnostic radiation procedures and risk of prostate cancer. Br J Cancer 2008; 98:1852.

-Medication

- Long-term intake (= daily for 5 years or more) of NSAIDS: risk x 0.82 (0.71-0.94)
- Long-term intake (= daily for 5 years or more) of aspirin: risk x 0.85 (0.73-0.99)

Reference: Jacobs EJ, Rodriguez C, Mondul AM, et al. A large cohort study of aspirin and other nonsteroidal anti-inflammatory drugs and prostate cancer incidence. J Natl Cancer Inst 2005; 97:975.

- Finasteride intake: risk x 0.70 (0.65-0.76)
Reference: Thompson IM Jr, Goodman PJ, Tangen CM, et al. Long-term survival of participants in the prostate cancer prevention trial. N Engl J Med 2013; 369:603.

- Dutasteride intake: risk x 0.772 (0.702-0.848)
Reference: Andriole GL, Bostwick DG, Brawley OW, et al. Effect of dutasteride on the risk of prostate cancer. N Engl J Med 2010; 362:1192.

-Statin intake: risk x 0.93 (0.87–0.99)
Reference: Bansal D, Undela K, D'Cruz S, Schifano F. Statin use and risk of prostate cancer: a meta-analysis of observational studies. PLoS One. 2012;7(10):e46691. doi:10.1371/journal.pone.0046691

-Night work: risk x 2.77 (1.96-3.92)
Reference: Parent, M. -E.; El-Zein, M.; Rousseau, M. -C.; Pintos, J.; Siemiatycki, J. (2012). "Night Work and the Risk of Cancer Among Men". American Journal of Epidemiology. 176(9):751–759.

- Coffee: risk x 0.79 (0.61-0.98)
Reference: Yu X, Bao Z, Zou J, Dong J. Coffee consumption and risk of cancers: a meta-analysis of cohort studies. BMC Cancer. 2011;11:96. Published 2011 Mar 15. doi:10.1186/1471-2407-11-96

- History of cancer

- History of Basocellular skin carcinoma:

Number of BCCs:	1	risk x	1.11	(1.06–1.17)
	6+	risk x	1.32	(1.17–1.47)
	12+	risk x	1.43	(1.15–1.79)

Reference: Cho HG et al. Frequent basal cell cancer development is a clinical marker for inherited cancer susceptibility. JCI Insight. 2018; 3(15): e122744.

- History of rectal cancer treated with radiotherapy: risk x 0.28 (0.17-0.43)
Reference: Hoffman KE, Hong TS, Zietman AL, Russell AH. External beam radiation treatment for rectal cancer is associated with a decrease in subsequent prostate cancer diagnosis. Cancer 2008; 112:943.

-Exposure

- Exposure to arsenic: risk x 1.28 (1.21-1.35)
Reference: Roh T, Lynch CF, Weyer P, et al. Low-level arsenic exposure from drinking water is associated with prostate cancer in Iowa. Environ Res 2017; 159:338.

- Exposure to Agent Orange: risk x 2.19 (1.75-2.75)
Reference: Chamie K, DeVere White RW, Lee D, et al. Agent Orange exposure, Vietnam War veterans, and the risk of prostate cancer. Cancer 2008; 113:2464.

- Exposure to Chlordecone: risk x 1.77 (1.21-2.58)
Reference: Multigner L, Ndong JR, Giusti A, et al. Chlordecone exposure and risk of prostate cancer. J Clin Oncol 2010; 28:3457.

Melanoma

- Use sunbed: Ever: risk x 1.16 (1.05-1.28)
More than 1 year: risk x 1.61 (0.98-2.67)

Reference: Colantonio S, Bracken MB, Beecker J. The association of indoor tanning and melanoma in adults: systematic review and meta-analysis. J Am Acad Dermatol 2014; 70:847.

- History of PUVA treatment: risk x 8.4 (3.4-17.3)

Reference: Stern RS, PUVA Follow up Study. The risk of melanoma in association with long-term exposure to PUVA. J Am Acad Dermatol 2001; 44:755.

- Mutation

- BRCA2 mutation: risk x 2.58 (1.28-5.17)

Reference: Easton D, The Breast Cancer Linkage Consortium. Cancer risks in BRCA2 mutation carriers. J Natl Cancer Inst 1999; 91:1310.

- CDKN2A mutation: risk x 53
- MC1R mutation: risk x 2.75

Reference: High WA, Robinson WA. Genetic mutations involved in melanoma: a summary of our current understanding. Adv Dermatol 2007; 23:61.

- Family History

- Parent risk x 2.40 (2.10–2.72)
- Sibling risk x 2.98 (2.54–3.47)
- Two first-degree relatives: risk x 8.92 (4.25–15.31)
- Parent with multiple primary melanomas: risk x 61.78 (5.82–227.19)

Reference: Hemminki K, Zhang H, Czene K. Familial and attributable risks in cutaneous melanoma: effects of proband and age. J Invest Dermatol 2003; 120:217.

- Physical attributes

- Birthmarks (normal vs atypical):

Atypical nevi

0	risk x	1.00	
1	risk x	1.45	(1.31-1.60)
2	risk x	2.10	(1.71-2.54)
3	risk x	3.03	(2.23-4.06)
4	risk x	4.39	(2.91-6.47)
5	risk x	6.36	(3.80-10.33)

Typical nevi

0–15	risk x	1.00	
16–40	risk x	1.47	(1.36-1.59)
41–60	risk x	2.24	(1.90-2.64)
61–80	risk x	3.26	(2.55-4.15)
81–100	risk x	4.74	(3.44-6.53)
101–120	risk x	6.89	(4.63-10.25)

Reference: Gandini S, Sera F, Cattaruzza MS, Pasquini P, Abeni D, Boyle P, Melchi CF. Meta-analysis of risk factors for cutaneous melanoma: I. Common and atypical nevi. Eur J Cancer. 2005 Jan;41(1):28-44. doi: 10.1016/j.ejca.2004.10.015. PMID: 15617989.

Actinic damage indicators:		4.28 (2.80-6.55)
Density of freckles	High vs. Low	2.10 (1.80-2.45)
Eye color	Blue vs. Dark	1.47 (1.28-1.69)
	Green vs. Dark	1.61 (1.06-2.45)
	Hazel vs. Dark	1.52 (1.26-1.83)
Hair color	Red vs. Dark	3.64 (2.56-5.37)
	Blonde vs. Dark	1.96 (1.41-2.74)
	Light brown vs. Dark	1.62 (1.11-2.34)

Reference: Gandini S, Sera F, Cattaruzza MS, et al. Meta-analysis of risk factors for cutaneous melanoma: III. Family history, actinic damage and phenotypic factors. Eur J Cancer 2005; 41:2040.

- Solar Exposure:	Intermittent	risk x	1.61	(1.31-1.99)
	Chronic	risk x	0.95	(0.87-1.04)
	High total solar exposure	risk x	1.34	(1.02-1.77)
- History of sunburn:		risk x	2.03	(1.73-2.37)

Reference: Gandini S, Sera F, Cattaruzza MS, Pasquini P, Picconi O, Boyle P, Melchi CF., Meta-analysis of risk factors for cutaneous melanoma: II. Sun exposure, Eur J Cancer. 2005 Jan;41(1):45-60.

- Alcohol: risk x 1.20 (1·06–1·37)

Reference: Alcohol drinking and cutaneous melanoma risk: a systematic review and dose-risk meta-analysis. M. Rota, E. Pasquali, R. Bellocco, V. Bagnardi, L. Scotti, F. Islami, E. Negri, P. Boffetta, C. Pelucchi, G. Corrao, et al. Br J Dermatol. 2014 May; 170(5): 1021–1028. doi: 10.1111/bjd.12856

- Medication

-Sildenafil: risk x 1.84 (1.04-3.22)

Reference: Li WQ, Qureshi AA, Robinson KC, Han J. Sildenafil use and increased risk of incident melanoma in US men: a prospective cohort study. JAMA Intern Med 2014; 174:964.

- Medications for long term daily use

Bendroflumethiazide:	risk x	1.3	(1.0-1.6)
Enalapril:	risk x	1.1	(1.0-1.2)
Methyldopa	risk x	1.5	(1.0-2.3)
Sotalol	risk x	1.2	(1.0-1.4)
Verapamil	risk x	1.1	(1.0-1.2)
Methotrexate	risk x	2.9	(1.3-6.5)

- Medications for short term use

Acyclovir	risk x	1.1	(1.0-1.2)
Doxycycline	risk x	1.1	(1.0-1.2)
Ketoconazole	risk x	1.1	(1.0-1.2)
Tetracycline	risk x	1.1	(1.1-1.3)
Hydroxychloroquine	risk x	1.2	(1.1-1.3)
Acitretin	risk x	1.2	(0.7-2.0)
Isotretinoin	risk x	1.3	(1.0-1.8)

Reference: Kaae J, Boyd HA, Hansen AV, Wulf HC, Wohlfahrt J, Melbye M. Photosensitizing medication use and risk of skin cancer. Cancer Epidemiol Biomarkers Prev. 2010 Nov;19(11):2942-9. doi: 10.1158/1055-9965.EPI-10-0652. Epub 2010 Sep 22. PMID: 20861398.

- For men, per 5 kg/m² increase in BMI (above 25): risk x 1.17 (1.05-1.30)

Reference: Renehan AG, Tyson M, Egger M, et al. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 2008; 371:569.

- Flight crew, women: risk x 2.27 (1.27–4.06)

Reference: McNeely E, Mordukhovich I, Staffa S, Tideman S, Gale S, Coull B. Cancer prevalence among flight attendants compared to the general population. Environ Health. 2018;17(1):49. Published 2018 Jun 26. doi:10.1186/s12940-018-0396-8

-Chronic Condition:

- History of Endometriosis:	risk x	1.62	(1.15–2.29)
- History of Fibroma:	risk x	1.33	(1.06–1.67)

Reference: Kvaskoff M, Mesrine S, Fournier A, et al. Personal history of endometriosis and risk of cutaneous melanoma in a large prospective cohort of French women. Arch Intern Med 2007; 167:2061.

- History of Parkinson's: risk x 1.95 (1.4–2.6)

Reference: Olsen JH, Friis S, Frederiksen K, et al. Atypical cancer pattern in patients with Parkinson's disease. Br J Cancer 2005; 92:201.

- Xeroderma pigmentosum: risk x 2000
Reference: Kraemer KH, DiGiovanna JJ. Forty years of research on xeroderma pigmentosum at the US National Institutes of Health. Photochem Photobiol. 2015;91(2):452-9.

- Cowden syndrome: risk x 8.5 (4.1–15.6)
Reference: Tan MH, Mester JL, Ngeow J, et al. Lifetime cancer risks in individuals with germline PTEN mutations. Clin Cancer Res 2012; 18:400.

- Celiac disease: risk x 5.0 (2.1–12)
Reference: Green PH, Fleischauer AT, Bhagat G, et al. Risk of malignancy in patients with celiac disease. Am J Med 2003; 115:191.

- Epidermolysis bullosa: risk x 2
Reference: Mallipeddi R. Epidermolysis bullosa and cancer. Clin Exp Dermatol. 2002 Nov;27(8):616-23. doi: 10.1046/j.1365-2230.2002.01130.x. PMID: 12472531.

- HIV positivity: risk x 1.24 (1·04–1·48)
- History of organ transplantation: risk x 2.34 (1·98–2·77)
Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

-History of cancer

- History of childhood cancer: risk x 4.04 (2.43-6.32)
Reference: Neglia JP, Friedman DL, Yasui Y, Mertens AC, Hammond S, Stovall M, Donaldson SS, Meadows AT, Robison LL, Second malignant neoplasms in five-year survivors of childhood cancer: childhood cancer survivor study., J Natl Cancer Inst. 2001 Apr 18;93(8):618-29.

- History of Basocellular skin carcinoma (if active, the risk increase for non-melanoma skin cancer should disappear):
Number of BCCs: 1 risk x 5.44 (5.22–5.67)
6+ risk x 16.04 (15.06–17.10)
12+ risk x 19.93 (17.73–22.40)
Reference: Cho HG et al. Frequent basal cell cancer development is a clinical marker for inherited cancer susceptibility. JCI Insight. 2018; 3(15): e122744.

- History of Prostate Cancer: risk x 1.83 (1.32-2.54)
Reference: Li WQ, Qureshi AA, Ma J, et al. Personal history of prostate cancer and increased risk of incident melanoma in the United States. J Clin Oncol 2013; 31:4394.

Stomach cancer

- Nutrition

- High salt intake:		risk x	2.98	(1.53–5.82)

Reference: Shikata K, Kiyohara Y, Kubo M, et al. A prospective study of dietary salt intake and gastric cancer incidence in a defined Japanese population: the Hisayama study. Int J Cancer 2006; 119:196.

- Intake of processed meat:		risk x	1.15	(1.04-1.27)

Reference: Larsson SC, Orsini N, Wolk A. Processed meat consumption and stomach cancer risk: a meta-analysis. J Natl Cancer Inst 2006; 98:1078.

- Fruit intake:		risk x	0.60	
	[Cardia]	risk x	0.58	(0.38-0.89)
	[Non-cardia]	risk x	0.61	(0.44-0.84)
- Vegetables intake:		risk x	0. 69	
	[Cardia]	risk x	0.63	(0.50-0.79)
	[Non-cardia]	risk x	0.75	(0.59-0.95)

Reference: Lunet N, Valbuena C, Vieira AL, et al. Fruit and vegetable consumption and gastric cancer by location and histological type: case-control and meta-analysis. Eur J Cancer Prev 2007; 16:312.

- Fiber intake:		risk x	0.58	(0.49-0.67)
	[Cardia]	risk x	0.66	(0.37–1.15)
	[Non-cardia]	risk x	0.55	(0.36–0.83)

Reference: Zhang Z, Xu G, Ma M, et al. Dietary fiber intake reduces risk for gastric cancer: a meta-analysis. Gastroenterology 2013; 145:113.

- BMI: 25 or more:		risk x	1.22	(1.06–1.41)

Reference: Yang P, Zhou Y, Chen B, et al. Overweight, obesity and gastric cancer risk: results from a meta-analysis of cohort studies. Eur J Cancer 2009; 45:2867.

- Smoking:	Men:	Active smoker:	risk x	1.62	(1.50-1.75)
		Ex-smoker:	risk x	1.34	(1.22-1.47)
	Women:	Active smoker:	risk x	1.20	(1.01-1.43)
		Ex-smoker:	risk x	1.16	(0.92-1.46)

Reference: Ladeiras-Lopes R, Pereira AK, Nogueira A, et al. Smoking and gastric cancer: systematic review and meta-analysis of cohort studies. Cancer Causes Control 2008; 19:689.

- History of infection with Helicobacter Pylori:		risk x	1.92	(1.32-2.78)

Reference: Huang JQ, Sridhar S, Chen Y, Hunt RH. Meta-analysis of the relationship between Helicobacter pylori seropositivity and gastric cancer. Gastroenterology 1998; 114:1169.

- Eradication of H pylori infection:		risk x	0.53	(0.44−0.64)

Reference: Lee YC, Chiang TH, Chou CK, Tu YK, Liao WC, Wu MS, Graham DY. Association Between Helicobacter pylori Eradication and Gastric Cancer Incidence: A Systematic Review and Meta-analysis. Gastroenterology. 2016 May;150(5):1113-1124.e5. doi: 10.1053/j.gastro.2016.01.028. Epub 2016 Feb 2. PMID: 26836587.

- Medication

- Intake of NSAIDs :		risk x	0.79	(0.77-0.81)

Reference: Wu CY, Wu MS, Kuo KN, et al. Effective reduction of gastric cancer risk with regular use of nonsteroidal anti-inflammatory drugs in Helicobacter pylori-infected patients. J Clin Oncol 2010; 28:2952.

-Statin intake:		risk x	0.85	(0.80–0.91)

Reference: Wu XD, Zeng K, Xue FQ, Chen JH, Chen YQ (October 2013). "Statins are associated with reduced risk of gastric cancer: a meta-analysis". European Journal of Clinical Pharmacology. 69(10): 1855–60. doi:10.1007/s00228-013-1547-z. PMID 23748751.

- Aspirin intake [Cardia] risk x 0.61 (0.49–0.77)
All Stomach cancer risk x 0.64 (0.51–0.82)
Reference: Bosetti C, Santucci C, Gallus S, Martinetti M, La Vecchia C. Aspirin and the risk of colorectal and other digestive tract cancers: an updated meta-analysis through 2019. Ann Oncol. 2020 May;31(5):558-568. doi: 10.1016/j.annonc.2020.02.012. Epub 2020 Apr 1. PMID: 32272209.

- Selenium intake: [Cardia] risk x 0.47 (0.33–0.65)
Reference: Mark SD, Qiao YL, Dawsey SM, et al. Prospective study of serum selenium levels and incident esophageal and gastric cancers. J Natl Cancer Inst 2000; 92:1753.

- Blood group A: risk x 1.2 (1.02-1.42)
Reference: Edgren G, Hjalgrim H, Rostgaard K, et al. Risk of gastric cancer and peptic ulcers in relation to ABO blood type: a cohort study. Am J Epidemiol 2010; 172:1280.

- History of peptic ulcer: risk x 1.8 (1.6–2.0)
Reference: Hansson LE, Nyrén O, Hsing AW, et al. The risk of stomach cancer in patients with gastric or duodenal ulcer disease. N Engl J Med 1996; 335:242.

-Mutation

- CDH1 gene mutation: risk x 74.12
Reference: Hansford S, Kaurah P, Li-Chang H, et al. Hereditary Diffuse Gastric Cancer Syndrome: CDH1 Mutations and Beyond. JAMA Oncol 2015; 1:23.

- BRCA2: risk x 2.59 (1.46-4.61)
Reference: Breast Cancer Linkage Consortium. Cancer risks in BRCA2 mutation carriers. J Natl Cancer Inst 1999; 91:1310.

- ATM gene variant: risk x 4.74 (3.03–7.40)
Reference: Helgason H, Rafnar T, Olafsdottir HS, et al. Loss-of-function variants in ATM confer risk of gastric cancer. Nat Genet 2015; 47:906.

- CHEK2 mutation: risk x 5.76 (2.12-15.6)
Reference: Näslund-Koch C, Nordestgaard BG, Bojesen SE. Increased Risk for Other Cancers in Addition to Breast Cancer for CHEK2*1100delC Heterozygotes Estimated From the Copenhagen General Population Study. J Clin Oncol 2016; 34:1208.

-Chronic Condition

Mucosal status at baseline	[Cardiac]	[Non-cardia]	All gastric cancer
Gastritis	1.8 (1.2-2.9)	2.8 (2.3-3.5)	2.6 (2.2-3.2)
Atrophic gastritis	2.4 (1.1-4.8)	5.0 (3.8-6.7)	4.5 (3.5-5.8)
Intestinal metaplasia	4.7 (2.3-9.5)	6.5 (4.8-8.9)	6.2 (4.7-8.2)
Dysplasia	6.0 (2.3-15.9)	12.1 (8.3-17.6)	10.9 (7.7-15.4)

Reference: Song H, Ekheden IG, Zheng Z, et al. Incidence of gastric cancer among patients with gastric precancerous lesions: observational cohort study in a low risk Western population. BMJ 2015; 351:h3867.

-Peutz-Jeghers syndrome (STK11): risk x 213 (96-368)
Reference: Francis M. Giardiello, Jill D. Brensinger, Anne C. Tersmette, Steven N. Goodman, Gloria M. Petersen, Susan V. Booker, Marcia Cruz–Correa, Johan A. Offerhaus. Very high risk of cancer in familial Peutz–Jeghers syndrome. Gastroenterology, Volume 119, Issue 6, December 2000, Pages 1447-1453

- Lynch syndrome (mismatch repair genes MLH1, MSH2, MSH6): risk x 9.78 (1.18-35.30)
Reference: Win AK, Young JP, Lindor NM, et al. Colorectal and other cancer risks for carriers and noncarriers from families with a DNA mismatch repair gene mutation: a prospective cohort study. J Clin Oncol 2012; 30:958.

- HIV positivity: risk x 1.90 (1·53–2·36)
- History of organ transplantation: risk x 2.04 (1·49–2·79)
Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

- Diabetes (Women): risk x 1.61 (1.02-2.54)
Reference: Inoue M, Iwasaki M, Otani T, et al. Diabetes Mellitus and the Risk of Cancer: Results From a Large-Scale Population-Based Cohort Study in Japan. Arch Intern Med. 2006;166(17):1871–1877.

- Rheumatism, unspecified risk x 4.91 (1.56-15.4)
- Graves' / autoimmune thyroiditis risk x 5.90 (1.47-23.8)

Reference: He MM, Lo CH, Wang K, Polychronidis G, Wang L, Zhong R, Knudsen MD, Fang Z, Song M. Immune-Mediated Diseases Associated With Cancer Risks. JAMA Oncol. 2021 Dec 2:e215680. doi: 10.1001/jamaoncol.2021.5680. Epub ahead of print. PMID: 34854871; PMCID: PMC8640951.

- Hepatitis B: risk x 1.41 (1.11-1.80)

Reference: Song C, Lv J, Liu Y, Chen JG, Ge Z, Zhu J, Dai J, Du LB, Yu C, Guo Y, Bian Z, Yang L, Chen Y, Chen Z, Liu J, Jiang J, Zhu L, Zhai X, Jiang Y, Ma H, Jin G, Shen H, Li L, Hu Z; China Kadoorie Biobank Collaborative Group. Associations Between Hepatitis B Virus Infection and Risk of All Cancer Types. JAMA Netw Open. 2019 Jun 5;2(6):e195718. doi: 10.1001/jamanetworkopen.2019.5718. PMID: 31199446; PMCID: PMC6575146.

-History of Multiple myeloma: risk x 1.30 (1.09-1.53)
-History of MGUS risk x 1.25 (1.05-1.48)

Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

- History of cancer

- History of Basocellular skin carcinoma:

Number of BCCs 12+: risk x 2.87 (1.43–5.77)

Reference: Cho HG et al. Frequent basal cell cancer development is a clinical marker for inherited cancer susceptibility. JCI Insight. 2018; 3(15): e122744.

- Exposure

- Asbestos risk x 1.2 (1.1-1.3)
- Lead compounds risk x 1.3 (1.2-1.5)

Reference: Marant Micallef C, Shield KD, Baldi I, Charbotel B, Fervers B, Gilg Soit Ilg A, Guénel P, Olsson A, Rushton L, Hutchings SJ, Straif K, Soerjomataram I. Occupational exposures and cancer: a review of agents and relative risk estimates. Occup Environ Med. 2018 Aug;75(8):604-614. doi: 10.1136/oemed-2017-104858. Epub 2018 May 7. PMID: 29735747.

- Exposure to Agent Orange: risk x 1.14 (1.04-1.24)

Reference: Sang‐Wook Yi, Heechoul Ohrr. Agent Orange exposure and cancer incidence in Korean Vietnam veterans: A prospective cohort study. Cancer. 2014 Dec 1;120(23):3699-706.

Testicular cancer

- Male history

- History of cryptorchidism (testicular malposition): risk x 3.71 (3.29-4.19)
- History of hypospadias: risk x 2.13 (1.26-3.61)

Reference: Schnack TH, Poulsen G, Myrup C, et al. Familial coaggregation of cryptorchidism, hypospadias, and testicular germ cell cancer: a nationwide cohort study. J Natl Cancer Inst 2010; 102:187.

- History of contralateral testicular cancer: risk x 12.4 (11.0-13.9)

Reference: Fosså SD, Chen J, Schonfeld SJ, et al. Risk of contralateral testicular cancer: a population-based study of 29,515 US men. J Natl Cancer Inst 2005; 97:1056.

- Testicular microlithiasis: risk x 8.5 (4.5-16.1)

Reference: Tan IB, Ang KK, Ching BC, et al. Testicular microlithiasis predicts concurrent testicular germ cell tumors and intratubular germ cell neoplasia of unclassified type in adults: a meta-analysis and systematic review. Cancer 2010; 116:4520.

- Transgender surgery for men: risk x 0 (risk falls to zero)

Reference: /

- Family history

- First-degree relative with testicular cancer
  - Brother: risk x 10.2 (6.22-15.77)
  - Son: risk x 4.3 (1.6-9.3)
  - Father: risk x 5.7 (0.7-23.2)

Reference: Heimdal K, Olsson H, Tretli S, et al. Familial testicular cancer in Norway and southern Sweden. Br J Cancer 1996; 73:964.

- Chronic Condition

- HIV positivity: risk x 1.35 (1·01–1·79)
- History of organ transplantation: risk x 1.61 (0·69–3·79)

Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

- Hypercholesterolemia: risk x 4.5 (1.3–16.2)

Reference: Wiréhn AB, Törnberg S, Carstensen J. Serum cholesterol and testicular cancer incidence in 45,000 men followed for 25 years. Br J Cancer 2005; 92:1785.

-History of: MGUS: risk x 1.32 (1.11-1.57)

Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

- Marijuana use: risk x 2.59 (1.60–4.19)

Reference: Gurney J, Shaw C, Stanley J, et al. Cannabis exposure and risk of testicular cancer: a systematic review and meta-analysis. BMC Cancer 2015; 15:897.

Thyroid cancer

- Family history

- Thyroid carcinoma	Parent:	risk x	3.2 1	(1.53–5.9)
	Brother/sister:	risk x	6.2 4	(2.67–12.36)

Reference: Hemminki K, Eng C, Chen B. Familial risks for nonmedullary thyroid cancer. J Clin Endocrinol Metab 2005; 90:5747.

-Female History

- Breastfeeding during the last 5 years:	risk x	1.9	(1.1-3.1)
- Two or more pregnancies during the last 5 years:	risk x	4.2	(2.0-8.9)

Reference: Rossing MA, Voigt LF, Wicklund KG, Daling JR. Reproductive factors and risk of papillary thyroid cancer in women. Am J Epidemiol 2000; 151:765.

-BMI

- Men, per 5 kg/m² increase in BMI (above 25):	risk x	1.33	(1.03-1.70)
- Women, per 5 kg/m² increase in BMI (above 25):	risk x	1.14	(1.06-1.23)

Reference: Renehan AG, Tyson M, Egger M, et al. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 2008; 371:569.

- Chronic Condition

- Hepatitis C infection:	risk x	12.2	(1.9–77.5)

Reference: Antonelli A, Ferri C, Fallahi P, et al. Thyroid cancer in HCV-related chronic hepatitis patients: a case-control study. Thyroid 2007; 17:447.

- History of organ transplantation:	risk x	5.91	(4·41–7·90)

Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

- Cowden syndrome:	risk x	51.1	(38.1 – 67.1)

Reference: Tan MH, Mester JL, Ngeow J, et al. Lifetime cancer risks in individuals with germline PTEN mutations. Clin Cancer Res 2012; 18:400.

-History of: MGUS:	risk x	2.76	(1.69-4.27)

Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

- Myasthenia gravis	risk x	12.1	(1.69-86.6)

Reference: He MM, Lo CH, Wang K, Polychronidis G, Wang L, Zhong R, Knudsen MD, Fang Z, Song M. Immune-Mediated Diseases Associated With Cancer Risks. JAMA Oncol. 2021 Dec 2:e215680. doi: 10.1001/jamaoncol.2021.5680. Epub ahead of print. PMID: 34854871; PMCID: PMC8640951.

-Surgery

- Thyroidectomy: risk x 0 (risk falls to zero)
Reference: /

- History of cancer in childhood risk x 11.34 (8.20-15.27)
Reference: Neglia JP, Friedman DL, Yasui Y, Mertens AC, Hammond S, Stovall M, Donaldson SS, Meadows AT, Robison LL, Second malignant neoplasms in five-year survivors of childhood cancer: childhood cancer survivor study., J Natl Cancer Inst. 2001 Apr 18;93(8):618-29.

Uterine cancer

- Female History

- Estrogen intake WITHOUT progesterone:	risk x	1.45	(1·02–2·06)
- Taking estrogen WITH progesterone:	risk x	0.71	(0·56–0·90)
- Tibolone intake:	risk x	1.79	(1·43–2·25)

Reference: Beral V, Bull D, Reeves G, Million Women Study Collaborators. Endometrial cancer and hormone-replacement therapy in the Million Women Study. Lancet 2005; 365:1543.

- Tamoxifen intake (in postmenopausal women):	risk x	3.32	

Reference: Iqbal J, Ginsburg OM, Wijeratne TD, et al. Endometrial cancer and venous thromboembolism in women under age 50 who take tamoxifen for prevention of breast cancer: a systematic review. Cancer Treat Rev 2012; 38:318.

- Age at Menarche:

≤11	risk x	1.00	
12	risk x	0.99	(0.81-1.20)
13	risk x	0.80	(0.66-0.98)
14	risk x	0.90	(0.70-1.16)
≥15	risk x	0.76	(0.55-1.04)

- Age at Menopause:

<45	risk x	1.22	(0.85-1.75)
45–49	risk x	1.00	
50–54	risk x	1.49	(1.22-1.82)
≥55	risk x	1.53	(1.13-2.06)

Reference: Karageorgi S, Hankinson SE, Kraft P, De Vivo I. Reproductive factors and postmenopausal hormone use in relation to endometrial cancer risk in the Nurses' Health Study cohort 1976-2004. Int J Cancer 2010; 126:208.

- Parity:

● 1	risk x	1	
● 2	risk x	0.92	(0.76–1.11)
● 3	risk x	0.80	(0.64–0.99)
● 4 or more	risk x	0.58	(0.44–0.78)
- Ever taking oral contraceptives:	risk x	0. 65	(0.56–0.75)
- Age at last pregnancy:			
● 25 or less	risk x	1	
● 26-30	risk x	1.05	(0.84–1.33)
● 31-35	risk x	0.85	(0.66–1.10)
● More than 35	risk x	0.75	(0.55–1.03)

Reference: Dossus L, Allen N, Kaaks R. Reproductive risk factors and endometrial cancer: the European Prospective Investigation into Cancer and Nutrition. Int J Cancer. 2010;127:442–451.

-Per 3 months of breastfeeding:	risk x	0.97	(0.96–0.98)

Reference: Jordan SJ, Na R, Johnatty SE, et al. Breastfeeding and Endometrial Cancer Risk: An Analysis From the Epidemiology of Endometrial Cancer Consortium. Obstet Gynecol 2017; 129:1059.

- Hysterectomy:	risk x	0 (risk falls to zero)
- Transgender surgery for women:	risk x	0 (risk falls to zero)

Reference: /

- Smoking

Ex-smoker:	risk x	0.88	(0.78-0.99)
Current smoker:	risk x	0.74	(0.64-0.84)

Reference: Zhou B, Yang L, Sun Q, et al. Cigarette smoking and the risk of endometrial cancer: a meta-analysis. Am J Med 2008; 121:501.

-Nutrition

- Large soy intake:	risk x	0.70	(0.57-0.86)

Reference: Myung SK, Ju W, Choi HJ, et al. Soy intake and risk of endocrine-related gynecological cancer: a meta-analysis. BJOG 2009; 116:1697.

- Coffee:	risk x	0.74	(0.63-0.84)

Reference: Yu X, Bao Z, Zou J, Dong J. Coffee consumption and risk of cancers: a meta-analysis of cohort studies. BMC Cancer 2011; 11:96.

- Regularly drink green tea: risk x 0.78 (0.62-0.98)
- Regularly drink black tea: risk x 1.20 (1.05-1.38)
Reference: Butler LM, Wu AH. Green and black tea in relation to gynecologic cancers. Mol Nutr Food Res 2011; 55:931.

- Aspirin intake: risk x 0.54 (0.38-0.78)
Reference: Neill AS, Nagle CM, Protani MM, et al. Aspirin, nonsteroidal anti-inflammatory drugs, paracetamol and risk of endometrial cancer: a case-control study, systematic review and meta-analysis. Int J Cancer 2013; 132:1146.

- BRCA1 mutation: risk x 2.65 (1.69-4.16)
Reference: Thompson D, Easton DF, Breast Cancer Linkage Consortium. Cancer Incidence in BRCA1 mutation carriers. J Natl Cancer Inst 2002; 94:1358.

-BMI: per 5 kg/m² increase (above 25): risk x 1.59 (1.50-1.68)
Reference: Renehan AG, Tyson M, Egger M, et al. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 2008; 371:569.

- Physical activity (hours per week):
- between 1 and 3 hours: risk x 0.94 (0.74–1.20)
- between 3 and 7 hours: risk x 0.79 (0.64–0.98)
- more than 7 hours: risk x 0.87 (0.71–1.06)
Reference: Schmid D, Behrens G, Keimling M, Jochem C, Ricci C, Leitzmann M. A systematic review and meta-analysis of physical activity and endometrial cancer risk. Eur J Epidemiol. 2015 May;30(5):397-412. doi:10.1007/s10654-015-0017-6. Epub 2015 Mar 24. PMID: 25800123.

- Chronic Condition
- Lynch syndrome (mismatch repair genes MLH1, MSH2, MSH6): risk x 30.62 (11.24-66.64)
Reference: Win AK, Young JP, Lindor NM, et al. Colorectal and other cancer risks for carriers and noncarriers from families with a DNA mismatch repair gene mutation: a prospective cohort study. J Clin Oncol 2012; 30:958.

- Cowden syndrome: risk x 42.9 (28.1 – 62.8)
Reference: Tan MH, Mester JL, Ngeow J, et al. Lifetime cancer risks in individuals with germline PTEN mutations. Clin Cancer Res 2012; 18:400.

- Polycystic ovary syndrome: risk x 2.70 (1.00–7.29)
Reference: Chittenden BG, Fullerton G, Maheshwari A, Bhattacharya S. Polycystic ovary syndrome and the risk of gynecological cancer: a systematic review. Reprod Biomed Online 2009; 19:398.

-Peutz-Jeghers syndrome (STK11): risk x 16 (1.9-56)
Reference: Francis M. Giardiello, Jill D. Brensinger, Anne C. Tersmette, Steven N. Goodman, Gloria M. Petersen, Susan V. Booker, Marcia Cruz–Correa, Johan A. Offerhaus. Very high risk of cancer in familial Peutz–Jeghers syndrome. Gastroenterology, Volume 119, Issue 6, December 2000, Pages 1447-1453

-Family history
- First-degree relative with endometrial carcinoma: risk x 1.82 (1.65-1.98)
- First-degree relative with colorectal carcinoma: risk x 1.17 (1.03-1.31)
Reference: Win AK, Reece JC, Ryan S. Family history and risk of endometrial cancer: a systematic review and meta-analysis. Obstet Gynecol 2015; 125:89.

Sinonasal cancer

- Exposure:

- Nickel compounds	risk x	8.7	(1.1-31.4)
- Chrome VI	risk x	5.2	(2.4-11.3)

Reference: Marant Micallef C, Shield KD, Baldi I, Charbotel B, Fervers B, Gilg Soit Ilg A, Guénel P, Olsson A, Rushton L, Hutchings SJ, Straif K, Soerjomataram I. Occupational exposures and cancer: a review of agents and relative risk estimates. Occup Environ Med. 2018 Aug;75(8):604-614. doi: 10.1136/oemed-2017-104858. Epub 2018 May 7. PMID: 29735747.

- Wood dust:	risk x	48.47	(13.30-176.63)

Reference: Pesch B, Pierl CB, Gebel M, Gross I, Becker D, Johnen G, Rihs HP, Donhuijsen K, Lepentsiotis V, Meier M, Schulze J, Brüning T. Occupational risks for adenocarcinoma of the nasal cavity and paranasal sinuses in the German wood industry. Occup Environ Med. 2008 Mar;65(3):191-6. doi: 10.1136/oem.2007.033886. Epub 2007 Sep 19. PMID: 17881467.

Small intestine cancer

- Medical History

-Cystic fibrosis: risk x 18.94 (9·37–38·27)
Reference: Yamada A, Komaki Y, Komaki F, et al. Risk of gastrointestinal cancers in patients with cystic fibrosis: a systematic review and meta-analysis. Lancet Oncol 2018; 19:758.

- Lynch syndrome: risk x 25
Reference: Watson P, Lynch HT. Extracolonic cancer in hereditary nonpolyposis colorectal cancer. Cancer. 1993 Feb 1;71(3):677-85. doi: 10.1002/1097-0142(19930201)71:3<677::aid-cncr2820710305>3.0.co;2-#. PMID: 8431847.

-Peutz-Jeghers syndrome (STK11): risk x 520 (220-1306)
Reference: Francis M. Giardiello, Jill D. Brensinger, Anne C. Tersmette, Steven N. Goodman, Gloria M. Petersen, Susan V. Booker, Marcia Cruz–Correa, Johan A. Offerhaus. Very high risk of cancer in familial Peutz–Jeghers syndrome. Gastroenterology, Volume 119, Issue 6, December 2000, Pages 1447-1453

- Familial Adenomatous Polyposis : risk x 300
Reference: Augustin T, Muslim MA, Cengiz TB, El-Hayek K, Simon R, Bhatt A, Tang A, Burke CA, Matthew Walsh R. Survival outcomes after surgical management of sporadic or familial adenomatous polyposis associated duodenal cancer. J Surg Oncol. 2020 Nov;122(6):1132-1144. doi:10.1002/jso.26131. Epub 2020 Aug 10. PMID: 33124067.

- Celiac disease risk x 6.89 (2.18-21.8)
- Sjögren syndrome risk x 8.49 (1.18-61.3)
- Guillain-Barre syndrome risk x 16.1 (2.25-116)
- Bullous disorders risk x 21.8 (3.04-157)
Reference: He MM, Lo CH, Wang K, Polychronidis G, Wang L, Zhong R, Knudsen MD, Fang Z, Song M. Immune-Mediated Diseases Associated With Cancer Risks. JAMA Oncol. 2021 Dec 2:e215680. doi: 10.1001/jamaoncol.2021.5680. Epub ahead of print. PMID: 34854871; PMCID: PMC8640951.

- Crohn's disease: risk x risk x 66.7 (18.1–170.7)
Reference: Jess T, Winther KV, Munkholm P, Langholz E, Binder V. Intestinal and extra-intestinal cancer in Crohn's disease: follow-up of a population-based cohort in Copenhagen County, Denmark. Aliment Pharmacol Ther. 2004 Feb 1;19(3):287-93. doi: 10.1111/j.1365-2036.2004.01858.x. PMID: 14984375.

- History of Multiple myeloma: risk x 1.30 (1.09-1.53)
- History of MGUS: risk x 1.25 (1.05-1.48)
Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

-Nutrition

Alcohol (drinks/day)	
Non-drinkers	1
≤2	0.59 (0.22–1.55)
Coffee (cups/day)	
>2	0.37 (0.10–1.34)
Bread/pasta/rice (portions/week)	
≤14	1
14.5–21	3.76 (1.13–12.50)
Sugar (spoonful/day)	
2–3.9	2.88 (0.93–8.92)
Red meat (portions/week)	
>5	4.57 (1.01–20.81)
Fish (portions/week)	
>1	0.33 (0.09–1.20)
Vegetables (portions/week)	
>9	0.27 (0.09–0.85)
Fruits (portions/week)	
>14	0.62 (0.26–1.49)

Reference: Negri E, Bosetti C, La Vecchia C, et al. Risk factors for adenocarcinoma of the small intestine. Int J Cancer 1999; 82:171.

- Exposure

- Agent Orange: risk x 2.30 (1.03-5.15)

Reference: Sang‐Wook Yi, Heechoul Ohrr. Agent Orange exposure and cancer incidence in Korean Vietnam veterans: A prospective cohort study. Cancer. 2014 Dec 1;120(23):3699-706.

Soft Tissue Sarcoma

-Genetics

-TP53: risk x 7700

Reference: Bougeard G, Renaux-Petel M, Flaman JM, Charbonnier C, Fermey P, Belotti M, Gauthier-Villars M, Stoppa-Lyonnet D, Consolino E, Brugières L, Caron O, Benusiglio PR, Bressac-de Paillerets B, Bonadona V, Bonaïti-Pellié C, Tinat J, Baert-Desurmont S, Frebourg T. Revisiting Li-Fraumeni Syndrome From TP53 Mutation Carriers. J Clin Oncol. 2015 Jul 20;33(21):2345-52. doi: 10.1200/JCO.2014.59.5728. Epub 2015 May 26. PMID: 26014290.

- CHEK2 mutation: risk x 3.45 (1.09-10.9)

Reference: Näslund-Koch C, Nordestgaard BG, Bojesen SE. Increased Risk for Other Cancers in Addition to Breast Cancer for CHEK2*1100delC Heterozygotes Estimated From the Copenhagen General Population Study. J Clin Oncol 2016; 34:1208.

- Medical History

- Neurofibromatosis Type 1: risk x 122 (61.0–219)

Reference: Walker L, Thompson D, Easton D, Ponder B, Ponder M, Frayling I, Baralle D. A prospective study of neurofibromatosis type 1 cancer incidence in the UK. Br J Cancer. 2006 Jul 17;95(2):233-8. doi: 10.1038/sj.bjc.6603227. Epub 2006 Jun 20. PMID: 16786042; PMCID: PMC2360616.

-Nevoid basal cell carcinoma syndrome: risk x 300

Reference: Singer S, Maki RG, O'Sullivan B: Soft tissue sarcoma. In: DeVita VT Jr, Lawrence TS, Rosenberg SA: Cancer: Principles and Practice of Oncology. 9th ed. Lippincott Williams & Wilkins, 2011, pp 1533-77.

- Graves'/autoimmune thyroiditis risk x 9.19 (2.93-28.8)
- Guillain-Barre syndrome risk x 11.2 (1.56-79.8)
- Autoimmune hepatitis risk x 15.1 (2.10-108)

Reference: He MM, Lo CH, Wang K, Polychronidis G, Wang L, Zhong R, Knudsen MD, Fang Z, Song M. Immune-Mediated Diseases Associated With Cancer Risks. JAMA Oncol. 2021 Dec 2:e215680. doi: 10.1001/jamaoncol.2021.5680. Epub ahead of print. PMID: 34854871; PMCID: PMC8640951.

- History of cancer

- History of childhood cancer: risk x 6.33 (4.33-8.94)

Reference: Neglia JP, Friedman DL, Yasui Y, Mertens AC, Hammond S, Stovall M, Donaldson SS, Meadows AT, Robison LL, Second malignant neoplasms in five-year survivors of childhood cancer: childhood cancer survivor study., J Natl Cancer Inst. 2001 Apr 18;93(8):618-29.

Spinocellular skin cancer

-Ethnicity

- African:		risk x	0.012	
- Asian:		risk x	0.090	
- Hispanic, Pacific Islanders, Native American:		risk x	0.087	

Reference: Gloster HM Jr, Neal K. Skin cancer in skin of color. J Am Acad Dermatol 2006; 55:741.

- Physical attributes

- Hair color	Brown	risk x	1.50	(0.79-2.86)
	Light/brown	risk x	1.57	(0.81-3.04)
	Blonde	risk x	1.64	(0.79-3.42)
	Light blonde	risk x	5.02	(2.30-10.94)
	Red	risk x	13.00	(4.29- 39.38)
- Light eye color		risk x	1.65	(1.11-2.43)
- Skin reaction to sun exposure	Tan, no burn	risk x	1	
	Burn, then tan	risk x	1.35	(0.93- 1.96)
	Burn, never tan	risk x	1.97	(1.19-3.26)

Reference: Zanetti R, Rosso S, Martinez C, et al. The multicentre south European study 'Helios'. I: Skin characteristics and sunburns in basal cell and squamous cell carcinomas of the skin. Br J Cancer. 1996;73(11):1440–1446. doi:10.1038/bjc.1996.274

-Treatments

- PUVA:	risk x	20.92	(14.08-31.08)

Reference: Stern RS, PUVA Follow-Up Study. The risk of squamous cell and basal cell cancer associated with psoralen and ultraviolet A therapy: a 30-year prospective study. J Am Acad Dermatol 2012; 66:553.

- Habits

-Solar exposure High OR Medium - Chronic:	risk x	1.95	(1·19–3·18)

Reference: Schmitt J, Haufe E, Trautmann F, et al. Is ultraviolet exposure acquired at work the most important risk factor for cutaneous squamous cell carcinoma? Results of the population-based case-control study FB-181. Br J Dermatol 2018; 178:462.

-Use of sunbed:	risk x	1.67	(1.29-2.17)

Reference: Wehner MR, Shive ML, Chren MM, et al. Indoor tanning and non-melanoma skin cancer: systematic review and meta-analysis. BMJ 2012; 345:e5909.

- Medical History

- HIV positivity:	- without treatment:	risk x	1.7	(0.7–3.6)
	- with treatment:	risk x	3.3	(2.1–4.9)

Reference: Franceschi S, Lise M, Clifford GM, et al. Changing patterns of cancer incidence in the early- and late-HAART periods: the Swiss HIV Cohort Study. Br J Cancer 2010; 103:416.

- History of organ transplantation:	risk x	28.62	(9·39–87·2)

Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

- Xeroderma pigmentosum:	risk x	10000	

Reference: Kraemer KH, DiGiovanna JJ. Forty years of research on xeroderma pigmentosum at the US National Institutes of Health. Photochem Photobiol. 2015;91(2):452-9.

- History of Parkinson's:	risk x	1.25	(1.1–1.4)

Reference: Olsen JH, Friis S, Frederiksen K, et al. Atypical cancer pattern in patients with Parkinson's disease. Br J Cancer 2005; 92:201.

- Epidermolysis bullosa:	risk x	8.5	

Reference: Mallipeddi R. Epidermolysis bullosa and cancer. Clin Exp Dermatol. 2002 Nov;27(8):616-23. doi: 10.1046/j.1365-2230.2002.01130.x. PMID: 12472531.

-History of Multiple myeloma:	risk x	2.22	(1.74-2.80)
-History of MGUS:	risk x	3.30	(2.76-3.90)

Reference: Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes after multiple myeloma and its precursor disease (MGUS). Blood. 2011;118(15):4086-4092. doi:10.1182/blood-2011-05-355743

- Genital Warts: risk x 2.2 (1.5–3.2)
Reference: Blomberg M, Friis S, Munk C, Bautz A, Kjaer SK. Genital warts and risk of cancer: a Danish study of nearly 50,000 patients with genital warts. J Infect Dis. 2012 May 15;205(10):1544-53. doi: 10.1093/infdis/jis228. Epub 2012 Mar 15. PMID: 22427679.

- Exposure

- Arsenic: risk x 1.37 (1.04-1.80)
Reference: D. Gilbert-Diamond, Z. Li, AE Perry, SK Spencer, A. Jay Gandolfi, MR Karagas. A population-based case-control study of urinary arsenic species and squamous cell carcinoma in New Hampshire, USA Environ. Health Perspect., 121 (2013), pp. 1154-1160

- Flight crew - women: risk x 4.09 (2.70–6.20)
Reference: McNeely E, Mordukhovich I, Staffa S, Tideman S, Gale S, Coull B. Cancer prevalence among flight attendants compared to the general population. Environ Health. 2018;17(1):49. Published 2018 Jun 26. doi:10.1186/s12940-018-0396-8

- Nutrition

-Intake of citrus fruits 2x/week or more: risk x 1.14 (1.00–1.30)
Reference: Wu S, Cho E, Feskanich D, et al. Citrus consumption and risk of basal cell carcinoma and squamous cell carcinoma of the skin. Carcinogenesis 2015; 36:1162.

- Genetics

-(MC1R) gene 151Cys variant: risk x 1.67 (1.12-2.49)
Reference: Han J, Kraft P, Colditz GA, et al. Melanocortin 1 receptor variants and skin cancer risk. Int J Cancer 2006; 119:1976.

-Medication

-Diuretics: risk x 1.3 (0.9–2.0)
Reference: Robinson SN, Zens MS, Perry AE, et al. Photosensitizing agents and the risk of non-melanoma skin cancer: a population-based case-control study. J Invest Dermatol 2013; 133:1950.

-Methotrexate: risk x 2.35 (1.57-3.38)
Reference: Lange E, Blizzard L, Venn A, et al. Disease-modifying anti-rheumatic drugs and non-melanoma skin cancer in inflammatory arthritis patients: a retrospective cohort study. Rheumatology (Oxford) 2016; 55:1594.

- Thiazide diuretics: risk x 1.93 (1.59–2.35)
Reference: Bendinelli B., Masala G., Garamella G., Palli D., Caini S. Do thiazide diuretics increase the risk of skin cancer? A critical review of the scientific evidence and updated meta-analysis. Curr. Cardiol. Rep. 2019;21:92. doi:10.1007/s11886-019-1183-z.

-NSAIDs: risk x 0.90 (0.83–0.98)
Reference: Ma Y., Yu P., Lin S., Li Q., Fang Z., Huang Z. The association between nonsteroidal anti-inflammatory drugs and skin cancer: Different responses in American and European populations. Pharmacol. Res. 2019;152:104499. doi: 10.1016/j.phrs.2019.104499.

- Medications for long term daily use

Bumetanide	risk x	1.2	(1.0-1.4)
Furosemide	risk x	1.4	(1.3-1.4)
Diclofenac	risk x	1.1	(1.0-1.1)
Indomethacin	risk x	1.2	(1.1-1.4)
Captopril	risk x	1.2	(1.0-1.4)
Enalapril	risk x	1.1	(1.0-1.2)
Simvastatin	risk x	1.1	(1.0-1.2)
Sotalol	risk x	1.1	(1.0-1.3)
Verapamil	risk x	1.1	(1.0-1.3)
Metformin	risk x	1.1	(1.0-1.3)
Carbamazepine	risk x	1.3	(1.1-1.5)
Valproate	risk x	1.3	(1.1-1.6)

- Medications for short term use

Acyclovir	risk x	1.5	(1.4-1.7)
Ciprofloxacin	risk x	1.3	(1.2-1.4)
Doxycycline	risk x	1.3	(1.2-1.5)
Ketoconazole	risk x	1.5	(1.4-1.7)
Sulfamethazole with trimethoprim	risk x	1.7	(1.4-2.0)

Tetracycline	risk x	1.5	(1.4-1.7)
Hydroxychloroquine	risk x	1.4	(1.3-1.6)
Acitretin	risk x	4.1	(3.0-5.6)
Isotretinoin	risk x	2.1	(1.1-3.8)

Reference: Kaae J, Boyd HA, Hansen AV, Wulf HC, Wohlfahrt J, Melbye M. Photosensitizing medication use and risk of skin cancer. Cancer Epidemiol Biomarkers Prev. 2010 Nov;19(11):2942-9. doi: 10.1158/1055-9965.EPI-10-0652. Epub 2010 Sep 22. PMID: 20861398.

- Voriconazole:	risk x	1.86	(1.36–2.55)

Reference: Tang H., Shi W., Song Y., Han J. Voriconazole exposure and risk of cutaneous squamous cell carcinoma among lung or hematopoietic cell transplant patients: A systematic review and meta-analysis. *J. Am. Acad. Dermatol.* 2019;80:500–507. doi: 10.1016/j.jaad.2018.08.010.

- Vemurafenib:	risk x	1.18	(1.12–1.26)

Reference: Chen P., Chen F., Zhou B. Systematic review and meta-analysis of prevalence of dermatological toxicities associated with vemurafenib treatment in patients with melanoma. *Clin. Exp. Dermatol.* 2019;44:243–251. doi:10.1111/ced.13751.

-Family history of skin cancer

- SCC only	risk x	3.3	(1.1–9.8)
- BCC only	risk x	13.0	(3.8–44.8)
- Melanoma only	risk x	5.0	(1.7–14.6)
- Multiple skin cancer types	risk x	11.1	(4.5–27.4)

Reference: Asgari MM, Warton EM, Whittemore AS. Family history of skin cancer is associated with increased risk of cutaneous squamous cell carcinoma. Dermatol Surg. 2015;41(4):481–486.

- History of cancer

- History BCC:	1	risk x	10.33	(10.02–10.66)
	6+	risk x	48.23	(46.17–50.38)
	12+	risk x	68.9	(63.62–74.63)

Reference: Cho HG et al. Frequent basal cell cancer development is a clinical marker for inherited cancer susceptibility. JCI Insight. 2018; 3(15): e122744.

Vulva/vagina cancer

- Medical History

- HIV positivity: risk x 6.45 (4·07–10·2)
- History of organ transplantation: risk x 22.76 (15·8–32·7)

Reference: Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet 2007; 370:59.

- Genital warts: risk x 5.9 (2.2–12.9)

Reference: Blomberg M, Friis S, Munk C, Bautz A, Kjaer SK. Genital warts and risk of cancer: a Danish study of nearly 50,000 patients with genital warts. J Infect Dis. 2012 May 15;205(10):1544-53. doi: 10.1093/infdis/jis228. Epub 2012 Mar 15. PMID: 22427679.

- Treatments

- Transgender surgery for women: risk x 0 (risk falls to zero)

Reference: /

Chapter 4: Assessing the Impact of the Developed Application on Cancer Risk Health Literacy

Background

The surge of technology and mobile applications in the field of healthcare has transformed the ways in which individuals access health-related information and participate in disease prevention efforts. There are now even randomized controlled trials demonstrating the usefulness of mobile applications in impacting outcomes in selected settings [1–3].

As per the World Health Organization, cancer is the second leading cause of death globally, accounting for nearly 10 million deaths in 2020 alone [4]. Thus, there is a substantial need for tools and strategies that can help individuals understand their risk and potentially encourage them to adopt healthier behaviors.

The field of oncology as a whole has already benefited from the development of many mobile applications with a variety of uses. Mobile applications have been developed for children with cancer [2], in order to address the information needs of young cancer patients, their parents, and health care providers; for patients in chemotherapy treatment [6], in order to provide self-management support on quality of life and health care utilization and for patients receiving palliative therapy [7], in order to improve adherence to medications prescribed for cancer pain management, among many others. Previous studies have shown that providing risk information by mobile applications may motivate health behavior changes, particularly for behaviors that impact the risk of cancer screening [8]. However, it is not clear to what extent mobile applications might be able to inform users about their risks of developing cancers or their risk factors.

Health Literacy Concerning Cancer Risk

Health literacy, defined as the ability to obtain, process, and understand basic health information and services needed to make appropriate health decisions, plays a critical role in cancer prevention, early detection, and treatment. The complexity of cancer information and the diversity of sources from which it can be accessed pose significant challenges, particularly for individuals with low health literacy [9]. By contrast, improved health literacy can lead to better outcomes in cancer prevention, detection, and treatment.

Low health literacy has been linked to poor knowledge of cancer risk factors and preventive measures and cancer-causing factors are inversely correlated with health literacy [10]. Studies have shown that individuals with limited health literacy are less likely to participate in preventive behaviors such as regular cancer screenings or HPV vaccinations [11]. Deficits in health literacy can lead to misconceptions about cancer risk and delay the adoption of preventive measures. Early detection of cancer significantly increases the chances of successful treatment and survival. Health literacy influences an individual's ability to recognize early signs of cancer, understand the importance of screening tests, and engage with healthcare providers effectively. Lack of understanding about the need for screening can result in underutilization of these services, particularly among communities with low health literacy [12].

Once diagnosed, cancer treatment involves complex decisions about options that vary in their risks and benefits. Patients with high health literacy are better equipped to understand treatment modalities, adhere to prescribed treatments, and manage side effects. Conversely, those with low health literacy may experience challenges in navigating the healthcare system, understanding medication instructions, and communicating effectively with healthcare providers [13]. Recent studies have provided evidence that online health information seeking is an effective mechanism for reducing cancer fatalism and minimizing cancer information avoidance is necessary to allay fatalistic beliefs about cancer prevention [14].

Improving health literacy will likely require a multifaceted approach, but stakeholders in healthcare and public health should prioritize health literacy to improve health outcomes and reduce the burden of cancer.

Prior Work in Risk Calculators

Risk calculators are becoming increasingly popular tools in the healthcare sector. They utilize algorithms that consider a variety of patient characteristics, including age, gender, family history, and lifestyle habits, to predict the likelihood of developing certain diseases. The Framingham Heart Study Risk Score calculator, for instance, was first introduced in 1991 [15] and has been instrumental in predicting cardiovascular risk and guiding treatment decisions [15,16]. In the realm of oncology, the Gail model for breast cancer was the first widely recognized risk prediction tool [17] and an updated version is still available on the National Cancer Institute's website [18]. Other tools have been developed, but their implementation remains limited, predominantly due to the necessity of a clinician to interpret the results and the need for dedicated and maintained software, and systematic analysis has revealed that many publicly available tools are very limited in scope and for many cancers there are no tools available [19]. Notably, it is not clear how these tools might impact patient awareness of either their risks or their risk factors, nor has it been studied if they might be able to influence behavior.

Goal of This Study

The aim of this study is to examine the effects of using the 'Cancer Risk Calculator' app, and to what extent it can inform users about their risk, possible risk factors for cancer and possible behavior change they might make to impact their risks.

The app has been designed with the intention of being an easy-to-use, informative tool that assists individuals in understanding their potential risk for developing cancer. It is based on its own heuristic aimed at providing users with an estimation of their cancer risk, but also includes a large number of validated models for various indications and cancers [20].

We attempted to understand the user engagement with the application and their perceptions of the information provided in the app by using a standardized questionnaire. We managed to demonstrate that respondents found the application useful and reported learning something new, more than half indicated a willingness to change their habits based on the information provided.

Given the prevalence and public health impact of cancer, tools like the 'Cancer Risk' study Calculator app could potentially play a significant role in encouraging individuals to adopt healthier behaviors and decrease their risk of cancer. Thus, it is crucial to understand users' experiences with the app and determine whether it succeeds in increasing awareness and influencing behaviors.

Methods

Mobile application

The Cancer Risk Calculator is an innovative mobile application, designed to estimate an individual's risk of developing cancer, based on a comprehensive array of risk factors identified in scientific literature. The application's risk analysis is subdivided into 38 types of cancer and is informed by a database of 450 distinct risk factors. It provides estimates for 10-, 20-, 30-year and lifetime timeframes as well as death rates and, when possible, further subdivides these estimates by anatomical or pathological subtypes.

Usage of the application involves creating an account and entering personal information into various fields. The data requested span multiple factors known to influence cancer risk, with age, gender, and racial background being critical, while all other information is optional. Users are advised to provide accurate and comprehensive data for the most dependable risk estimates. Users also have the option to edit their input data to see how such modifications influence their results.

The lifetime probabilities of developing cancer used by this application draw from data gathered by the National Cancer Institute's (NCI) Surveillance, Epidemiology, and End Results (SEER) Program, which has collected data since 1973, and the Centers for Disease Control and Prevention's (CDC) National Program of Cancer Registries (NPCR), which has gathered data since 1995 [21,22]. These statistics have been adapted through hazard ratios found in published, peer-reviewed literature. Notably, only quantifiable risk factors were included, and complex tests unavailable to the average clinician were excluded from consideration. A detailed list of a person's risk factors, along with their impact, is available for each cancer, with an additional list of possible actions or interventions one could undergo to decrease the risk of cancers in question.The application also separately includes a supplementary list of suggestions for modifiable risk factors associated with neoplasms.

The Cancer Risk Calculator bears the CE conformity mark, which indicates its status as a Class I low-risk medical device . This designation is predicated on the Class I conformity assessment procedures delineated in Annex VII Module A, EC Declaration of Conformity. Furthermore, because the application is considered a minimal-risk medical device, it falls under the U.S. Food and Drug Administration's (FDA) exercise enforcement discretions [23].

While the Cancer Risk Calculator is a groundbreaking tool, it is important to note that its purpose is strictly educational, and it should not replace a thorough assessment by a healthcare provider. The application strives to provide a comprehensive and convenient method for cancer risk assessment, but the results are inevitably influenced by a myriad of assumptions, extrapolations, and estimates due to the complexities and potential controversies in cancer risk studies. As scientific literature continually evolves, users should regard the figures generated by the application as indicative rather than precise.

To assure privacy, the application ensures that any information entered is stored solely on the user's device, without transmission to any other party.

Data Available

The survey, included in the addendum, was completed by 168 patients undergoing radiotherapy or by their family members at the Radiation Oncology Department of the CHU de Liège. This population was chosen to approximate those in the general population developing different types of cancer, which could provide insights into how these groups may differ in their responses to the application. Among them, 6 respondents expressed doubts regarding the correct use of the "Cancer Risk Calculator" app and were subsequently removed from the study. This resulted in a final sample size of N=162 patients.

The application was designed to be used only once, and depending on patient characteristics, this was estimated to take roughly 20 minutes, with an additional 10 minutes to complete the questionnaire.
The collected data comprised of the following information:

- Gender (Male/Female)
- Date of Birth (in DD/MM/YYYY format)
- Date of Entry (in DD/MM/YYYY format)
- From the Date of Birth and Date of Entry, the age of the patient was calculated. If the date of entry was unspecified, the age was calculated based on the date 01/05/2022.
- Type of respondent (Patient, Companion, Family). If the respondent was a companion or family member, it was clarified whether they answered the survey for themselves or for the patient.
- Type of Cancer (Assumed to be the patient's cancer type if the respondent was a companion or family member)
- Responses to Questions Q1 to Q12.
- Name of the Radiation Therapist who first saw the patient (this information was collected but not used in the analysis).

Statistical Methods

The age of the respondents was analyzed using mean and standard deviation, along with minimum and maximum values. Other variables were described using frequency tables (numbers and percents). Specifically, responses from the two most common cancer subgroups (breast and lung) were also depicted.
Multiple regression models were constructed to determine the impact of certain respondent characteristics on their responses to the survey questions. The considered explanatory variables were sex, age, type of respondent (patient or not), and presence of breast or lung cancer. The results of these models are presented via estimated coefficients, their standard errors, and the corresponding p-values.
The analysis was conducted on the maximum available data, with missing values not replaced. Statistical significance was determined at the 5% level ($p<0.05$). All statistical analysis was performed using SAS software (version 9.4).

Results

Description of Respondents

Table 1 provides an in-depth description of the patients and respondents. Their ages spanned from 21 to 87 years, with a mean age of 62.6 years (± 10.8 standard deviation). The majority of them (64.2%) were 60 years or older. In 96.3% of instances, the patients themselves completed the questionnaire. Predominantly, the type of cancer among these patients was breast cancer (60.5%). A more detailed breakdown of the types of cancer is provided in Table 2.

Table 1. Description of patients and respondents (N=162)

	N (%) or Mean ± SD
Sex	
Women	123 (75.9%)
Men	39 (24.1%)

Age (Years)	62.6 ± 10.8
< 60 years	58 (35.8%)
≥ 60 years	104 (64.2%)
Respondent	
Patient	156 (96.3%)
Companion	1 (0.6%)
Family	5 (3.1%)
Type of Cancer	
Breast	98 (60.5%)
Lung	19 (11.7%)
Prostate	10 (6.2%)
Rectum	7 (4.3%)
ENT (Ear-Nose-Throat)	7 (4.3%)
Skin	3 (1.9%)
Others	18 (11.4%)

Table 2. Types of cancer - detail of responses (N=162)

Cancer	N	%
HL	1	0.6
NHL	1	0.6
ENT - Oropharynx	1	0.6
ENT - Epiglottis	1	0.6
ENT - Larynx	1	0.6
ENT - Parotid	1	0.6
ENT - Pharynx	1	0.6
ENT - Sinus Piriformis	2	1.2
Unknown Primary & Metastases	6	3.7
Brain	2	1.2
Cervix	1	0.6
Colon	1	0.6
Endometrium	2	1.2
Esophagus	2	1.2
Pancreas	2	1.2
Skin	1	0.6
Pleura	1	0.6
Lung	19	11.7
Prostate	10	6.2
Rectum	6	3.7
Breast	98	60.5
Vagina	1	0.6
Bladder	1	0.6

Application Questions

The answers to the 12 questions are described in Table 3. Since we employed a cross-sectional design, we took several measures to address potential common method bias, which could arise from using a single data collection method. Firstly, we ensured participant anonymity and confidentiality, which helps reduce social desirability bias. Second, the questionnaire was designed with randomized question orders to diminish the likelihood of response pattern biases.

In total, 67.1% of the respondents consider that the application is (rather yes or completely) interesting and 63.4% have learned something thanks to the application. 52.5% of respondents will

make changes to their habits thanks to the information provided by the application. Overall, the risks and their impact are rather greater than they would have thought. They are not really surprised by the risk of death (average score of 2.9 which corresponds to 'neither yes nor no').

Table 3. Responses to application-related questions (N=162)

	N not missing	NOT (%)	Mean ± SD
1) Is the application interesting?	161		3.9 ± 1.0
1 = Not at all		3 (1.9)	
2 = Rather not		10 (6.2)	
3 = Neither yes nor no		40 (24.8)	
4 = Rather yes		60 (37.3)	
5 = Completely		48 (29.8)	
2) Did you learn anything from the app?	161		3.6 ± 1.2
1 = Not at all		13 (8.1)	
2 = Rather not		14 (8.7)	
3 = Neither yes nor no		32 (19.9)	
4 = Rather yes		66 (41.0)	
5 = Completely		36 (22.4)	
3) Do you think you will make changes in your habits thanks to the information provided by the application?	161		3.3 ± 1.2
1 = Not at all		18 (11.1)	
2 = Rather not		17 (10.5)	
3 = Neither yes nor no		42 (25.9)	
4 = Rather yes		62 (38.3)	
5 = Completely		23 (14.2)	
4) Do you think that the application has provided you with additional information compared to the various media (brochure, internet, etc.) that already exist?	161		3.3 ± 1.3
1 = Not at all		22 (13.7)	
2 = Rather not		19 (11.8)	
3 = Neither yes nor no		41 (25.5)	
4 = Rather yes		51 (31.7)	
5 = Completely		28 (17.4)	
5) Are certain risks described in the application more important than you would have thought?	161		3.6 ± 1.2
1 = Not at all		9 (5.6)	
2 = Rather not		24 (14.9)	
3 = Neither yes nor no		36 (22.4)	
4 = Rather yes		53 (32.9)	
5 = Completely		39 (24.2)	

6) Are some of the risks described in the application less important than you would have thought?	157		2.6 ± 1.1
1 = Not at all		31 (19.7)	
2 = Rather not		44 (28.0)	
3 = Neither yes nor no		53 (33.8)	
4 = Rather yes		21 (13.4)	
5 = Completely		8 (5.1)	
7) Are the impacts of certain risk factors described in the application more important than you would have thought?	162		3.4 ± 1.1
1 = Not at all		8 (4.9)	
2 = Rather not		22 (13.6)	
3 = Neither yes nor no		52 (32.1)	
4 = Rather yes		54 (33.3)	
5 = Completely		26 (16.0)	
8) Are the impacts of certain risk factors described in the application less important than you would have thought?	158		2.6 ± 1.0
1 = Not at all		21 (13.3)	
2 = Rather not		45 (28.5)	
3 = Neither yes nor no		70 (44.3)	
4 = Rather yes		16 (10.1)	
5 = Completely		6 (3.8)	
9) Are you surprised by the number of risk factors described in the application?	161		3.7 ± 1.2
1 = Not at all		13 (8.1)	
2 = Rather not		15 (9.3)	
3 = Neither yes nor no		28 (17.4)	
4 = Rather yes		59 (36.6)	
5 = Completely		46 (28.6)	
10) Are you surprised by the progression of risks over time (at 10 years, 20 years, 30 years and for life)?	161		3.5 ± 1.2
1 = Not at all		12 (7.5)	
2 = Rather not		21 (13.0)	
3 = Neither yes nor no		40 (24.8)	
4 = Rather yes		57 (35.4)	
5 = Completely		31 (19.3)	
11) Are you surprised by the risk of developing any cancer described in the app?	161		3.5 ± 1.2

1 = Not at all		17 (10.6)	
2 = Rather not		15 (9.3)	
3 = Neither yes nor no		35 (21.7)	
4 = Rather yes		55 (34.2)	
5 = Completely		39 (24.2)	
12) Are you surprised by the risk of death from cancer?	159		2.9 ± 1.4
1 = Not at all		34 (21.4)	
2 = Rather not		28 (17.6)	
3 = Neither yes nor no		41 (25.8)	
4 = Rather yes		25 (15.7)	
5 = Completely		31 (19.5)	

Application Questions – Breast Cancers

There were 98 respondents whose type of cancer was breast cancer. They were all women, aged between 33 and 79 (Mean ± Standard deviation = 60.9 ± 10.1). A member of the family completed 1 questionnaire, for the 97 others it is the patient. Table 4 gives the results of the questionnaires for these 98 patients.

Table 4. Answers to questions relating to the application (N=98 breast cancers)

	N not missing	NOT (%)	Mean ± SD
1) Is the application interesting?	97		3.8 ± 1.0
1 = Not at all		2 (2.1)	
2 = Rather not		8 (8.2)	
3 = Neither yes nor no		26 (26.8)	
4 = Rather yes		34 (35.1)	
5 = Completely		27 (27.8)	
2) Did you learn anything from the app?	98		3.5 ± 1.1
1 = Not at all		9 (9.2)	
2 = Rather not		7 (7.1)	
3 = Neither yes nor no		25 (25.5)	
4 = Rather yes		39 (39.8)	
5 = Completely		18 (18.4)	
3) Do you think you will make changes in your habits thanks to the information provided by the application?	98		3.2 ± 1.2
1 = Not at all		12 (12.2)	
2 = Rather not		10 (10.2)	
3 = Neither yes nor no		28 (28.6)	
4 = Rather yes		38 (38.8)	
5 = Completely		10 (10.2)	

4) Do you think that the application has provided you with additional information compared to the various media (brochure, internet, etc.) that already exist?	98		3.1 ± 1.2
1 = Not at all		13 (13.3)	
2 = Rather not		15 (15.3)	
3 = Neither yes nor no		26 (26.5)	
4 = Rather yes		33 (33.7)	
5 = Completely		11 (11.2)	
5) Are certain risks described in the application more important than you would have thought?	97		3.5 ± 1.1
1 = Not at all		6 (6.2)	
2 = Rather not		13 (13.4)	
3 = Neither yes nor no		25 (25.8)	
4 = Rather yes		33 (34.0)	
5 = Completely		20 (20.6)	
6) Are some of the risks described in the application less important than you would have thought?	94		2.5 ± 1.0
1 = Not at all		19 (20.2)	
2 = Rather not		27 (28.7)	
3 = Neither yes nor no		33 (35.1)	
4 = Rather yes		12 (12.8)	
5 = Completely		3 (3.2)	
7) Are the impacts of certain risk factors described in the application more important than you would have thought?	98		3.3 ± 1.0
1 = Not at all		5 (5.1)	
2 = Rather not		15 (15.3)	
3 = Neither yes nor no		37 (37.8)	
4 = Rather yes		30 (30.6)	
5 = Completely		11 (11.2)	
8) Are the impacts of certain risk factors described in the application less important than you would have thought?	96		2.6 ± 0.9
1 = Not at all		12 (12.5)	
2 = Rather not		28 (29.2)	
3 = Neither yes nor no		43 (44.8)	
4 = Rather yes		11 (11.5)	
5 = Completely		2 (2.1)	
9) Are you surprised by the number of risk factors described in the application?	98		3.7 ± 1.2
1 = Not at all		6 (6.1)	
2 = Rather not		11 (11.2)	
3 = Neither yes nor no		18 (18.4)	
4 = Rather yes		37 (37.8)	

5 = Completely		26 (26.5)	
10) Are you surprised by the progression of risks over time (at 10 years, 20 years, 30 years and for life)?	98		3.3 ± 1.2
1 = Not at all		8 (8.2)	
2 = Rather not		17 (17.3)	
3 = Neither yes nor no		25 (25.5)	
4 = Rather yes		32 (32.7)	
5 = Completely		16 (16.3)	
11) Are you surprised by the risk of developing any cancer described in the app?	98		3.4 ± 1.3
1 = Not at all		11 (11.2)	
2 = Rather not		13 (13.3)	
3 = Neither yes nor no		21 (21.4)	
4 = Rather yes		31 (31.6)	
5 = Completely		22 (22.4)	
12) Are you surprised by the risk of death from cancer?	97		2.8 ± 1.4
1 = Not at all		23 (23.7)	
2 = Rather not		18 (18.6)	
3 = Neither yes nor no		24 (24.7)	
4 = Rather yes		16 (16.5)	
5 = Completely		16 (16.5)	

Application Questions – Lung Cancers

Respondents with lung cancer as the type of cancer are 19, including 9 women and 10 men. They are between 53 and 87 years old (Mean ± Standard Deviation = 66.8 ± 7.4). A family member completed 1 questionnaire, a companion for 1 other questionnaire, and the patient for the other 17. Table 5 gives the results of the questionnaires for these 19 patients.

Table 5. Responses to application-related questions (N=19 lung cancers)

	N not missing	NOT (%)	Mean ± SD
1) Is the application interesting?	19		4.0 ± 0.8
1 = Not at all		0 (0.0)	
2 = Rather not		0 (0.0)	
3 = Neither yes nor no		6 (31.6)	
4 = Rather yes		7 (36.8)	
5 = Completely		6 (31.6)	
2) Did you learn anything from the app?	19		3.7 ± 1.1
1 = Not at all		1 (5.3)	
2 = Rather not		2 (10.6)	
3 = Neither yes nor no		3 (15.8)	
4 = Rather yes		9 (47.4)	

5 = Completely		4 (21.1)	
3) Do you think you will make changes in your habits thanks to the information provided by the application?	19		3.1 ± 1.3
1 = Not at all		3 (15.8)	
2 = Rather not		4 (21.1)	
3 = Neither yes nor no		2 (10.5)	
4 = Rather yes		8 (42.1)	
5 = Completely		2 (10.5)	
4) Do you think that the application has provided you with additional information compared to the various media (brochure, internet, etc.) that already exist?	19		3.5 ± 1.3
1 = Not at all		2 (10.5)	
2 = Rather not		2 (10.5)	
3 = Neither yes nor no		4 (21.1)	
4 = Rather yes		7 (36.8)	
5 = Completely		4 (21.1)	
5) Are certain risks described in the application more important than you would have thought?	19		3.5 ± 1.2
1 = Not at all		0 (0.0)	
2 = Rather not		5 (26.3)	
3 = Neither yes nor no		4 (21.1)	
4 = Rather yes		5 (26.3)	
5 = Completely		5 (26.3)	
6) Are some of the risks described in the application less important than you would have thought?	19		2.4 ± 1.0
1 = Not at all		3 (15.8)	
2 = Rather not		7 (36.8)	
3 = Neither yes nor no		8 (42.1)	
4 = Rather yes		0 (0.0)	
5 = Completely		1 (5.3)	
7) Are the impacts of certain risk factors described in the application more important than you would have thought?	19		3.4 ± 1.2
1 = Not at all		2 (10.5)	
2 = Rather not		2 (10.5)	
3 = Neither yes nor no		3 (15.8)	
4 = Rather yes		10 (52.6)	
5 = Completely		2 (10.5)	
8) Are the impacts of certain risk factors described in the application less important than you would have thought?	19		2.6 ± 1.1
1 = Not at all		3 (15.8)	

2 = Rather not		5 (26.3)	
3 = Neither yes nor no		8 (42.1)	
4 = Rather yes		2 (10.5)	
5 = Completely		1 (5.3)	
9) Are you surprised by the number of risk factors described in the application?	19		3.8 ± 1.3
1 = Not at all		2 (10.5)	
2 = Rather not		1 (5.3)	
3 = Neither yes nor no		2 (10.5)	
4 = Rather yes		8 (42.1)	
5 = Completely		6 (31.6)	
10) Are you surprised by the progression of risks over time (at 10 years, 20 years, 30 years and for life)?	19		3.7 ± 1.1
1 = Not at all		1 (5.3)	
2 = Rather not		1 (5.3)	
3 = Neither yes nor no		6 (31.6)	
4 = Rather yes		5 (26.3)	
5 = Completely		6 (31.6)	
11) Are you surprised by the risk of developing any cancer described in the app?	19		3.7 ± 1.1
1 = Not at all		1 (5.3)	
2 = Rather not		1 (5.3)	
3 = Neither yes nor no		5 (26.3)	
4 = Rather yes		7 (36.8)	
5 = Completely		5 (26.3)	
12) Are you surprised by the risk of death from cancer?	19		3.2 ± 1.4
1 = Not at all		3 (15.8)	
2 = Rather not		3 (15.8)	
3 = Neither yes nor no		5 (26.3)	
4 = Rather yes		3 (15.8)	
5 = Completely		5 (26.3)	

Factors influencing responses

Multiple regression models were built in order to identify whether certain characteristics of the respondents have an impact on the answers to the different questions. The explanatory variables considered are gender, age, type of respondent (patient or not), breast cancer, lung cancer (Table 6).
We highlight that patients with breast cancer have a lower response to question 3 (p=0.044), that is to say that these patients think less of making changes to their habits thanks to the information provided by the patient. 'application. We also show that the answer to question 10 decreases with age (p=0.049),

i.e. older patients are less surprised by the progression of risks over time. No other impact of the respondent's characteristics on the different answers is highlighted (all p-values > 0.05).

Table 6. Analysis of the impact of respondent characteristics on responses (N=162) – Multiple regression models

		Coef . ± SE	P-value
Question 1	Intercept	3.4 ± 0.52	-
N=161	Sex (Ref =M)	0.079 ± 0.25	0.76
	Age (Years)	0.0078 ± 0.0074	0.29
	Respondent (Ref = Patient)	0.25 ±0.42	0.55
	Breast (Ref = No)	-0.13 ± 0.24	0.61
	Lung (Ref = No)	0.033 ± 0.27	0.90
Question 2	Intercept	3.9 ± 0.62	-
N=161	Sex (Ref =M)	0.26 ± 0.30	0.76
	Age (Years)	-0.0038 ± 0.0088	0.67
	Respondent (Ref = Patient)	-0.011 ± 0.50	0.98
	Breast (Ref = No)	-0.13 ± 0.29	0.66
	Lung (Ref = No)	-0.066 ± 0.33	0.84
Question 3	Intercept	4.8 ± 0.62	-
N=162	Sex (Ref =M)	-0.19 ± 0.30	0.52
	Age (Years)	-0.016 ± 0.0088	0.077
	Respondent (Ref = Patient)	-0.32 ± 0.50	0.52
	Breast (Ref = No)	-0.59 ± 0.29	0.044
	Lung (Ref = No)	-0.49 ± 0.32	0.14
Question 4	intercept	3.7 ± 0.68	-
N=161	Sex (Ref =M)	-0.0001 ± 0.33	0.99
	Age (Years)	-0.0035 ± 0.0096	0.71
	Respondent (Ref = Patient)	0.077 ± 0.54	0.89
	Breast (Ref = No)	-0.34 ± 0.32	0.29
	Lung (Ref = No)	0.0083 ± 0.36	0.98
Question 5	Intercept	4.4 ± 0.63	-
N=161	Sex (Ref =M)	-0.094 ± 0.30	0.76
	Age (Years)	-0.011 ± 0.0089	0.23
	Respondent (Ref = Patient)	0.74 ± 0.50	0.14

	Breast (Ref = No)	-0.25 ± 0.29	0.40
	Lung (Ref = No)	-0.16 ± 0.32	0.63
Question 6	Intercept	1.6 ± 0.59	-
N=157	Sex (Ref =M)	0.44 ± 0.29	0.13
	Age (Years)	0.013 ± 0.0084	0.11
	Respondent (Ref = Patient)	-0.35 ± 0.47	0.45
	Breast (Ref = No)	0.067 ± 0.28	0.81
	Lung (Ref = No)	-0.31 ± 0.31	0.30
Question 7	Intercept	4.1 ± 0.56	-
N=162	Sex (Ref =M)	0.13 ± 0.29	0.65
	Age (Years)	-0.0080 ± 0.0080	0.32
	Respondent (Ref = Patient)	0.30 ± 0.45	0.50
	Breast (Ref = No)	-0.38 ± 0.26	0.15
	Lung (Ref = No)	-0.28 ± 0.29	0.35
Question 8	Intercept	2.1 ± 0.52	-
N=158	Sex (Ref =M)	0.35 ± 0.26	0.17
	Age (Years)	0.0050 ± 0.0074	0.50
	Respondent (Ref = Patient)	-0.25 ± 0.42	0.54
	Breast (Ref = No)	0.19 ±0.25	0.44
	Lung (Ref = No)	0.013 ± 0.27	0.96
Question 9	Intercept	3.9 ± 0.66	-
N=161	Sex (Ref =M)	-0.080 ± 0.32	0.80
	Age (Years)	-0.0036 ± 0.0093	0.70
	Respondent (Ref = Patient)	0.11 ±0.52	0.83
	Breast (Ref = No)	-0.042 ± 0.31	0.89
	Lung (Ref = No)	0.13 ±0.34	0.70
Question 10	intercept	4.9 ± 0.62	-
N=161	Sex (Ref =M)	-0.23 ± 0.30	0.44
	Age (Years)	-0.017 ± 0.0087	0.049
	Respondent (Ref = Patient)	0.14 ±0.49	0.78
	Breast (Ref = No)	-0.54 ± 0.29	0.061
	Lung (Ref = No)	0.11 ±0.32	0.72

Question 11	Intercept	4.3 ± 0.67	-
N=161	Sex (Ref =M)	0.11 ± 0.33	0.73
	Age (Years)	-0.011 ± 0.0095	0.23
	Respondent (Ref = Patient)	0.0032 ± 0.53	0.99
	Breast (Ref = No)	-0.24 ± 0.31	0.44
	Lung (Ref = No)	0.11 ±0.35	0.75
Question 12	Intercept	3.3 ± 0.76	-
N=159	Sex (Ref =M)	-0.014 ± 0.37	0.97
	Age (Years)	-0.0030 ± 0.011	0.78
	Respondent (Ref = Patient)	-0.27 ± 0.61	0.65
	Breast (Ref = No)	-0.27 ± 0.36	0.45
	Lung (Ref = No)	0.16 ± 0.40	0.69

Discussion

The term "health literacy" first appeared in 1974 as a policy issue affecting the health care system [24]. Over the years, definitions have evolved. The most recent definition was provided by the Centers for Disease Control and Prevention (CDC) in August 2020, defining health literacy as "the degree to which individuals have the ability to find, understand, and use information and services to inform health-related decisions and actions for themselves and others" [25]. The need to enhance eHealth literacy is continuously emphasized and discussed among health literacy experts and health professionals [26]. Health literacy is crucial for navigating the numerous cancer risk factors and low knowledge regarding health literacy is associated with poor medication adherence, poor health status, and increased healthcare costs [27]. And while there is little doubt that eHealth will play an even more significant role in the future, currently available tools seem to be coming up short in educating the public about their risk of cancers and the risk factors impacting it [19].

Numerous investigations have delved into the utilization of mobile applications within health-related scenarios, their objectives varying from managing diseases [28], physical and mental health interventions [29], modifying lifestyles [30], and facilitating health education [31]. The broader pattern evident in these studies aligns with our findings: effectively constructed health applications can enhance health literacy, empower individuals in managing their health, and potentially stimulate behavioral modifications.

Mobile applications have similarly started emerging as an influential tool in cancer care. Symptom tracking apps allow patients to document their symptoms in real-time, leading to more accurate reporting and timely interventions [32]. Self-management apps can also aid in medication adherence by offering medication reminders and dosage instructions, which are particularly beneficial for managing complex cancer treatment regimens [33]. Through survivorship apps, cancer survivors can monitor their quality of life (QOL) via participant reported outcomes (PROs), which is followed by automatically generated individually tailored feedback and personalized advice on supportive care

services [34]. Usability evaluations have allowed for patient feedback to improve these applications across various devices [35]

In the realm of cancer prevention and early detection, mobile applications are thus far less well established, but there are apps available that can provide personalized recommendations based on user input, such as smoking cessation strategies [36] or advice on maintaining a healthy diet and regular physical activity [37]. They can also provide tailored information about routine screenings for different types of cancer [38]. These functions contribute to raising awareness about modifiable risk factors, promoting early detection, and ultimately reducing cancer incidence and mortality.

The "Cancer Risk Calculator" application sits at the intersection of these domains. By providing tailored, accessible information about cancer risks, it equips individuals with the knowledge they need to take proactive steps in mitigating those risks [20]. To the best of our knowledge, it is the first mobile application to be tested for its potential to inform patients about their risk of various cancers and cancer risk factors.

Our results reveal a promising picture regarding the application's acceptance and potential for impact, with roughly two-thirds of respondents considering the application interesting and stating that they had learned something from it, with over half indicating that they were planning to make changes to their habits due to the information they obtained from the application. When contrasted with the existing literature, this response is very encouraging, since qualitative patient education features have only been reported in a minority of applications [39] and extensive reviews have concluded that there were no interventions designed to meet patients' full range of cancer-related information needs [40]. Furthermore, our results confirm the potential for mHealth applications to motivate users to adopt healthier habits [41], which could significantly reduce cancer risks, and dovetails nicely with the positive feedback to the broader effort of telehealth solutions that have been introduced in recent years [42,43].

In terms of risk perception, respondents tended to overestimate their risk of developing cancer. This is consistent with the existing literature, which suggests that patients tend to think they are at an increased risk of developing cancer, even when they are actually at a decreased risk [44,45]. Through multiple regression analysis, we identified some respondent characteristics that appeared to influence responses to the application's questions. Age and type of cancer (specifically breast cancer) were the primary influencing factors. Patients diagnosed with breast cancer were found to be less likely to consider making changes to their habits due to the information provided by the app ($p=0.044$). Older patients were less surprised by the progression of risks over time ($p=0.049$). The influence of age aligns with previous research that has highlighted how health perceptions and behaviors can change as people age [46].

The influence of the type of cancer on a patient's response is an intriguing finding. While our study showed that breast cancer patients were less likely to consider changing their habits, further research is needed to unpack why this is so. It may be related to the nature of the disease, the stage of the disease, or the psychological impacts that come with a cancer diagnosis.

We acknowledge several limitations. First, participation was voluntary, with fear of other cancers and not having a smartphone being cited as the main reasons for non-participation. This does not seem a large concern, since smartphone ownership will only become more ubiquitous in the future and more widespread usage of the application will depend on patient interest, allowing for self-selection of users. Second, the questionnaire's self-report nature could introduce response bias. Third, we did not capture certain potential influencing variables such as the respondents' educational background, socio-economic status, and prior knowledge about cancer, which may have affected their perceptions and responses to the app.

Conclusions

In conclusion, our study demonstrates the potential of health-based mobile applications to inform patients and change their behavior. With most respondents finding the app interesting, learning from it, and considering changes in their habits as a result, the app's promise in cancer risk education is evident. Furthermore, our study illustrates the importance of considering patient characteristics, like age and cancer type, in tailoring health information delivery.

Considering these results, we encourage policy makers to include mobile applications in their public health initiatives, to allow for better patient education, preventative care and screening efforts.

References

[1] Thiengwittayaporn S, Wattanapreechanon P, Sakon P, Peethong A, Ratisoontorn N, Charoenphandhu N, et al. Development of a mobile application to improve exercise accuracy and quality of life in knee osteoarthritis patients: a randomized controlled trial. Arch Orthop Trauma Surg 2023;143:729–38. https://doi.org/10.1007/s00402-021-04149-8.

[2] Buller DB, Borland R, Bettinghaus EP, Shane JH, Zimmerman DE. Randomized trial of a smartphone mobile application compared to text messaging to support smoking cessation. Telemed J E-Health Off J Am Telemed Assoc 2014;20:206–14. https://doi.org/10.1089/tmj.2013.0169.

[3] Al Ansari FS, Alfayez A, Alsalman D, Alanezi F, Alhodaib H, Al-Rayes S, et al. Using mobile health applications to enhance physical activity in Saudi Arabia: a cross-sectional study on users' perceptions. Int Health 2023;15:47–55. https://doi.org/10.1093/inthealth/ihac008.

[4] "World Health Organization. 'Cancer.' World Health Organization, 2022." https://www.who.int/news-room/fact-sheets/detail/cancer. n.d.

[5] Berntsen E, Babic A. Cherry: mobile application for children with cancer. Stud Health Technol Inform 2013;192:1168.

[6] Graetz I, Hu X, Curry AN, Robles A, Vidal GA, Schwartzberg LS. Mobile application to support oncology patients during treatment on patient outcomes: Evidence from a randomized controlled trial. Cancer Med 2023;12:6190–9. https://doi.org/10.1002/cam4.5351.

[7] Gopichandran L, Garg R, Chalga MS, Joshi P, Dhandapani M, Bhatnagar S. Development of Mobile Application-Based System for Improving Medication Adherence Among Cancer Patients Receiving Palliative Therapy. Indian J Palliat Care 2023;29:51–6. https://doi.org/10.25259/IJPC_12_2021.

[8] Ruco A, Dossa F, Tinmouth J, Llovet D, Jacobson J, Kishibe T, et al. Social Media and mHealth Technology for Cancer Screening: Systematic Review and Meta-analysis. J Med Internet Res 2021;23:e26759. https://doi.org/10.2196/26759.

[9] Lamb LR, Baird GL, Roy IT, Choi PHS, Lehman CD, Miles RC. Are English-language online patient education materials related to breast cancer risk assessment understandable, readable, and actionable? Breast Edinb Scotl 2022;61:29–34. https://doi.org/10.1016/j.breast.2021.11.012.

[10] Ahmed HG, Abboh E a. A, Alnajib AMA, Elhussein GMO, Mustafa SA, Abdalla R a. H, et al. Shared thoughts and practices on some modifiable cancer risk factors. Eur Rev Med Pharmacol Sci 2023;27:3612–21. https://doi.org/10.26355/eurrev_202304_32145.

[11] Galvin AM, Garg A, Griner SB, Moore JD, Thompson EL. Health Literacy Correlates to HPV Vaccination Among US Adults Ages 27-45. J Cancer Educ Off J Am Assoc Cancer Educ 2023;38:349–56. https://doi.org/10.1007/s13187-021-02123-x.

[12] Poon PKM, Tam KW, Lam T, Luk AKC, Chu WCW, Cheung P, et al. Poor health literacy associated with stronger perceived barriers to breast cancer screening and overestimated breast cancer risk. Front Oncol 2022;12:1053698. https://doi.org/10.3389/fonc.2022.1053698.

[13] Gansler T, Henley SJ, Stein K, Nehl EJ, Smigal C, Slaughter E. Sociodemographic determinants of cancer treatment health literacy. Cancer 2005;104:653–60. https://doi.org/10.1002/cncr.21194.

[14] Zhang L, Jiang S. Examining the Role of Information Behavior in Linking Cancer Risk Perception and Cancer Worry to Cancer Fatalism in China: Cross-Sectional Survey Study. J Med Internet Res 2024;26:e49383. https://doi.org/10.2196/49383.
[15] Anderson KM, Wilson PW, Odell PM, Kannel WB. An updated coronary risk profile. A statement for health professionals. Circulation 1991;83:356–62. https://doi.org/10.1161/01.cir.83.1.356.
[16] Eichler K, Puhan MA, Steurer J, Bachmann LM. Prediction of first coronary events with the Framingham score: a systematic review. Am Heart J 2007;153:722–31, 731.e1-8. https://doi.org/10.1016/j.ahj.2007.02.027.
[17] Gail MH, Brinton LA, Byar DP, Corle DK, Green SB, Schairer C, et al. Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. J Natl Cancer Inst 1989;81:1879–86. https://doi.org/10.1093/jnci/81.24.1879.
[18] "Breast Cancer Risk Assessment Tool," Breast Cancer Risk Assessment Tool. https://www.cancer.gov/bcrisktool (accessed Jun. 22, 2023). n.d.
[19] Westerlinck P, Coucke P. Review of interactive digital solutions improving health literacy of personal cancer risks in the general public. Int J Med Inf 2021;154:104564. https://doi.org/10.1016/j.ijmedinf.2021.104564.
[20] Westerlinck P, Coucke P, Albert A. Development of a cancer risk model and mobile health application to inform the public about cancer risks and risk factors. Int J Med Inf 2024;189:105503. https://doi.org/10.1016/j.ijmedinf.2024.105503.
[21] National Cancer Institute. (2021). Surveillance, Epidemiology, and End Results (SEER) Program. [Online] Available at: https://seer.cancer.gov/. n.d.
[22] Centers for Disease Control and Prevention. (2021). National Program of Cancer Registries (NPCR). [Online] Available at: https://www.cdc.gov/cancer/npcr/. n.d.
[23] Food and Drug Administration. (2021). Mobile Medical Applications. [Online] Available at: https://www.fda.gov/medical-devices/digital-health-center-excellence/mobile-medical-applications. n.d.
[24] C. Zarcadoolas, A. Pleasant, and D. S. Greer, Advancing Health Literacy: A Framework for Understanding and Action. John Wiley & Sons, 2012. n.d.
[25] CDC (2020). Health Literacy. Retrieved from https://www.cdc.gov/healthliteracy/learn/index.html. n.d.
[26] Institute of Medicine, Board on Population Health and Public Health Practice, and Roundtable on Health Literacy, Health Literacy, eHealth, and Communication: Putting the Consumer First: Workshop Summary. National Academies Press, 2009. n.d.
[27] Berkman ND, Sheridan SL, Donahue KE, Halpern DJ, Crotty K. Low Health Literacy and Health Outcomes: An Updated Systematic Review. Ann Intern Med 2011;155:97. https://doi.org/10.7326/0003-4819-155-2-201107190-00005.
[28] Silva BMC, Rodrigues JJPC, De La Torre Díez I, López-Coronado M, Saleem K. Mobile-health: A review of current state in 2015. J Biomed Inform 2015;56:265–72. https://doi.org/10.1016/j.jbi.2015.06.003.
[29] Rathbone AL, Prescott J. The Use of Mobile Apps and SMS Messaging as Physical and Mental Health Interventions: Systematic Review. J Med Internet Res 2017;19:e295. https://doi.org/10.2196/jmir.7740.
[30] Payne HE, Lister C, West JH, Bernhardt JM. Behavioral Functionality of Mobile Apps in Health Interventions: A Systematic Review of the Literature. JMIR MHealth UHealth 2015;3:e20. https://doi.org/10.2196/mhealth.3335.
[31] Jang I. A Systematic Review on Mobile Health Applications' Education Program for Patients Taking Oral Anticoagulants. Int J Environ Res Public Health 2021;18:8902. https://doi.org/10.3390/ijerph18178902.
[32] Basch E, Deal AM, Kris MG, Scher HI, Hudis CA, Sabbatini P, et al. Symptom Monitoring With Patient-Reported Outcomes During Routine Cancer Treatment: A Randomized Controlled Trial. J Clin Oncol 2016;34:557–65. https://doi.org/10.1200/JCO.2015.63.0830.
[33] Klasnja P, Pratt W. Healthcare in the pocket: Mapping the space of mobile-phone health interventions. J Biomed Inform 2012;45:184–98. https://doi.org/10.1016/j.jbi.2011.08.017.
[34] Duman-Lubberding S, Van Uden-Kraan CF, Jansen F, Witte BI, Van Der Velden LA, Lacko

M, et al. Feasibility of an eHealth application “OncoKompas” to improve personalized survivorship cancer care. Support Care Cancer 2016;24:2163–71. https://doi.org/10.1007/s00520-015-3004-2.
[35] Mirkovic J, Kaufman DR, Ruland CM. Supporting cancer patients in illness management: usability evaluation of a mobile app. JMIR MHealth UHealth 2014;2:e33. https://doi.org/10.2196/mhealth.3359.
[36] Lana A, Faya-Ornia G, López ML. Impact of a web-based intervention supplemented with text messages to improve cancer prevention behaviors among adolescents: Results from a randomized controlled trial. Prev Med 2014;59:54–9. https://doi.org/10.1016/j.ypmed.2013.11.015.
[37] Martin CK, Miller AC, Thomas DM, Champagne CM, Han H, Church T. Efficacy of SmartLoss ^{SM} , a smartphone-based weight loss intervention: Results from a randomized controlled trial: SmartLoss Weight Loss Intervention. Obesity 2015;23:935–42. https://doi.org/10.1002/oby.21063.
[38] Salmani H, Ahmadi M, Shahrokhi N. The Impact of Mobile Health on Cancer Screening: A Systematic Review. Cancer Inform 2020;19:117693512095419. https://doi.org/10.1177/1176935120954191.
[39] Vaffis S, Whaley S, Axon DR, Hall-Lipsy E, Hincapie A, Slack M, et al. Features of Cancer mHealth Apps and Evidence for Patient Preferences: Scoping Literature Review. JMIR Cancer 2023;9:e37330. https://doi.org/10.2196/37330.
[40] Richards R, Kinnersley P, Brain K, McCutchan G, Staffurth J, Wood F. Use of Mobile Devices to Help Cancer Patients Meet Their Information Needs in Non-Inpatient Settings: Systematic Review. JMIR MHealth UHealth 2018;6:e10026. https://doi.org/10.2196/10026.
[41] Lee M, Lee H, Kim Y, Kim J, Cho M, Jang J, et al. Mobile App-Based Health Promotion Programs: A Systematic Review of the Literature. Int J Environ Res Public Health 2018;15:2838. https://doi.org/10.3390/ijerph15122838.
[42] Alhassan GN, Öztürk İ, AdedoyiN FF, Bekun FV. Telehealth as a Panacea Amidst Global Pandemic (COVID-19) in Africa. Düzce Tıp Fakültesi Derg 2021;23:43–7. https://doi.org/10.18678/dtfd.898373.
[43] Alhassan GN, Bosnak AS, Hamurtekin E. Perceived satisfaction and outcomes from drug information center services provided with a telehealth approach. Niger J Clin Pract 2022;25:2053–61. https://doi.org/10.4103/njcp.njcp_552_22.
[44] Gonzalez S, Mora Hurtado AC, Syder NC, Rodman J, Elbuluk N. Perception of skin cancer risk and sun protective practices in individuals with vitiligo: a prospective international cross-sectional survey. Arch Dermatol Res 2024;316:189. https://doi.org/10.1007/s00403-024-02942-0.
[45] Abittan B, Pachtman S, Herman S, Indelicato J, Herman J. Perception of Breast Cancer Risk in Over 11,000 Patients During Routine Mammography Exam. J Cancer Educ 2020;35:782–7. https://doi.org/10.1007/s13187-019-01530-5.
[46] J. Kerr, D. Rosenberg, and L. Frank, “The role of the built environment in healthy aging,” J. Plan. Lit., vol. 27, no. 1, pp. 43–60, Feb. 2012. N.d.

Conclusion:

This thesis investigated the development and impact of a novel mobile health application, "Cancer Risk Calculator" (CRC), designed to enhance public understanding of cancer risks and promote preventative behaviors. Addressing the limitations of existing cancer risk assessment tools, this research sought to provide a comprehensive, personalized, and accessible resource for the general public.

The thesis makes several significant contributions to the field. First, it presents the development of a unique cancer risk model incorporated within the CRC application. This model considers a broad spectrum of cancer types and associated risk factors, offering users a more comprehensive assessment of their individual cancer risks. Second, the development of the CRC application itself signifies an important step toward leveraging mobile technology for public health education, specifically in the crucial area of cancer prevention. By making risk information readily available and understandable, the application empowers individuals to actively participate in their health management.

The evaluation of the CRC application's impact on cancer risk health literacy constitutes a key aspect of this research. Findings from a study involving 162 participants indicate a positive response to the application, with a majority finding it engaging, informative, and potentially motivating behavior change. These results align with broader research on the potential of health-focused mobile applications to enhance health literacy and encourage healthier behaviors. Notably, this research provides crucial evidence supporting the effectiveness of mHealth interventions in the context of cancer prevention, a previously less explored area.

However, the research also acknowledges limitations, including potential response bias inherent in self-reported data and the absence of specific socio-economic and educational background information in the evaluation phase. Future studies could address these limitations by incorporating diverse data collection methods and considering a broader range of demographic factors.

The potential of mobile health applications like the CRC to bridge the gap between complex medical information and public understanding is vast. By providing personalized risk assessments, promoting health literacy, and potentially influencing preventative behaviors, the CRC application exemplifies a significant advancement in digital health interventions for cancer prevention. The findings underscore the need for further exploration and integration of mHealth strategies into public health initiatives to empower individuals and enhance population health outcomes.

Ongoing efforts

Now that the initial impact of the Cancer Risk Calculator (CRC) application on cancer patients has been successfully assessed, two additional studies are currently underway to further explore the broader implications and benefits of the tool. These studies aim to evaluate the impact of the CRC application in diverse populations: the general public and high-risk individuals, specifically smokers. By recruiting participants from a general practitioner's cabinet and consulting with tabacologists within the CHU (Centre Hospitalier Universitaire) and CHC (Centre Hospitalier Chrétien) networks, these studies aim to extend the application’s reach and evaluate its effectiveness in diverse contexts.

The first study involves recruiting participants from general practitioner (GP) clinics to understand how the CRC application affects the general public. General practitioners are often the first point of contact for health concerns, making them an ideal setting for engaging a broad cross-section of the population. By targeting individuals who may not have an immediate cancer diagnosis but are interested in preventive health, this study will assess the application's ability to raise awareness and encourage lifestyle changes in a non-specialist setting.

The inclusion of participants from GP cabinets provides a unique opportunity to gauge how well the CRC application can integrate into routine healthcare settings and influence the behavior of individuals who may not otherwise consider themselves at high risk for cancer. The value of this study lies in its potential to identify the CRC's broader public health impact—specifically, how personalized risk assessments can motivate preventative behaviors among the general population. If successful, this integration into general practice could enhance proactive health behaviors, improve early detection of cancer risks, and reduce the overall burden on healthcare systems through increased prevention and early intervention. Since the application has been shown to have positive effects on habit changes for people who have already had cancer, it stands to reason that there would be a similar or even greater impact on people who have not had cancer. For individuals without a cancer history, the focus is primarily on prevention rather than prognosis, which could lead to a broader engagement with preventive health behaviors. In contrast, cancer survivors may be more focused on managing their existing condition and less motivated by the prevention of future cancers. Therefore, the CRC application has the potential to play a significant role in motivating healthy lifestyle changes among the general public, who may be more receptive to proactive prevention strategies.

The second study focuses on smokers, a population with a particularly high risk of developing various types of cancers, notably lung cancer. By recruiting participants through tabacologists in the CHU and CHC networks, the research aims to assess the CRC application's utility in a high-risk population that stands to benefit significantly from tailored health interventions. Smokers represent a unique demographic for studying the application's effectiveness in not only raising awareness but potentially also encouraging smoking cessation and other preventive health behaviors.

Smokers are at increased risk for multiple cancers, and an intervention like the CRC could serve as both an educational tool and a motivational catalyst for quitting smoking. By providing personalized risk assessments, the application can present a compelling, individualized picture of the potential consequences of continued smoking, which could foster greater motivation for behavioral change. The use of tabacologists as a recruitment point also offers a strategic advantage—smokers consulting specialists are likely to be already considering changes to their habits, and the CRC's integration into their consultations could further enhance their readiness to quit and adopt healthier lifestyles.

This study could provide valuable evidence on how mobile health tools can serve as an adjunct to traditional cessation programs, potentially leading to increased success rates in quitting smoking and reducing cancer incidence. The results could pave the way for incorporating such digital tools into broader cessation strategies, creating a more holistic approach to cancer prevention.

These studies will provide foundational data that could inform the integration of the CRC application into public health initiatives, allowing healthcare providers to leverage digital tools to promote early detection and prevention on a larger scale. They will also help identify any unique barriers or facilitators for adoption in these populations, ultimately guiding further enhancements to the application's design and functionality. This expansion of the research scope holds promise for

enhancing cancer prevention strategies, empowering individuals with diverse health profiles, and advancing public health outcomes through innovative mobile health solutions.

Possible Improvements for the Application and Model

One of the primary strengths of the CRC approach is that it allows for easy updating based on new data appearing in the scientific literature. This flexibility is crucial because our understanding of cancer risk factors is continuously evolving. The CRC can be updated to include new risk factors as they are identified, or to incorporate new data, such as more fine-grained analyses of existing risk factors. For example, for a given cancer, the model might currently be accounting for the impact of tobacco by categorizing individuals based on smoking status (i.e., smoker vs. non-smoker), but if better data become available, the model could be updated to consider both the length of smoking history and the intensity of smoking, providing a more accurate risk assessment for each user. This ability to evolve with new research findings ensures that the CRC remains at the cutting edge of cancer prevention science.

Moreover, the model allows for the creation of separate versions tailored for different populations, which is particularly important given that many cancer risk factors vary in their impact across different regions of the world. For example, the influence of certain dietary habits or environmental exposures may be different in Western populations compared to populations in Asia or Africa. By developing population-specific versions of the CRC, we can ensure that risk assessments are as relevant and accurate as possible for diverse users. This tailoring can improve the applicability of the CRC for different cultural and geographical contexts, ultimately making the tool more effective globally.

Similar improvements are possible when considering the validated models. The application has already incorporated many validated models for assessing risks of various cancers, making it adaptable for incorporating additional models in the future. This flexibility is an important feature that enhances the relevance and utility of the application as new scientific knowledge emerges. Each of the incorporated models has been validated for specific cancer types, ensuring that users receive reliable risk assessments tailored to different types of cancer. The application is also capable of determining whether a particular model is applicable to an individual based on the data they provide, such as age, gender, family history, and other relevant risk factors. This capacity could be further refined to ensure users are matched with the most appropriate validated model based on more nuanced criteria, such as the similarity of the user to the population used to develop the model. For instance, if a model was developed using data from a particular demographic group, users with characteristics that closely resemble this group could be prioritized for use of that specific model, thereby increasing the accuracy of the risk prediction.

Another potential improvement involves enhancing the user interface and user experience based on user feedback and usability testing. Ensuring that the application is accessible, easy to use, and engaging is key to encouraging sustained use and maximizing its impact. Additional features, such as goal-setting tools, personalized reminders, and connections to local health resources, could also be integrated to provide further support for behavior change.

Embedding the CRC into existing electronic health records (EHR) and healthcare information systems could enable healthcare providers to use CRC data as part of routine medical assessments. This integration could facilitate personalized preventive recommendations during medical appointments

and ensure healthcare professionals are equipped with the most up-to-date insights on their patients' cancer risks. Additionally, integrating the CRC application with other health apps or wearable devices could provide a more comprehensive view of individual health, tracking physical activity, diet, sleep patterns, and other behaviors that impact cancer risk.

Another important perspective is how the CRC could be used as part of public health campaigns. Governments and public health organizations could adopt CRC as a tool to reach broader populations, particularly in underserved communities. With appropriate consent and healthcare provider participation, the CRC could also provide anonymized data that informs policymakers on high-risk groups within populations, helping direct resources and targeted interventions where they are most needed. Furthermore, the insights gained from using CRC in real-world settings could drive policy changes related to cancer prevention and early detection strategies.

With the information gathered from the CRC, more targeted interventions could be developed. By identifying specific behaviors that individuals are most likely to change, the CRC could provide personalized follow-up support tailored to each user's risk profile. Such support could include personalized messaging, interactive coaching, or connections to local resources, providing sustained motivation to maintain positive lifestyle changes. Additionally, targeted interventions could be directed toward high-risk groups, such as individuals with a family history of cancer or those in high-exposure environments, providing them with more proactive support.

Building a sense of community and ongoing support could significantly enhance the user experience and the long-term effectiveness of the CRC application. Adding features that allow users to connect with others facing similar risk factors or pursuing similar health goals could foster a sense of solidarity and shared purpose. Community forums, peer support groups, and success stories could help motivate users to sustain behavior changes. Moreover, incorporating feedback mechanisms where users can provide input on the app's features could ensure that it continuously evolves to meet user needs and preferences.

Finally, leveraging machine learning and artificial intelligence techniques could further improve the predictive accuracy of the CRC model. By continuously learning from new data, the CRC could become increasingly accurate in predicting individual cancer risks, while also identifying patterns in behavior change that can inform future interventions. These improvements would not only enhance the application's accuracy and effectiveness but also contribute to its capacity to support sustained health behavior change and cancer prevention efforts.

Future Perspectives & Research Opportunities:

1) Validation of the Cancer Risk Model

Since the cancer risk model integrated into the CRC application has not yet undergone formal validation, a study specifically designed to validate the model could be extremely useful. Validation is an essential process to ensure that the predictions and risk assessments provided by the CRC are accurate, reliable, and applicable across different populations. A validated model would provide users, healthcare providers, and policymakers with greater confidence in the tool's utility for assessing cancer risk.

Validating the model would involve comparing its predictions with real-world outcomes, ideally using longitudinal data that tracks participants' health status over time. Such a study would help determine how well the CRC model predicts actual cancer incidence and whether its risk factors are weighted appropriately. Moreover, validation is key to identifying any biases within the model, ensuring that it performs equally well across diverse demographic groups, including different ages, genders, socio-economic backgrounds, and ethnicities.

Conducting a validation study would also open up opportunities for refining the CRC model to improve its predictive power. If the model is found to underpredict or overpredict cancer risk for specific subgroups, adjustments can be made to enhance its accuracy. Ultimately, this would lead to a more trustworthy and effective tool that could be recommended for widespread use in preventive health initiatives.

A validated CRC model could also facilitate integration into clinical settings, which is discussed below.

2) Promoting Participation in Screening Examinations

Another promising research opportunity lies in exploring how the CRC application could be used to promote participation in cancer screening examinations, thereby facilitating early detection of cancer and improving prognoses. By leveraging the personalized cancer risk assessments provided by the CRC, future research could assess how effectively the application can highlight the importance of timely screenings for individuals at elevated risk. This could include evaluating the effectiveness of tailored educational content, reminders, and actionable guidance in encouraging users to schedule and participate in appropriate screening tests, such as mammograms, colonoscopies, or skin checks, based on their individual risk profiles.

The potential to promote participation in screening dovetails nicely with the validated models included in the application, as many of these models were developed to guide screening and early detection programs. By aligning users with validated models that are specifically designed to identify individuals at high risk, the CRC can educate users on the benefits of regular screening in a targeted manner. Encouraging participation in screenings is particularly crucial, as early detection of cancer is often associated with better treatment outcomes and higher survival rates.

This research could also investigate ways to further enhance the CRC by incorporating features that facilitate the actual scheduling of screening appointments. Integrating the application with local healthcare systems and screening facilities could allow users to directly book their screening examinations through the app, effectively reducing barriers to accessing these services. Automated notifications and reminders could be used to prompt users to follow through with their scheduled screenings, reducing the risk of missed appointments and ensuring adherence to recommended screening intervals.

Ultimately, examining how the CRC promotes participation in cancer screening examinations could offer significant contributions to cancer prevention research. This proactive approach aligns well with the CRC's goal of empowering users with knowledge and tools to take meaningful action toward maintaining their health. Understanding the effectiveness of these strategies could help enhance individual health management, reduce the burden of late-stage cancer on healthcare systems, and contribute to better outcomes for at-risk individuals.

3) Long-term Behavior Change and Risk Analysis

While our findings suggest that the CRC application can be very effective in promoting behavior change for modifiable cancer risk factors, long-term follow-up is necessary to verify whether such changes are maintained over time. Behavior change, particularly in the context of health risks, often requires sustained motivation and support, and it is unclear if the positive changes observed in the short term will persist in the absence of ongoing intervention. Conducting long-term studies would provide valuable insights into the durability of behavior changes prompted by the CRC application, helping to determine if additional support or follow-up features might be needed to maintain these positive health behaviors.

Moreover, a more detailed analysis is required to understand which specific risk factors are most likely to be impacted and maintained as a result of using the CRC. Different modifiable risk factors—such as smoking cessation, dietary changes, physical activity, and alcohol consumption—may vary in the degree to which individuals can sustain changes over time. Understanding which behaviors are most amenable to long-term change can help refine the CRC application to focus on the most impactful areas and provide targeted resources to support sustained behavior modification. This detailed analysis would further enhance the effectiveness of the CRC, ensuring that it delivers meaningful, lasting improvements in cancer prevention and overall health.

4) Psychological Evaluation & Implications on Quality of Life

In addition to promoting physical health changes, future research should explore the impact of the CRC application on psychological well-being. This includes understanding whether personalized risk assessments and the subsequent behavior changes positively influence mental health, particularly by reducing anxiety associated with health uncertainties. Being informed about one's risk can lead to greater empowerment, a sense of control, and proactive health management, potentially reducing the fear of the unknown and prompting beneficial lifestyle changes. This sense of empowerment and the ability to make informed choices about one's health can lead to improved quality of life, as users take steps to mitigate their cancer risk.

However, there is also the potential for negative psychological effects, particularly for individuals who may experience increased worry and anxiety upon learning about their elevated cancer risk. It is crucial to recognize that for some, the detailed information provided by the CRC might provoke anxiety rather than prompt action. Interestingly, feedback from recruiting caregivers for the studies mentioned above suggests that individuals who tend to worry excessively about their health often indicate that they prefer not to know too many details about their risk. This implies that those who decide to download and use the CRC application are likely to be individuals who are less prone to anxiety about their health status, thereby reducing the potential negative impact of the application. By self-selecting, the users of the CRC are more likely to be those who will benefit from the information without experiencing undue psychological distress.

These implications on quality of life are an important aspect of the CRC's broader impact and merit investigation. It may also be valuable to conduct a more in-depth psychological evaluation to assess how users respond emotionally over time and whether adaptive support features could mitigate any potential negative effects, such as increased anxiety or health-related stress.

5) Longitudinal Outcomes and Cost-Benefit Analysis

Finally, conducting a cost-benefit analysis over time could be valuable for assessing the CRC's broader impact on healthcare costs and outcomes. If the CRC application successfully reduces cancer incidence and promotes earlier detection, it could result in significant cost savings for healthcare systems. Understanding these economic benefits could facilitate greater buy-in from healthcare providers, insurance companies, and public health entities. Longitudinal studies should also examine how the CRC impacts cancer morbidity and mortality rates over extended periods, providing clear evidence of its long-term effectiveness in reducing the cancer burden at the population level.

Appendix 1: Included risk models

First Author	Name of model	Year	Type	Discrimination (AUROC or C-statistic)	Applicability	Reference
Cha	Cytology & Immunocytology Model	2012	Bladder cancer	0.908	Patients with painless hematuria	Cha EK, Tirsar LA, Schwentner C, Christos PJ, Mian C, Hennenlotter J, Martini T, Stenzl A, Pycha A, Shariat SF, Schmitz-Dräger BJ. Immunocytology is a strong predictor of bladder cancer presence in patients with painless hematuria: a multicentre study. Eur Urol. 2012 Jan;61(1):185-92. doi: 10.1016/j.eururo.2011.08.073. Epub 2011 Sep 9. PMID: 21924544; PMCID: PMC3628750.
Hee	/	2013	Bladder cancer	0.804	Patients with hematuria	Hee TG, Shah SA, Ann HS, Hemdan SN, Shen LC, Al-Fahmi Abdul Galib N, Singam P, Chee Kong CH, Hong GE, Bahadzor B, Zainuddin ZM. Stratifying patients with haematuria into high or low risk groups for bladder cancer: a novel clinical scoring system. Asian Pac J Cancer Prev. 2013;14(11):6327-30. doi: 10.7314/apjcp.2013.14.11.6327. PMID: 24377526.
Lotan	Base + NMP22 model	2009	Bladder cancer	0.824	General public	Lotan Y, Capitanio U, Shariat SF, Hutterer GC, Karakiewicz PI. Impact of clinical factors, including a point-of-care nuclear matrix protein-22 assay and cytology, on bladder cancer detection. BJU Int. 2009 May;103(10):1368-74. doi: 10.1111/j.1464-410X.2009.08360.x. Epub 2009 Mar 11. Erratum in: BJU Int. 2010 Apr;105(7):1036. PMID: 19338566.
Tan	Haematuria Cancer Risk Score (HCRS)	2019	Urinary tract cancer	Development: 0.768 (0.741–0.795) Validation: 0.835 (0.789–0.880)	Patients with hematuria	Tan WS, Ahmad A, Feber A, Mostafid H, Cresswell J, Fankhauser CD, Waisbrod S, Hermanns T, Sasieni P, Kelly JD; DETECT I trial collaborators. Development and validation of a haematuria cancer risk score to identify patients at risk of harbouring cancer. J Intern Med. 2019 Apr;285(4):436-445. doi: 10.1111/joim.12868. Epub 2019 Jan 4. PMID: 30521125; PMCID: PMC6446724.
Matulewicz	/	2020	Bladder cancer	Development: 0.79 (0.75–0.83) Validation: 0.74 (0.67–0.80)	Patients with new diagnosis of microscopic hematuria	Matulewicz RS, Rademaker A, Meeks JJ. A simplified nomogram to assess risk of bladder cancer in patients with a new diagnosis of microscopic hematuria. Urol Oncol. 2020 Apr;38(4):240-246. doi: 10.1016/j.urolonc.2019.12.010. Epub 2020 Jan 14. PMID: 31952999; PMCID: PMC7150636.
Wu	Epidemiologic model	2007	Bladder cancer	0.70 (0.67-0.73)	General public	Wu X, Lin J, Grossman HB, Huang M, Gu J, Etzel CJ, Amos CI, Dinney CP, Spitz MR. Projecting individualized probabilities of developing bladder cancer in white individuals. J Clin Oncol. 2007 Nov 1;25(31):4974-81. doi: 10.1200/JCO.2007.10.7557. PMID: 17971596.

Wu	Epidemiologic-genetic model.	2007	Bladder cancer	0.80 (0.72-0.82)	General public	Wu X, Lin J, Grossman HB, Huang M, Gu J, Etzel CJ, Amos CI, Dinney CP, Spitz MR. Projecting individualized probabilities of developing bladder cancer in white individuals. J Clin Oncol. 2007 Nov 1;25(31):4974-81. doi: 10.1200/JCO.2007.10.7557. PMID: 17971596.
Huang	/	2016	Bladder cancer	0.891 (0.86–0.92)	General public	Huang S, Kou L, Furuya H, Yu C, Goodison S, Kattan MW, Garmire L, Rosser CJ. A Nomogram Derived by Combination of Demographic and Biomarker Data Improves the Noninvasive Evaluation of Patients at Risk for Bladder Cancer. Cancer Epidemiol Biomarkers Prev. 2016 Sep;25(9):1361-6. doi: 10.1158/1055-9965.EPI-16-0260. Epub 2016 Jul 6. PMID: 27383773; PMCID: PMC5106243.
Gail	Breast Cancer Risk Assessment Tool	1989	Breast cancer (invasive or in situ)	0.58–0.74	Women in the general public	Gail MH, Brinton LA, Byar DP, Corle DK, Green SB, Schairer C, Mulvihill JJ. Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. J Natl Cancer Inst. 1989 Dec 20;81(24):1879-86. doi: 10.1093/jnci/81.24.1879. PMID: 2593165.
Banegas	Hispanic risk model (HRM) - US-born	2016	Breast cancer (invasive)	0.564 (0.485-0.644)	US Hispanic Women	Banegas MP, John EM, Slattery ML, Gomez SL, Yu M, LaCroix AZ, Pee D, Chlebowski RT, Hines LM, Thompson CA, Gail MH. Projecting Individualized Absolute Invasive Breast Cancer Risk in US Hispanic Women. J Natl Cancer Inst. 2016 Dec 20;109(2):djw215. doi: 10.1093/jnci/djw215. PMID: 28003316; PMCID: PMC5174188.
Banegas	Hispanic risk model (HRM) - foreign-born	2016	Breast cancer (invasive)	0.625 (0.487-0.764)	US Hispanic Women	Banegas MP, John EM, Slattery ML, Gomez SL, Yu M, LaCroix AZ, Pee D, Chlebowski RT, Hines LM, Thompson CA, Gail MH. Projecting Individualized Absolute Invasive Breast Cancer Risk in US Hispanic Women. J Natl Cancer Inst. 2016 Dec 20;109(2):djw215. doi: 10.1093/jnci/djw215. PMID: 28003316; PMCID: PMC5174188.

Pankratz	BBD-BC model	2015	Breast cancer (invasive or in situ)	5-year: 0.692 (0.62-0.77) (Derivation) 0.644 (0.57-0.72) (Validation) 10-year: 0.665 (0.61-0.72) (Derivation) 0.629 (0.58-0.68) (Validation) Lifetime year: 0.636 (0.60-0.67) (Derivation) 0.650 (0.62-0.68) (Validation)	Women with benign breast disease	Pankratz VS, Degnim AC, Frank RD, Frost MH, Visscher DW, Vierkant RA, Hieken TJ, Ghosh K, Tarabishy Y, Vachon CM, Radisky DC, Hartmann LC. Model for individualized prediction of breast cancer risk after a benign breast biopsy. J Clin Oncol. 2015 Mar 10;33(8):923-9. doi: 10.1200/JCO.2014.55.4865. Epub 2015 Jan 26. PMID: 25624442; PMCID: PMC4348637.
Claus	/	1993	Breast cancer	NA	women with a first degree family history of ovarian cancer	Claus EB, Risch N, Thompson WD. The calculation of breast cancer risk for women with a first degree family history of ovarian cancer. Breast Cancer Res Treat. 1993 Nov;28(2):115-20. doi: 10.1007/BF00666424. PMID: 8173064.
Cook	/	2009	Breast cancer	/	/	Cook NR, Rosner BA, Hankinson SE, Colditz GA. Mammographic screening and risk factors for breast cancer. Am J Epidemiol. 2009 Dec 1;170(11):1422-32. doi: 10.1093/aje/kwp304. Epub 2009 Oct 29. PMID: 19875646; PMCID: PMC2800262.
Novotny	First variant of the Czech model	2006	Breast cancer	NR	Women in general public	Novotny J, Pecen L, Petruzelka L, Svobodnik A, Dusek L, Danes J, Skovajsova M. Breast cancer risk assessment in the Czech female population--an adjustment of the original Gail model. Breast Cancer Res Treat. 2006 Jan;95(1):29-35. doi: 10.1007/s10549-005-9027-5. Epub 2005 Dec 1. PMID: 16319995.
Novotny	Second variant of the Czech model	2006	Breast cancer	NR	Women in general public	Novotny J, Pecen L, Petruzelka L, Svobodnik A, Dusek L, Danes J, Skovajsova M. Breast cancer risk assessment in the Czech female population--an adjustment of the original Gail model. Breast Cancer Res Treat. 2006 Jan;95(1):29-35. doi: 10.1007/s10549-005-9027-5. Epub 2005 Dec 1. PMID: 16319995.
Rosner	/	1996	Breast cancer	NR	Women in	Rosner B, Colditz GA. Nurses' health study: log-incidence mathematical model of breast cancer incidence. J Natl

					general public	Cancer Inst. 1996 Mar 20;88(6):359-64. doi: 10.1093/jnci/88.6.359. PMID: 8609645.
Rosner	/	2008	ER+ Breast cancer (invasive)	0.645 (0.38-0.652)	Women in general public	Rosner B, Colditz GA, Iglehart JD, Hankinson SE. Risk prediction models with incomplete data with application to prediction of estrogen receptor-positive breast cancer: prospective data from the Nurses' Health Study. Breast Cancer Res. 2008;10(4):R55. doi: 10.1186/bcr2110. Epub 2008 Jul 3. PMID: 18598349; PMCID: PMC2575548.
Sun	BRCA-CRisk	2022	Contralateral breast cancer	Development: 5-year: 0.775, 10-year : 0.702 Validation: 5-year: 0.750, 10-year: 0.691	BRCA1/2 with unilateral breast cancer	Sun J, Chu F, Pan J, Zhang Y, Yao L, Chen J, Hu L, Zhang J, Xu Y, Wang X, Cao W, Xie Y. BRCA-CRisk: A Contralateral Breast Cancer Risk Prediction Model for BRCA Carriers. J Clin Oncol. 2023 Feb 10;41(5):991-999. doi: 10.1200/JCO.22.00833. Epub 2022 Dec 8. PMID: 36480783.
Zhu	/	2023	Breast cancer	Development: 0.607 (1 year) 0.604 (3 year) 0.594 (5 year) Validation: 0.643 (1 year)	Women in general public	Zhu J, Wang L, Gong W, Li X, Wang Y, Zhu C, Li H, Shi L, Yang C, Du L. Development and evaluation of a risk assessment tool for the personalized screening of breast cancer in Chinese populations: A prospective cohort study. Cancer. 2023 Nov 2. doi: 10.1002/cncr.35095. Epub ahead of print. PMID: 37916832.
Giardiello	PredictCBC-1A	2019	Contralateral breast cancer	5 years: 0.63 (0.52–0.74) 10 years: 0.63 (0.53–0.72)	Women with previous breast cancer	Giardiello D, Steyerberg EW, Hauptmann M, Adank MA, Akdeniz D, Blomqvist C, Bojesen SE, Bolla MK, Brinkhuis M, Chang-Claude J, Czene K, Devilee P, Dunning AM, Easton DF, Eccles DM, Fasching PA, Figueroa J, Flyger H, García-Closas M, Haeberle L, Haiman CA, Hall P, Hamann U, Hopper JL, Jager A, Jakubowska A, Jung A, Keeman R, Kramer I, Lambrechts D, Le Marchand L, Lindblom A, Lubiński J, Manoochehri M, Mariani L, Nevanlinna H, Oldenburg HSA, Pelders S, Pharoah PDP, Shah M, Siesling S, Smit VTHBM, Southey MC, Tapper WJ, Tollenaar RAEM, van den Broek AJ, van Deurzen CHM, van Leeuwen FE, van Ongeval C, Van't Veer LJ, Wang Q, Wendt C, Westenend PJ, Hooning MJ, Schmidt MK. Prediction and clinical utility of a contralateral breast cancer risk model. Breast Cancer Res. 2019 Dec 17;21(1):144. doi: 10.1186/s13058-019-1221-1. PMID: 31847907; PMCID: PMC6918633.
Giardiello	PredictCBC-1B	2019	Contralateral breast cancer	5 years: 0.59 (0.54–0.63) 10 years: 0.59 (0.56–0.62)	Women with previous breast cancer	Giardiello D, Steyerberg EW, Hauptmann M, Adank MA, Akdeniz D, Blomqvist C, Bojesen SE, Bolla MK, Brinkhuis M, Chang-Claude J, Czene K, Devilee P, Dunning AM, Easton DF, Eccles DM, Fasching PA, Figueroa J, Flyger H, García-Closas M, Haeberle L, Haiman CA, Hall P, Hamann U, Hopper JL, Jager A, Jakubowska A, Jung A, Keeman R, Kramer I, Lambrechts D, Le Marchand L, Lindblom A, Lubiński J, Manoochehri M, Mariani L, Nevanlinna H, Oldenburg HSA, Pelders S, Pharoah PDP, Shah M, Siesling S, Smit VTHBM, Southey MC, Tapper WJ, Tollenaar RAEM, van den Broek AJ, van Deurzen CHM, van Leeuwen FE, van Ongeval C, Van't Veer LJ, Wang Q,

						Wendt C, Westenend PJ, Hooning MJ, Schmidt MK. Prediction and clinical utility of a contralateral breast cancer risk model. Breast Cancer Res. 2019 Dec 17;21(1):144. doi: 10.1186/s13058-019-1221-1. PMID: 31847907; PMCID: PMC6918633.
Driver	/	2007	Colorectal	0.695 (Derivation), 0.686 (Validation)	General public	Driver JA, Gaziano JM, Gelber RP, Lee IM, Buring JE, Kurth T. Development of a risk score for colorectal cancer in men. Am J Med. 2007 Mar;120(3):257-63. doi: 10.1016/j.amjmed.2006.05.055. PMID: 17349449.
Ma	/	2010	CRC	0.70 (0.68-0.72)	General Public (Japanese men)	Ma E, Sasazuki S, Iwasaki M, Sawada N, Inoue M; Shoichiro Tsugane; Japan Public Health Center-based Prospective Study Group. 10-Year risk of colorectal cancer: development and validation of a prediction model in middle-aged Japanese men. Cancer Epidemiol. 2010 Oct;34(5):534-41. doi: 10.1016/j.canep.2010.04.021. Epub 2010 May 31. PMID: 20554262.
Wells	CRC-PRO Female model	2014	CRC	0.679 (0.665–0.692)	General Public	Wells BJ, Kattan MW, Cooper GS, Jackson L, Koroukian S. Colorectal cancer predicted risk online (CRC-PRO) calculator using data from the multi-ethnic cohort study. J Am Board Fam Med. 2014 Jan-Feb;27(1):42-55. doi: 10.3122/jabfm.2014.01.130040. PMID: 24390885; PMCID: PMC4219857.
Betes	Broad criteria model	2003	ACN+	0.6537	General Public	Betés M, Muñoz-Navas MA, Duque JM, Angós R, Macías E, Súbtil JC, Herraiz M, De La Riva S, Delgado-Rodríguez M, Martínez-González MA. Use of colonoscopy as a primary screening test for colorectal cancer in average risk people. Am J Gastroenterol. 2003 Dec;98(12):2648-54. doi: 10.1111/j.1572-0241.2003.08771.x. PMID: 14687811.
Betes	Restricted criteria model	2003	ACN	0.6724	General Public	Betés M, Muñoz-Navas MA, Duque JM, Angós R, Macías E, Súbtil JC, Herraiz M, De La Riva S, Delgado-Rodríguez M, Martínez-González MA. Use of colonoscopy as a primary screening test for colorectal cancer in average risk people. Am J Gastroenterol. 2003 Dec;98(12):2648-54. doi: 10.1111/j.1572-0241.2003.08771.x. PMID: 14687811.
Cai	/	2012	ACN	0.74 (0.72-0.77) (Derivation) 0.74 (0.70-0.78) (Validation)	General Public	Cai QC, Yu ED, Xiao Y, Bai WY, Chen X, He LP, Yang YX, Zhou PH, Jiang XL, Xu HM, Fan H, Ge ZZ, Lv NH, Huang ZG, Li YM, Ma SR, Chen J, Li YQ, Xu JM, Xiang P, Yang L, Lin FL, Li ZS. Derivation and validation of a prediction rule for estimating advanced colorectal neoplasm risk in average-risk Chinese. Am J Epidemiol. 2012 Mar 15;175(6):584-93. doi: 10.1093/aje/kwr337. Epub 2012 Feb 10. PMID: 22328705.
Chen	/	2014	ACN	0.75 (0.70–0.82)	General Public	Chen G, Mao B, Pan Q, Liu Q, Xu X, Ning Y. Prediction rule for estimating advanced colorectal neoplasm risk in average-risk populations in southern Jiangsu Province. Chin J Cancer Res. 2014 Feb;26(1):4-11. doi: 10.3978/j.issn.1000-9604.2014.02.03. PMID: 24653621; PMCID: PMC3937762.

Kaminski	/	2014	ACRN	0.62 (0.60–0.64) (V)	General public	Kaminski MF, Polkowski M, Kraszewska E, Rupinski M, Butruk E, Regula J. A score to estimate the likelihood of detecting advanced colorectal neoplasia at colonoscopy. Gut. 2014 Jul;63(7):1112-9. doi: 10.1136/gutjnl-2013-304965. Epub 2014 Jan 2. PMID: 24385598; PMCID: PMC4078748.
Lin OS	/	2006	ACN	0.596	General public aged 50 years or more	Lin OS, Kozarek RA, Schembre DB, Ayub K, Gluck M, Cantone N, Soon MS, Dominitz JA. Risk stratification for colon neoplasia: screening strategies using colonoscopy and computerized tomographic colonography. Gastroenterology. 2006 Oct;131(4):1011-9. doi: 10.1053/j.gastro.2006.08.015. PMID: 17030171.
Yeoh	Asia-Pacific Colorectal Screening score	2011	ACRN	Derivation: 0.66 (0.62-0.70) Validation: 0.64 (0.60-0.68)	General public	Yeoh KG, Ho KY, Chiu HM, Zhu F, Ching JY, Wu DC, Matsuda T, Byeon JS, Lee SK, Goh KL, Sollano J, Rerknimitr R, Leong R, Tsoi K, Lin JT, Sung JJ; Asia-Pacific Working Group on Colorectal Cancer. The Asia-Pacific Colorectal Screening score: a validated tool that stratifies risk for colorectal advanced neoplasia in asymptomatic Asian subjects. Gut. 2011 Sep;60(9):1236-41. doi: 10.1136/gut.2010.221168. Epub 2011 Mar 14. PMID: 21402615.
Tao	/	2014	ACN	0.67 (0.65–0.69) (Derivation) 0.66 (0.63–0.69) (Validation)	General public	Tao S, Hoffmeister M, Brenner H. Development and validation of a scoring system to identify individuals at high risk for advanced colorectal neoplasms who should undergo colonoscopy screening. Clin Gastroenterol Hepatol. 2014 Mar;12(3):478-85. doi: 10.1016/j.cgh.2013.08.042. Epub 2013 Sep 8. PMID: 24022090.
Tao	/	2014	CRC	0.71 (0.67–0.75) (Derivation) 0.68 (0.57–0.79) (Validation)	General public	Tao S, Hoffmeister M, Brenner H. Development and validation of a scoring system to identify individuals at high risk for advanced colorectal neoplasms who should undergo colonoscopy screening. Clin Gastroenterol Hepatol. 2014 Mar;12(3):478-85. doi: 10.1016/j.cgh.2013.08.042. Epub 2013 Sep 8. PMID: 24022090.
Schroy III	/	2015	ACRN	0.69 (0.66–0.72)	General Public aged 50–79 years	Schroy PC 3rd, Wong JB, O'Brien MJ, Chen CA, Griffith JL. A Risk Prediction Index for Advanced Colorectal Neoplasia at Screening Colonoscopy. Am J Gastroenterol. 2015 Jul;110(7):1062-71. doi: 10.1038/ajg.2015.146. Epub 2015 May 26. PMID: 26010311; PMCID: PMC4705553.
Park	/	2017	ACRN	0.74 (0.72–0.76) (derivation) 0.72 (0.70–0.75) (validation)	General Public aged 40–49 years who had never had a colonoscopy	Park YM, Kim HS, Park JJ, Baik SJ, Youn YH, Kim JH, Park H. A simple scoring model for advanced colorectal neoplasm in asymptomatic subjects aged 40-49 years. BMC Gastroenterol. 2017 Jan 9;17(1):7. doi: 10.1186/s12876-016-0562-9. PMID: 28068908; PMCID: PMC5223374.

Sung	/	2017	ACRN	0.649 (0.608-0.691)	General Public aged 50–70 years	Sung JJY, Wong MCS, Lam TYT, Tsoi KKF, Chan VCW, Cheung W, Ching JYL. A modified colorectal screening score for prediction of advanced neoplasia: A prospective study of 5744 subjects. J Gastroenterol Hepatol. 2018 Jan;33(1):187-194. doi: 10.1111/jgh.13835. PMID: 28561279.
Yang	/	2017	ACRN	0.728 (0.709–0.748)	Population who had never had a colonoscopy	Yang HJ, Choi S, Park SK, Jung YS, Choi KY, Park T, Kim JY, Park DI. Derivation and validation of a risk scoring model to predict advanced colorectal neoplasm in adults of all ages. J Gastroenterol Hepatol. 2017 Jul;32(7):1328-1335. doi: 10.1111/jgh.13711. PMID: 28012211.
Sekiguchi	/	2018	ACRN	Derivation: 0.70 (0.67–0.73) Validation: 0.70 (0.67–0.73)	Population who had never had a colonoscopy	Sekiguchi M, Kakugawa Y, Matsumoto M, Matsuda T. A scoring model for predicting advanced colorectal neoplasia in a screened population of asymptomatic Japanese individuals. J Gastroenterol. 2018 Oct;53(10):1109-1119. doi: 10.1007/s00535-018-1433-7. Epub 2018 Jan 22. PMID: 29359244.
Hong	/	2017	ACRN	0.716 (derivation) 0.701 (validation)	Population who had never had a colonoscopy	Hong SN, Son HJ, Choi SK, Chang DK, Kim YH, Jung SH, Rhee PL. A prediction model for advanced colorectal neoplasia in an asymptomatic screening population. PLoS One. 2017 Aug 25;12(8):e0181040. doi: 10.1371/journal.pone.0181040. PMID: 28841657; PMCID: PMC5571924.
Hong	/	2017	ACRN	0.726 (derivation) 0.713 (validation)	Population who had never had a colonoscopy	Hong SN, Son HJ, Choi SK, Chang DK, Kim YH, Jung SH, Rhee PL. A prediction model for advanced colorectal neoplasia in an asymptomatic screening population. PLoS One. 2017 Aug 25;12(8):e0181040. doi: 10.1371/journal.pone.0181040. PMID: 28841657; PMCID: PMC5571924.
Jung	PAC-50	2017	ACRN	0.673 (0.648–0.697)	Population aged 30–49 years.	Jung YS, Park CH, Kim NH, Lee MY, Park DI. Impact of Age on the Risk of Advanced Colorectal Neoplasia in a Young Population: An Analysis Using the Predicted Probability Model. Dig Dis Sci. 2017 Sep;62(9):2518-2525. doi: 10.1007/s10620-017-4683-y. Epub 2017 Jul 21. PMID: 28733868.
Imperiale	/	2003	CRC	0.74 (0.68-0.80)	/	Imperiale TF, Wagner DR, Lin CY, Larkin GN, Rogge JD, Ransohoff DF. Using risk for advanced proximal colonic neoplasia to tailor endoscopic screening for colorectal cancer. Ann Intern Med. 2003 Dec 16;139(12):959-65. doi: 10.7326/0003-4819-139-12-200312160-00005. PMID: 14678915.

Chen	Model 1	2021	Colorectal cancer	0.72 (0.71-0.74)	General public	Chen CH, Tsai MK, Wen C, Wen CP. A user-friendly objective prediction model in predicting colorectal cancer based on 234 044 Asian adults in a prospective cohort. ESMO Open. 2021 Dec;6(6):100288. doi: 10.1016/j.esmoop.2021.100288. Epub 2021 Nov 20. PMID: 34808523; PMCID: PMC8609147.
Chen	Model 2	2021	Colorectal cancer	0.73 (0.71-0.74)	General public	Chen CH, Tsai MK, Wen C, Wen CP. A user-friendly objective prediction model in predicting colorectal cancer based on 234 044 Asian adults in a prospective cohort. ESMO Open. 2021 Dec;6(6):100288. doi: 10.1016/j.esmoop.2021.100288. Epub 2021 Nov 20. PMID: 34808523; PMCID: PMC8609147.
Chen	Model 3	2021	Colorectal cancer	0.81 (0.80-0.83)	General public	Chen CH, Tsai MK, Wen C, Wen CP. A user-friendly objective prediction model in predicting colorectal cancer based on 234 044 Asian adults in a prospective cohort. ESMO Open. 2021 Dec;6(6):100288. doi: 10.1016/j.esmoop.2021.100288. Epub 2021 Nov 20. PMID: 34808523; PMCID: PMC8609147.
Chen	Model 4	2021	Colorectal cancer	0.82 (0.81-0.84)	General public	Chen CH, Tsai MK, Wen C, Wen CP. A user-friendly objective prediction model in predicting colorectal cancer based on 234 044 Asian adults in a prospective cohort. ESMO Open. 2021 Dec;6(6):100288. doi: 10.1016/j.esmoop.2021.100288. Epub 2021 Nov 20. PMID: 34808523; PMCID: PMC8609147.
Chen	Model 5	2021	Colorectal cancer	0.83 (0.81-0.85)	General public	Chen CH, Tsai MK, Wen C, Wen CP. A user-friendly objective prediction model in predicting colorectal cancer based on 234 044 Asian adults in a prospective cohort. ESMO Open. 2021 Dec;6(6):100288. doi: 10.1016/j.esmoop.2021.100288. Epub 2021 Nov 20. PMID: 34808523; PMCID: PMC8609147.
Wong	/	2014	CN	0.62 (0.61-0.63)	General public, aged 50-70	Wong MC, Lam TY, Tsoi KK, Hirai HW, Chan VC, Ching JY, Chan FK, Sung JJ. A validated tool to predict colorectal neoplasia and inform screening choice for asymptomatic subjects. Gut. 2014 Jul;63(7):1130-6. doi: 10.1136/gutjnl-2013-305639. Epub 2013 Sep 17. PMID: 24045331.
Wong	Asia-Pacific Proximal Colon Neoplasia Risk Score	2021	Advanced proximal neoplasia	0.74 (0.68–0.79 Distal findings alone: 0.67 (0.60–0.74)	General public	Wong MCS, Rerknimitr R, Lee Goh K, Matsuda T, Kim HS, Wu DC, Wu KC, Yeoh KG, Chong VH, Ahmed F, Sollano JD, Menon J, Chiu HM, Li J, Ching JYL, Sung JJY. Development and Validation of the Asia-Pacific Proximal Colon Neoplasia Risk Score. Clin Gastroenterol Hepatol. 2021 Jan;19(1):119-127.e1. doi: 10.1016/j.cgh.2019.12.031. Epub 2020 Jan 7. PMID: 31923642.
Samarakoon	/	2019	Colorectal cancer	0.849 (0.8-0.9)	General public	Samarakoon YM, Gunawardena NS, Pathirana A, Perera MN, Hewage SA. Prediction of colorectal cancer risk among adults in a lower middle-income country. J Gastrointest Oncol. 2019 Jun;10(3):445-452. doi:

						10.21037/jgo.2019.01.27. PMID: 31183194; PMCID: PMC6534714.
Sharara	/	2020	Advanced colorectal neoplasia	0.73 (0.66-0.79)	General public	Sharara AI, El Mokahal A, Harb AH, Khalaf N, Sarkis FS, M El-Halabi M, Mansour NM, Malli A, Habib R. Risk prediction rule for advanced neoplasia on screening colonoscopy for average-risk individuals. World J Gastroenterol. 2020 Oct 7;26(37):5705-5717. doi: 10.3748/wjg.v26.i37.5705. PMID: 33088163; PMCID: PMC7545395.
Feng	/	2020	Colorectal cancer	Development: 0.713 (0.670–0.757) Validation: 0.708.	Type 2 diabetes patients	Feng LH, Su T, Bu KP, Ren S, Yang Z, Deng CE, Li BX, Wei WY. A clinical prediction nomogram to assess risk of colorectal cancer among patients with type 2 diabetes. Sci Rep. 2020 Sep 1;10(1):14359. doi: 10.1038/s41598-020-71456-2. PMID: 32873885; PMCID: PMC7463255.
Shen	/	2021	early colorectal neoplasm	Development: 0.624 (0.604–0.643) Validation: 0.630 (0.604–0.655)	General public	Shen J, Wu Y, Feng X, Liang F, Mo M, Cai B, Zhou C, Wang Z, Zhu M, Cai G, Zheng Y. Assessing Individual Risk for High-Risk Early Colorectal Neoplasm for Pre-Selection of Screening in Shanghai, China: A Population-Based Nested Case-Control Study. Cancer Manag Res. 2021 May 12;13:3867-3878. doi: 10.2147/CMAR.S301185. PMID: 34012295; PMCID: PMC8126801.
Imperiale	/	2015	Advanced colorectal neoplasia	0.72	Asymptomatic Adults	Imperiale TF, Monahan PO, Stump TE, Glowinski EA, Ransohoff DF. Derivation and Validation of a Scoring System to Stratify Risk for Advanced Colorectal Neoplasia in Asymptomatic Adults: A Cross-sectional Study. Ann Intern Med. 2015 Sep 1;163(5):339-46. doi: 10.7326/M14-1720. PMID: 26259154; PMCID: PMC4840411.
Kim	Young Adult Colorectal Screening (YCS) score	2019	Advanced colorectal neoplasia	0.66	Young adults aged <50 years	Kim JY, Choi S, Park T, Kim SK, Jung YS, Park JH, Kim HJ, Cho YK, Sohn CI, Jeon WK, Kim BI, Choi KY, Park DI. Development and validation of a scoring system for advanced colorectal neoplasm in young Korean subjects less than age 50 years. Intest Res 2019; 17: 253-264 [PMID: 30449080 DOI:10.5217/ir.2018.00062]
Cubiella	COLONPREDICT	2016	Colorectal cancer	Development: 0.92 (0.91–0.94) Validation: 0.92 (0.90–0.94)	Symptomatic patients	Cubiella J, Vega P, Salve M, Díaz-Ondina M, Alves MT, Quintero E, Álvarez-Sánchez V, Fernández-Bañares F, Boadas J, Campo R, Bujanda L, Clofent J, Ferrandez Á, Torrealba L, Piñol V, Rodríguez-Alcalde D, Hernández V, Fernández-Seara J; COLONPREDICT study investigators. Development and external validation of a faecal immunochemical test-based prediction model for colorectal cancer detection in symptomatic patients. BMC Med. 2016 Aug 31;14(1):128. doi: 10.1186/s12916-016-0668-5. PMID: 27580745; PMCID: PMC5007726.

Cubiella	FAST Score	2017	Colorectal cancer	Development: 0.88 (0.85–0.9) Validation: 0.91 (0.9–0.93)	Symptomatic patients	Cubiella J, Digby J, Rodríguez-Alonso L, Vega P, Salve M, Díaz-Ondina M, Strachan JA, Mowat C, McDonald PJ, Carey FA, Godber IM, Younes HB, Rodriguez-Moranta F, Quintero E, Álvarez-Sánchez V, Fernández-Bañares F, Boadas J, Campo R, Bujanda L, Garayoa A, Ferrandez Á, Piñol V, Rodríguez-Alcalde D, Guardiola J, Steele RJ, Fraser CG; COLONPREDICT study investigators. The fecal hemoglobin concentration, age and sex test score: Development and external validation of a simple prediction tool for colorectal cancer detection in symptomatic patients. Int J Cancer. 2017 May 15;140(10):2201-2211. doi: 10.1002/ijc.30639. Epub 2017 Mar 6. PMID: 28187494.
Fernandez-Banares	COLONOFIT score	2019	Advanced colorectal neoplasia	Development: CRC: 0.93 (0.91–0.95) CRC & Adenomas: 0.865 (0.83–0.89) Validation CRC: 0.86 CRC & Adenomas:: 0.79	Symptomatic patients	Fernández-Bañares F, Clèries R, Boadas J, Ribes J, Oliva JC, Alsius A, Sanz X, Martínez-Bauer E, Galter S, Pujals M, Pujol M, Del Pozo P, Campo R. Prediction of advanced colonic neoplasm in symptomatic patients: a scoring system to prioritize colonoscopy (COLONOFIT study). BMC Cancer. 2019 Jul 25;19(1):734. doi: 10.1186/s12885-019-5926-4. PMID: 31345180; PMCID: PMC6659265.
Law	Neoplasia score	2014	Advanced colorectal neoplasia	Development: 0.76 Validation: 0.76	General public	Law CW, Rampal S, Roslani AC, Mahadeva S. Development of a risk score to stratify symptomatic adults referred for colonoscopy. J Gastroenterol Hepatol. 2014 Nov;29(11):1890-6. doi: 10.1111/jgh.12638. PMID: 24909623.
Law	Colorectal cancer score	2014	Colorectal cancer	Development: 0.83 Validation: 0.83	General public	Law CW, Rampal S, Roslani AC, Mahadeva S. Development of a risk score to stratify symptomatic adults referred for colonoscopy. J Gastroenterol Hepatol. 2014 Nov;29(11):1890-6. doi: 10.1111/jgh.12638. PMID: 24909623.
Rodriguez-Alonso	/	2015	Advanced colorectal neoplasia	CRC: 0.94 (0.91–0.96) CRC & Adenomas: 0.76 (0.71–0.81)	Symptomatic patients	Rodríguez-Alonso L, Rodríguez-Moranta F, Ruiz-Cerulla A, Lobatón T, Arajol C, Binefa G, Moreno V, Guardiola J. An urgent referral strategy for symptomatic patients with suspected colorectal cancer based on a quantitative immunochemical faecal occult blood test. Dig Liver Dis. 2015 Sep;47(9):797-804. doi: 10.1016/j.dld.2015.05.004. Epub 2015 May 15. PMID: 26055489.
Chen	Full model	2020	SCC	3-year: Derivation: 0.805 (0.783-0.826) Validation: 0.795 (0.773-0.818)	General Public	Chen W, Li H, Ren J, Zheng R, Shi J, Li J, Cao M, Sun D, He S, Sun X, Cao X, Feng S, Zhou J, Luo P, Zha Z, Jia S, Wang J, Ma H, Zeng H, Canfell K, He J. Selection of high-risk individuals for esophageal cancer screening: A prediction model of esophageal squamous cell carcinoma based on a multicenter screening cohort in rural China. Int J Cancer. 2021 Jan 15;148(2):329-339. doi: 10.1002/ijc.33208. Epub 2020 Aug 6. PMID: 32663318.

Xie	Simple model	2016	AC	Derivation: 0.817 (0.783, 0.852) Validation: 0.791 (0.754, 0.828)	General Public	Xie SH, Lagergren J. A model for predicting individuals' absolute risk of esophageal adenocarcinoma: Moving toward tailored screening and prevention. Int J Cancer. 2016 Jun 15;138(12):2813-9. doi: 10.1002/ijc.29988. Epub 2016 Jan 30. PMID: 26756848.
Thrift	Standard model	2013	AC	Derivation: 0.76 (0.73–0.79). Validation: 0.75 (0.66 – 0.84)	General Public	Thrift AP, Kendall BJ, Pandeya N, Whiteman DC. A model to determine absolute risk for esophageal adenocarcinoma. Clin Gastroenterol Hepatol. 2013 Feb;11(2):138-44.e2. doi: 10.1016/j.cgh.2012.10.026. Epub 2012 Oct 25. PMID: 23103823.
Thrift	Alarm symptoms model	2013	AC	Validation: 0.85 (0.78 – 0.91)	General Public	Thrift AP, Kendall BJ, Pandeya N, Whiteman DC. A model to determine absolute risk for esophageal adenocarcinoma. Clin Gastroenterol Hepatol. 2013 Feb;11(2):138-44.e2. doi: 10.1016/j.cgh.2012.10.026. Epub 2012 Oct 25. PMID: 23103823.
Rubenstein	/	2011	AC	NA	Gastroesophageal reflux patients	Rubenstein JH, Scheiman JM, Sadeghi S, Whiteman D, Inadomi JM. Esophageal adenocarcinoma incidence in individuals with gastroesophageal reflux: synthesis and estimates from population studies. Am J Gastroenterol. 2011 Feb;106(2):254-60. doi: 10.1038/ajg.2010.470. Epub 2010 Dec 7. PMID: 21139576; PMCID: PMC3901355.
Kunzmann	EC Model	2018	AC, SCC	0.76 (0.73–0.79)	General Public	Kunzmann AT, Thrift AP, Cardwell CR, Lagergren J, Xie S, Johnston BT, Anderson LA, Busby J, McMenamin ÚC, Spence AD, Coleman HG. Model for Identifying Individuals at Risk for Esophageal Adenocarcinoma. Clin Gastroenterol Hepatol. 2018 Aug;16(8):1229-1236.e4. doi: 10.1016/j.cgh.2018.03.014. Epub 2018 Mar 17. PMID: 29559360.
Kunzmann	EAC Points-based Model	2018	AC	0.80 (0.77–0.82)	General Public	Kunzmann AT, Thrift AP, Cardwell CR, Lagergren J, Xie S, Johnston BT, Anderson LA, Busby J, McMenamin ÚC, Spence AD, Coleman HG. Model for Identifying Individuals at Risk for Esophageal Adenocarcinoma. Clin Gastroenterol Hepatol. 2018 Aug;16(8):1229-1236.e4. doi: 10.1016/j.cgh.2018.03.014. Epub 2018 Mar 17. PMID: 29559360.
Kunzmann	ESCC Model	2018	ESCC	0.71 (0.66–0.78)	General Public	Kunzmann AT, Thrift AP, Cardwell CR, Lagergren J, Xie S, Johnston BT, Anderson LA, Busby J, McMenamin ÚC, Spence AD, Coleman HG. Model for Identifying Individuals at Risk for Esophageal Adenocarcinoma. Clin Gastroenterol Hepatol. 2018 Aug;16(8):1229-1236.e4. doi: 10.1016/j.cgh.2018.03.014. Epub 2018 Mar 17. PMID: 29559360.
Yokoyama	HRA-F Model	2008	SCC	0.84	Men in the General Public	Yokoyama T, Yokoyama A, Kumagai Y, Omori T, Kato H, Igaki H, Tsujinaka T, Muto M, Yokoyama M, Watanabe H. Health risk appraisal models for mass screening of esophageal cancer in Japanese men. Cancer Epidemiol

						Biomarkers Prev. 2008 Oct;17(10):2846-54. doi: 10.1158/1055-9965.EPI-08-0397. PMID: 18843030.
Yokoyama	HRA-G Model	2008	SCC	0.86	Men in the General Public	Yokoyama T, Yokoyama A, Kumagai Y, Omori T, Kato H, Igaki H, Tsujinaka T, Muto M, Yokoyama M, Watanabe H. Health risk appraisal models for mass screening of esophageal cancer in Japanese men. Cancer Epidemiol Biomarkers Prev. 2008 Oct;17(10):2846-54. doi: 10.1158/1055-9965.EPI-08-0397. PMID: 18843030.
Yang X	Male Model	2021	SCC	nomograms: 0.75 (0.72-0.77) weighted analysis model: 0.81 (0.79-0.84)	General public	Yang X, Suo C, Zhang T, Yin X, Man J, Yuan Z, Chen H, Yu J, Jin L, Chen X, Lu M, Ye W. A nomogram for screening esophageal squamous cell carcinoma based on environmental risk factors in a high-incidence area of China: a population-based case-control study. BMC Cancer. 2021 Mar 31;21(1):343. doi: 10.1186/s12885-021-08053-7. PMID: 33789604; PMCID: PMC8011400.
Yang X	Female Model	2021	SCC	nomograms: 0.76 (0.73-0.79) weighted analysis model: 0.88 (0.85-0.90)	General public	Yang X, Suo C, Zhang T, Yin X, Man J, Yuan Z, Chen H, Yu J, Jin L, Chen X, Lu M, Ye W. A nomogram for screening esophageal squamous cell carcinoma based on environmental risk factors in a high-incidence area of China: a population-based case-control study. BMC Cancer. 2021 Mar 31;21(1):343. doi: 10.1186/s12885-021-08053-7. PMID: 33789604; PMCID: PMC8011400.
Wang	ESCaScore	2021	SCC	Derivation: 0.76 (0.58–0.93) Internal cross-validation: 0.71 (0.52–0.90) External validation: 0.70 (0.64–0.75)	General public	Wang QL, Ness-Jensen E, Santoni G, Xie SH, Lagergren J. Development and Validation of a Risk Prediction Model for Esophageal Squamous Cell Carcinoma Using Cohort Studies. Am J Gastroenterol. 2021 Apr;116(4):683-691. doi: 10.14309/ajg.0000000000001094. PMID: 33982937.
Han	Score Model	2021	ESCC	0.792 (0.761, 0.822) (d) 0.773 (0.736, 0.811) (v)	General public	Han J, Wang L, Zhang H, Ma S, Li Y, Wang Z, Zhu G, Zhao D, Wang J, Xue F. Development and Validation of an Esophageal Squamous Cell Carcinoma Risk Prediction Model for Rural Chinese: Multicenter Cohort Study. Front Oncol. 2021 Aug 30;11:729471. doi: 10.3389/fonc.2021.729471. PMID: 34527592; PMCID: PMC8435773.
Smith	/	2023	Myeloma	0.85 (0.83-0.87)	General Public	Smith L, Carmichael J, Cook G, Shinkins B, Neal RD. Development and Internal Validation of a Risk Prediction Model to Identify Myeloma Based on Routine Blood Tests: A Case-Control Study. Cancers (Basel). 2023 Feb 3;15(3):975. doi: 10.3390/cancers15030975. PMID: 36765931; PMCID: PMC9913376.
Landsman	unweighted Model	2013	renal cell carcinoma	NR	General public	Landsman V, Graubard BI. Efficient analysis of case-control studies with sample weights. Stat Med. 2013

						Jan 30;32(2):347-60. doi: 10.1002/sim.5530. Epub 2012 Jul 26. PMID: 22833421.
Landsman	SPL (sample pseudo likelihood) Model	2013	renal cell carcinoma	NR	General public	Landsman V, Graubard BI. Efficient analysis of case-control studies with sample weights. Stat Med. 2013 Jan 30;32(2):347-60. doi: 10.1002/sim.5530. Epub 2012 Jul 26. PMID: 22833421.
Landsman	Weighted Model	2013	renal cell carcinoma	NR	General public	Landsman V, Graubard BI. Efficient analysis of case-control studies with sample weights. Stat Med. 2013 Jan 30;32(2):347-60. doi: 10.1002/sim.5530. Epub 2012 Jul 26. PMID: 22833421.
Landsman	RSW (rescaled weighted) Model	2013	renal cell carcinoma	NR	General public	Landsman V, Graubard BI. Efficient analysis of case-control studies with sample weights. Stat Med. 2013 Jan 30;32(2):347-60. doi: 10.1002/sim.5530. Epub 2012 Jul 26. PMID: 22833421.
Landsman	SPW (semiparametric weighted) Model	2013	renal cell carcinoma	NR	General public	Landsman V, Graubard BI. Efficient analysis of case-control studies with sample weights. Stat Med. 2013 Jan 30;32(2):347-60. doi: 10.1002/sim.5530. Epub 2012 Jul 26. PMID: 22833421.
Singleton	EPIC RCC risk prediction model	2020	renal cell carcinoma	Derivation: 0.714 (0.694–0.735) Validation: 0.709	General Public	Singleton RK, Heath AK, Clasen JL, Scelo G, Johansson M, Calvez-Kelm FL, Weiderpass E, Liedberg F, Ljungberg B, Harbs J, Olsen A, Tjønneland A, Dahm CC, Kaaks R, Fortner RT, Panico S, Tagliabue G, Masala G, Tumino R, Ricceri F, Gram IT, Santiuste C, Bonet C, Rodriguez-Barranco M, Schulze MB, Bergmann MM, Travis RC, Tzoulaki I, Riboli E, Muller DC. Risk Prediction for Renal Cell Carcinoma: Results from the European Prospective Investigation into Cancer and Nutrition (EPIC) Prospective Cohort Study. Cancer Epidemiol Biomarkers Prev. 2021 Mar;30(3):507-512. doi: 10.1158/1055-9965.EPI-20-1438. Epub 2020 Dec 17. PMID: 33335022.
Iwasaki	Gene-environment interaction model	2020	Upper aerodigestive tract cancer (oral, pharynx, esophageal SCC, larynx)	0.71 (0.57-0.84)	General Public	Iwasaki M, Budhathoki S, Yamaji T, Tanaka-Mizuno S, Kuchiba A, Sawada N, Goto A, Shimazu T, Inoue M, Tsugane S; Japan Public Health Center-based Prospective Study (JPHC Study) Group. Inclusion of a gene-environment interaction between alcohol consumption and the aldehyde dehydrogenase 2 genotype in a risk prediction model for upper aerodigestive tract cancer in Japanese men. Cancer Sci. 2020 Oct;111(10):3835-3844. doi: 10.1111/cas.14573. Epub 2020 Aug 4. PMID: 32662535; PMCID: PMC7540993.
Amarasinghe	/	2010	Oral potentially malignant disorders (excluding	0.87 (95% CI: 0.83–0.91)	High-risk communities	Amarasinghe HK, Johnson NW, Lalloo R, Kumaraarachchi M, Warnakulasuriya S. Derivation and validation of a risk-factor model for detection of oral potentially malignant disorders in populations with high prevalence. Br J Cancer. 2010 Jul 27;103(3):303-9. doi: 10.1038/sj.bjc.6605778.

			lichen planus)			Epub 2010 Jul 13. PMID: 20628386; PMCID: PMC2920027.
Chen	Male model	2018	Oral cancer (tongue, buccal, gingiva, floor of mouth, palate, lip, and unspecified or overlapping)	0.768 (0.723-0.813)	General Public	Chen F, Lin L, Yan L, Liu F, Qiu Y, Wang J, Hu Z, Wu J, Bao X, Lin L, Wang R, Cai G, Aoyagi K, Cai L, He B. Nomograms and risk scores for predicting the risk of oral cancer in different sexes: a large-scale case-control study. J Cancer. 2018 Jun 22;9(14):2543-2548. doi: 10.7150/jca.24431. PMID: 30026853; PMCID: PMC6036893.
Chen	Female model	2018	Oral cancer (tongue, buccal, gingiva, floor of mouth, palate, lip, and unspecified or overlapping)	0.700 (0.635-0.765)	General Public	Chen F, Lin L, Yan L, Liu F, Qiu Y, Wang J, Hu Z, Wu J, Bao X, Lin L, Wang R, Cai G, Aoyagi K, Cai L, He B. Nomograms and risk scores for predicting the risk of oral cancer in different sexes: a large-scale case-control study. J Cancer. 2018 Jun 22;9(14):2543-2548. doi: 10.7150/jca.24431. PMID: 30026853; PMCID: PMC6036893.
Krishna Rao	/	2016	Oral cavity and oropharynx cancer	0.866	/	Krishna Rao S, Mejia GC, Logan RM, Kulkarni M, Kamath V, Fernandes DJ, Ray S, Roberts-Thomson K. A screening model for oral cancer using risk scores: development and validation. Community Dent Oral Epidemiol. 2016 Feb;44(1):76-84. doi: 10.1111/cdoe.12192. Epub 2015 Aug 26. PMID: 26308953.
Lau	/	2018	Head and neck cancer	0.79	General Public	Lau K, Wilkinson J, Moorthy R. A web-based prediction score for head and neck cancer referrals. Clin Otolaryngol. 2018 Aug;43(4):1043-1049. doi: 10.1111/coa.13098. Epub 2018 Apr 6. PMID: 29543399.

Tikka	HaNC-RC-V.2.	2020	Cancer of head and neck (primary cancers to the HaN regions, metastatic cancers to the HaN from other regions,and cancers in neighboring regions that manifested with HaN symptoms)	0.8856 (0.8818–0.8879)	General Public	Tikka T, Kavanagh K, Lowit A, Jiafeng P, Burns H, Nixon IJ, Paleri V, MacKenzie K. Head and neck cancer risk calculator (HaNC-RC)-V.2. Adjustments and addition of symptoms and social history factors. Clin Otolaryngol. 2020 May;45(3):380-388. doi: 10.1111/coa.13511. Epub 2020 Feb 20. PMID: 31985180; PMCID: PMC7318185.
Tota	/	2019	Oropharyngeal cancer	Internal validation: 0.94 (0.92-0.97) External validation: 0.87 (0.84-0.90)	General Public	Tota JE, Gillison ML, Katki HA, Kahle L, Pickard RK, Xiao W, Jiang B, Graubard BI, Chaturvedi AK. Development and validation of an individualized risk prediction model for oropharynx cancer in the US population. Cancer. 2019 Dec 15;125(24):4407-4416. doi: 10.1002/cncr.32412. Epub 2019 Aug 27. PMID: 31454434.
Tikka	/	2016	Head and neck cancer	0.77	General Public	Tikka T, Pracy P, Paleri V. Refining the head and neck cancer referral guidelines: a two-centre analysis of 4715 referrals. Clin Otolaryngol. 2016 Feb;41(1):66-75. doi: 10.1111/coa.12597. PMID: 26611658.
Yuen	"GAG-HCC" score	2009	hepatocellular carcinoma	5-year: 0.88 0.82–0.93) 10-year: 0.89 (0.85–0.93)	chronic hepatitis B patients	Yuen MF, Tanaka Y, Fong DY, Fung J, Wong DK, Yuen JC, But DY, Chan AO, Wong BC, Mizokami M, Lai CL. Independent risk factors and predictive score for the development of hepatocellular carcinoma in chronic hepatitis B. J Hepatol. 2009 Jan;50(1):80-8. doi: 10.1016/j.jhep.2008.07.023. Epub 2008 Sep 21. PMID: 18977053.
Yuen	Simple score	2009	hepatocellular carcinoma	5-year: 0.87 (0.82–0.93) 10-year: 0.88 (0.82–0.92)	chronic hepatitis B patients	Yuen MF, Tanaka Y, Fong DY, Fung J, Wong DK, Yuen JC, But DY, Chan AO, Wong BC, Mizokami M, Lai CL. Independent risk factors and predictive score for the development of hepatocellular carcinoma in chronic hepatitis B. J Hepatol. 2009 Jan;50(1):80-8. doi: 10.1016/j.jhep.2008.07.023. Epub 2008 Sep 21. PMID: 18977053.
Wong	CU-HCC	2010	hepatocellular carcinoma	5-year: 0.76 (0.66-0.86) 10-year: 0.78 (0.71-0.86)	chronic hepatitis B patients	Wong VW, Chan SL, Mo F, Chan TC, Loong HH, Wong GL, Lui YY, Chan AT, Sung JJ, Yeo W, Chan HL, Mok TS. Clinical scoring system to predict hepatocellular carcinoma in chronic hepatitis B carriers. J Clin Oncol. 2010 Apr

						1;28(10):1660-5. doi: 10.1200/JCO.2009.26.2675. Epub 2010 Mar 1. PMID: 20194845.
Wong	LSM-HCC	2014	hepatocellular carcinoma	Training cohort: 0.83 (0.76–0.91) at 3 years 0.83 (0.77–0.90) at 5 years Validation cohort: 0.89 (0.84–0.95) at 3 years 0.83 (0.71–0.94) at 5 years	chronic hepatitis B patients	Wong GL, Chan HL, Wong CK, Leung C, Chan CY, Ho PP, Chung VC, Chan ZC, Tse YK, Chim AM, Lau TK, Wong VW. Liver stiffness-based optimization of hepatocellular carcinoma risk score in patients with chronic hepatitis B. J Hepatol. 2014 Feb;60(2):339-45. doi: 10.1016/j.jhep.2013.09.029. Epub 2013 Oct 12. PMID: 24128413.
Yang	REACH-B	2011	hepatocellular carcinoma	In the validation cohort: 0·811 (0·790–0·831) at 3 years 0·796 (0·775–0·816) at 5 years 0·769 (0·747–0·790) at 10 years In the validation cohort after exclusion of cirhossis patients: 0·902 (0·884–0·918) at 3 years 0·783 (0·759–0·806) at 5 years 0·806 (0·783–0·828) at 10 years	anti-HCV-serone gative chronic hepatitis B patients	Yang HI, Yuen MF, Chan HL, Han KH, Chen PJ, Kim DY, Ahn SH, Chen CJ, Wong VW, Seto WK; REACH-B Working Group. Risk estimation for hepatocellular carcinoma in chronic hepatitis B (REACH-B): development and validation of a predictive score. Lancet Oncol. 2011 Jun;12(6):568-74. doi: 10.1016/S1470-2045(11)70077-8. Epub 2011 Apr 14. PMID: 21497551.

Yang	Model 1	2010	hepatocellular carcinoma	regression model: - Derivation: 84.8 (5 year), 83.3 (10 year) - Validation: 82.6 (5 year), 82.1 (10 year) nomogram: - Derivation: 84.7 (5 year), 83.2 (10 year) - Validation: 83.1 (5 year), 82.1 (10 year)	anti-HCV-seronegative chronic hepatitis B patients	Yang HI, Sherman M, Su J, Chen PJ, Liaw YF, Iloeje UH, Chen CJ. Nomograms for risk of hepatocellular carcinoma in patients with chronic hepatitis B virus infection. J Clin Oncol. 2010 May 10;28(14):2437-44. doi: 10.1200/JCO.2009.27.4456. Epub 2010 Apr 5. PMID: 20368541.
Yang	Model 2	2010	hepatocellular carcinoma	regression model: - Derivation: 88.2 (5 year), 87.5 (10 year) - Validation: 84.4 (5 year), 84.8 (10 year) nomogram: - Derivation: 85.2 (5 year), 85.1 (10 year) - Validation: 83.2 (5 year), 83.0 (10 year)	anti-HCV-seronegative chronic hepatitis B patients	Yang HI, Sherman M, Su J, Chen PJ, Liaw YF, Iloeje UH, Chen CJ. Nomograms for risk of hepatocellular carcinoma in patients with chronic hepatitis B virus infection. J Clin Oncol. 2010 May 10;28(14):2437-44. doi: 10.1200/JCO.2009.27.4456. Epub 2010 Apr 5. PMID: 20368541.
Yang	Model 3	2010	hepatocellular carcinoma	regression model: - Derivation: 88.3 (5 year), 88.5 (10 year) - Validation: 84.1 (5 year), 84.4 (10 year) nomogram: - Derivation: 86.1 (5 year), 86.6 (10 year) - Validation: 83.2 (5 year), 83.0 (10 year)	anti-HCV-seronegative chronic hepatitis B patients	Yang HI, Sherman M, Su J, Chen PJ, Liaw YF, Iloeje UH, Chen CJ. Nomograms for risk of hepatocellular carcinoma in patients with chronic hepatitis B virus infection. J Clin Oncol. 2010 May 10;28(14):2437-44. doi: 10.1200/JCO.2009.27.4456. Epub 2010 Apr 5. PMID: 20368541.

Lin	Model 1	2013	hepatocellular carcinoma	0.83	anti-HCV-seronegative chronic hepatitis B patients	Lin YJ, Lee MH, Yang HI, Jen CL, You SL, Wang LY, Lu SN, Liu J, Chen CJ. Predictability of liver-related seromarkers for the risk of hepatocellular carcinoma in chronic hepatitis B patients. PLoS One. 2013 Apr 17;8(4):e61448. doi: 10.1371/journal.pone.0061448. PMID: 23613855; PMCID: PMC3629190.
Lin	Model 2	2013	hepatocellular carcinoma	0.89	anti-HCV-seronegative chronic hepatitis B patients	Lin YJ, Lee MH, Yang HI, Jen CL, You SL, Wang LY, Lu SN, Liu J, Chen CJ. Predictability of liver-related seromarkers for the risk of hepatocellular carcinoma in chronic hepatitis B patients. PLoS One. 2013 Apr 17;8(4):e61448. doi: 10.1371/journal.pone.0061448. PMID: 23613855; PMCID: PMC3629190.
Lin	Model 3	2013	hepatocellular carcinoma	0.91	anti-HCV-seronegative chronic hepatitis B patients	Lin YJ, Lee MH, Yang HI, Jen CL, You SL, Wang LY, Lu SN, Liu J, Chen CJ. Predictability of liver-related seromarkers for the risk of hepatocellular carcinoma in chronic hepatitis B patients. PLoS One. 2013 Apr 17;8(4):e61448. doi: 10.1371/journal.pone.0061448. PMID: 23613855; PMCID: PMC3629190.
Lee	/	2013	hepatocellular carcinoma	Derivation set: 5-year: 0.89 10-year: 0.85 15-year: 0.86 Validation set: 5-year: 0.84 10-year: 0.86 15-year: 0.87	anti-HCV-seronegative chronic hepatitis B patients	Lee MH, Yang HI, Liu J, Batrla-Utermann R, Jen CL, Iloeje UH, Lu SN, You SL, Wang LY, Chen CJ; R.E.V.E.A.L.-HBV Study Group. Prediction models of long-term cirrhosis and hepatocellular carcinoma risk in chronic hepatitis B patients: risk scores integrating host and virus profiles. Hepatology. 2013 Aug;58(2):546-54. doi: 10.1002/hep.26385. PMID: 23504622.
Kim	/	2013	hepatocellular carcinoma	3-year: 0.806 (0.738–0.874)	chronic hepatitis B patients who had transient elastography examination	Kim DY, Song KJ, Kim SU, Yoo EJ, Park JY, Ahn SH, Han KH. Transient elastography-based risk estimation of hepatitis B virus-related occurrence of hepatocellular carcinoma: development and validation of a predictive model. Onco Targets Ther. 2013 Oct 16;6:1463-9. doi: 10.2147/OTT.S51986. PMID: 24204161; PMCID: PMC3804604.
Chang	/	2013	hepatocellular carcinoma	5-year: 0.79	chronic hepatitis C patients who had interferon-based therapy	Chang KC, Wu YY, Hung CH, Lu SN, Lee CM, Chiu KW, Tsai MC, Tseng PL, Huang CM, Cho CL, Chen HH, Hu TH. Clinical-guide risk prediction of hepatocellular carcinoma development in chronic hepatitis C patients after interferon-based therapy. Br J Cancer. 2013 Oct 29;109(9):2481-8. doi: 10.1038/bjc.2013.564. Epub 2013 Oct 1. PMID: 24084770; PMCID: PMC3817320.

Chang	scoreHCC	2012	hepatocellular carcinoma	8-year: 0.848	chronic hepatitis C patients who received combined pegylated interferon and ribavirin therapy and achieved SVR	Chang KC, Hung CH, Lu SN, Wang JH, Lee CM, Chen CH, Yen MF, Lin SC, Yen YH, Tsai MC, Tseng PL, Hu TH. A novel predictive score for hepatocellular carcinoma development in patients with chronic hepatitis C after sustained response to pegylated interferon and ribavirin combination therapy. J Antimicrob Chemother. 2012 Nov;67(11):2766-72. doi: 10.1093/jac/dks269. Epub 2012 Aug 16. PMID: 22899800.
Flemming	ADRESS-HCC	2014	hepatocellular carcinoma	1-year: 0.704 (derivation) 0.691 (validation)	cirrhosis patients	Flemming JA, Yang JD, Vittinghoff E, Kim WR, Terrault NA. Risk prediction of hepatocellular carcinoma in patients with cirrhosis: the ADRESS-HCC risk model. Cancer. 2014 Nov 15;120(22):3485-93. doi: 10.1002/cncr.28832. Epub 2014 Jul 16. PMID: 25042049; PMCID: PMC4553222.
Michikawa	/	2012	hepatocellular carcinoma	10-year: 0.9424	General public	Michikawa T, Inoue M, Sawada N, Iwasaki M, Tanaka Y, Shimazu T, Sasazuki S, Yamaji T, Mizokami M, Tsugane S; Japan Public Health Center-based Prospective Study Group. Development of a prediction model for 10-year risk of hepatocellular carcinoma in middle-aged Japanese: the Japan Public Health Center-based Prospective Study Cohort II. Prev Med. 2012 Aug;55(2):137-43. doi: 10.1016/j.ypmed.2012.05.017. Epub 2012 Jun 4. PMID: 22676909.
Wen	Health History Model	2012	hepatocellular carcinoma	subcohort without an HCV test: 0.807 (0.804 to 0.811) subcohort with an HCV test: 0.793 (0.790 to 0.802)	General public	Wen CP, Lin J, Yang YC, Tsai MK, Tsao CK, Etzel C, Huang M, Hsu CY, Ye Y, Mishra L, Hawk E, Wu X. Hepatocellular carcinoma risk prediction model for the general population: the predictive power of transaminases. J Natl Cancer Inst. 2012 Oct 17;104(20):1599-611. doi: 10.1093/jnci/djs372. PMID: 23073549; PMCID: PMC3692381.
Wen	Transaminase Model	2012	hepatocellular carcinoma	subcohort without an HCV test: 0.900 (0.894 to 0.906) subcohort with an HCV test: 0.912 (0.909 to 0.915)	General public	Wen CP, Lin J, Yang YC, Tsai MK, Tsao CK, Etzel C, Huang M, Hsu CY, Ye Y, Mishra L, Hawk E, Wu X. Hepatocellular carcinoma risk prediction model for the general population: the predictive power of transaminases. J Natl Cancer Inst. 2012 Oct 17;104(20):1599-611. doi: 10.1093/jnci/djs372. PMID: 23073549; PMCID: PMC3692381.

Wen	Transaminase and health history Model	2012	hepatocellular carcinoma	-	General public	Wen CP, Lin J, Yang YC, Tsai MK, Tsao CK, Etzel C, Huang M, Hsu CY, Ye Y, Mishra L, Hawk E, Wu X. Hepatocellular carcinoma risk prediction model for the general population: the predictive power of transaminases. J Natl Cancer Inst. 2012 Oct 17;104(20):1599-611. doi: 10.1093/jnci/djs372. PMID: 23073549; PMCID: PMC3692381.
Wen	Transaminase, health history, HBV test results and AFP Model	2012	hepatocellular carcinoma	subcohort without an HCV test: 0.918 (0.910 to 0.928) subcohort with an HCV test: 0.927 (0.918 to 0.945)	General public	Wen CP, Lin J, Yang YC, Tsai MK, Tsao CK, Etzel C, Huang M, Hsu CY, Ye Y, Mishra L, Hawk E, Wu X. Hepatocellular carcinoma risk prediction model for the general population: the predictive power of transaminases. J Natl Cancer Inst. 2012 Oct 17;104(20):1599-611. doi: 10.1093/jnci/djs372. PMID: 23073549; PMCID: PMC3692381.
Wen	Transaminase, health history, HBV/HCV test results and AFP Model	2012	hepatocellular carcinoma	subcohort without an HCV test: - subcohort with an HCV test: 0.933 (0.929 to 0.949)	General public	Wen CP, Lin J, Yang YC, Tsai MK, Tsao CK, Etzel C, Huang M, Hsu CY, Ye Y, Mishra L, Hawk E, Wu X. Hepatocellular carcinoma risk prediction model for the general population: the predictive power of transaminases. J Natl Cancer Inst. 2012 Oct 17;104(20):1599-611. doi: 10.1093/jnci/djs372. PMID: 23073549; PMCID: PMC3692381.
Hung	Model 1	2015	hepatocellular carcinoma	- Model: 0.78 (0.76-0.80; bootstrap-corrected c-statistic = 0.77) - Risk score for 3-, 5-, and 10-year risk: 0.73-0.78	/	Hung YC, Lin CL, Liu CJ, Hung H, Lin SM, Lee SD, Chen PJ, Chuang SC, Yu MW. Development of risk scoring system for stratifying population for hepatocellular carcinoma screening. Hepatology. 2015 Jun;61(6):1934-44. doi: 10.1002/hep.27610. Epub 2015 Apr 13. PMID: 25418332.
Hung	Model 2	2015	hepatocellular carcinoma	- Model: 0.79 (0.77-0.81; bootstrap-corrected c-statistic = 0.79) - Risk score for 3-, 5-, and 10-year risk: 0.76-0.80	/	Hung YC, Lin CL, Liu CJ, Hung H, Lin SM, Lee SD, Chen PJ, Chuang SC, Yu MW. Development of risk scoring system for stratifying population for hepatocellular carcinoma screening. Hepatology. 2015 Jun;61(6):1934-44. doi: 10.1002/hep.27610. Epub 2015 Apr 13. PMID: 25418332.
Hung	Model 3	2015	hepatocellular carcinoma	- Model: 0.85 (0.83-0.87; bootstrap-corrected c-statistic = 0.84)	/	Hung YC, Lin CL, Liu CJ, Hung H, Lin SM, Lee SD, Chen PJ, Chuang SC, Yu MW. Development of risk scoring system for stratifying population for hepatocellular carcinoma screening. Hepatology. 2015 Jun;61(6):1934-44. doi: 10.1002/hep.27610. Epub 2015 Apr 13. PMID: 25418332.

				- Risk score for 3-, 5-, and 10-year risk: 0.83-0.85		
Hung	Model 4	2015	hepatocellular carcinoma	- Model: NR (not significantly better than model 3) - Risk score for 3-, 5-, and 10-year risk: 0.83-0.86	/	Hung YC, Lin CL, Liu CJ, Hung H, Lin SM, Lee SD, Chen PJ, Chuang SC, Yu MW. Development of risk scoring system for stratifying population for hepatocellular carcinoma screening. Hepatology. 2015 Jun;61(6):1934-44. doi: 10.1002/hep.27610. Epub 2015 Apr 13. PMID: 25418332.
Sharma	Toronto HCC risk index	2017	hepatocellular carcinoma	0.76 (0.72–0.79)	cirrhosis patients	Sharma SA, Kowgier M, Hansen BE, Brouwer WP, Maan R, Wong D, Shah H, Khalili K, Yim C, Heathcote EJ, Janssen HLA, Sherman M, Hirschfield GM, Feld JJ. Toronto HCC risk index: A validated scoring system to predict 10-year risk of HCC in patients with cirrhosis. J Hepatol. 2017 Aug 24:S0168-8278(17)32248-1. doi: 10.1016/j.jhep.2017.07.033. Epub ahead of print. PMID: 28844936.
Papatheodoridis	PAGE-B	2016	hepatocellular carcinoma	0.82, 0.81 after bootstrap validation 0.82 in the validation dataset	chronic hepatitis B patients	Papatheodoridis G, Dalekos G, Sypsa V, Yurdaydin C, Buti M, Goulis J, Calleja JL, Chi H, Manolakopoulos S, Mangia G, Gatselis N, Keskin O, Savvidou S, de la Revilla J, Hansen BE, Vlachogiannakos I, Galanis K, Idilman R, Colombo M, Esteban R, Janssen HL, Lampertico P. PAGE-B predicts the risk of developing hepatocellular carcinoma in Caucasians with chronic hepatitis B on 5-year antiviral therapy. J Hepatol. 2016 Apr;64(4):800-6. doi: 10.1016/j.jhep.2015.11.035. Epub 2015 Dec 8. PMID: 26678008.
Kim	modified PAGE-B	2018	hepatocellular carcinoma	5-years: 0.82 (0.78–0.86) 0.81 (0.78–0.85) after bootstrap validation 0.82 (95% CI 0.76–0.88) in the validation dataset	chronic hepatitis B patients	Kim JH, Kim YD, Lee M, Jun BG, Kim TS, Suk KT, Kang SH, Kim MY, Cheon GJ, Kim DJ, Baik SK, Choi DH. Modified PAGE-B score predicts the risk of hepatocellular carcinoma in Asians with chronic hepatitis B on antiviral therapy. J Hepatol. 2018 Nov;69(5):1066-1073. doi: 10.1016/j.jhep.2018.07.018. Epub 2018 Aug 1. PMID: 30075230.
Papatheodoridis	CAGE-B	2020	hepatocellular carcinoma	Development: 0.814 Bootstrapped: 0.806	Caucasian public	Papatheodoridis GV, Sypsa V, Dalekos GN, Yurdaydin C, Van Boemmel F, Buti M, Calleja JL, Chi H, Goulis J, Manolakopoulos S, Loglio A, Voulgaris T, Gatselis N, Keskin O, Veelken R, Lopez-Gomez M, Hansen BE, Savvidou S, Kourikou A, Vlachogiannakos J, Galanis K, Idilman R, Esteban R, Janssen HLA, Berg T, Lampertico P. Hepatocellular carcinoma prediction beyond year 5 of oral therapy in a large cohort of Caucasian patients with chronic

						hepatitis B. J Hepatol. 2020 Jun;72(6):1088-1096. doi: 10.1016/j.jhep.2020.01.007. Epub 2020 Jan 22. PMID: 31981727.
Papatheodoridis	SAGE-B	2020	hepatocellular carcinoma	Development: 0.809 Bootstrapped: 0.805	Caucasian public	Papatheodoridis GV, Sypsa V, Dalekos GN, Yurdaydin C, Van Boemmel F, Buti M, Calleja JL, Chi H, Goulis J, Manolakopoulos S, Loglio A, Voulgaris T, Gatselis N, Keskin O, Veelken R, Lopez-Gomez M, Hansen BE, Savvidou S, Kourikou A, Vlachogiannakos J, Galanis K, Idilman R, Esteban R, Janssen HLA, Berg T, Lampertico P. Hepatocellular carcinoma prediction beyond year 5 of oral therapy in a large cohort of Caucasian patients with chronic hepatitis B. J Hepatol. 2020 Jun;72(6):1088-1096. doi: 10.1016/j.jhep.2020.01.007. Epub 2020 Jan 22. PMID: 31981727.
Hsu	CAMD	2018	hepatocellular carcinoma	Development: 0.83 (0.81–0.84) Validation: 0.74 (0.71–0.77)	patients with chronic hepatitis B on antiviral therapy	Hsu YC, Yip TC, Ho HJ, Wong VW, Huang YT, El-Serag HB, Lee TY, Wu MS, Lin JT, Wong GL, Wu CY. Development of a scoring system to predict hepatocellular carcinoma in Asians on antivirals for chronic hepatitis B. J Hepatol. 2018 Aug;69(2):278-285. doi: 10.1016/j.jhep.2018.02.032. Epub 2018 Mar 16. Erratum in: J Hepatol. 2019 Mar;70(3):581. PMID: 29551708.
Chen	APA-B	2017	hepatocellular carcinoma	Development: 2 years 0.877 (0.789–0.965) 3 years 0.842 (0.771–0.914) 4 years 0.857 (0.806–0.907) 5 years 0.827 (0.771–0.883) Validation: 2 years 0.939 (0.902–0.976) 3 years 0.892 (0.828–0.956) 4 years 0.883 (0.829–0.938) 5 years 0.862 (0.795–0.929)	Nucleos(t)ide analog (NA)-treated chronic hepatitis B patients	Chen CH, Lee CM, Lai HC, Hu TH, Su WP, Lu SN, Lin CH, Hung CH, Wang JH, Lee MH, Peng CY. Prediction model of hepatocellular carcinoma risk in Asian patients with chronic hepatitis B treated with entecavir. Oncotarget. 2017 Sep 28;8(54):92431-92441. doi: 10.18632/oncotarget.21369. PMID: 29190928; PMCID: PMC5696194.
Yang	REAL-B	2020	hepatocellular carcinoma	Development: 0.81 (0.78–0.84) Validation: 0.83 (0.78–0.87)	patients with chronic hepatitis B on oral antiviral therapy	Yang HI, Yeh ML, Wong GL, Peng CY, Chen CH, Trinh HN, Cheung KS, Xie Q, Su TH, Kozuka R, Lee DH, Ogawa E, Zhao C, Ning HB, Huang R, Li J, Zhang JQ, Ide T, Xing H, Iwane S, Takahashi H, Wong C, Wong C, Lin CH, Hoang J, Le A, Henry L, Toyoda H, Ueno Y, Gane EJ, Eguchi Y, Kurosaki M, Wu C, Liu C, Shang J, Furusyo N, Enomoto M, Kao JH, Yuen MF, Yu ML, Nguyen MH. Real-World Effectiveness From the Asia Pacific Rim Liver Consortium for HBV Risk Score for the Prediction of Hepatocellular Carcinoma in Chronic Hepatitis B Patients

						Treated With Oral Antiviral Therapy. J Infect Dis. 2020 Jan 14;221(3):389-399. doi: 10.1093/infdis/jiz477. PMID: 31550363.
Yu	AASL-HCC	2019	hepatocellular carcinoma	Development: 0.802 (0.716–0.888) Validation: 0.805 (0.671–0.939)	patients with chronic hepatitis B on oral antiviral therapy	Yu JH, Suh YJ, Jin YJ, Heo NY, Jang JW, You CR, An HY, Lee JW. Prediction model for hepatocellular carcinoma risk in treatment-naive chronic hepatitis B patients receiving entecavir/tenofovir. Eur J Gastroenterol Hepatol. 2019 Jul;31(7):865-872. doi: 10.1097/MEG.0000000000001357. PMID: 30694912.
Poh	RWS-HCC	2016	hepatocellular carcinoma	0.915 (0.880-0.949)	patients with chronic hepatitis B	Poh Z, Shen L, Yang HI, Seto WK, Wong VW, Lin CY, Goh BB, Chang PE, Chan HL, Yuen MF, Chen CJ, Tan CK. Real-world risk score for hepatocellular carcinoma (RWS-HCC): a clinically practical risk predictor for HCC in chronic hepatitis B. Gut. 2016 May;65(5):887-8. doi: 10.1136/gutjnl-2015-310818. Epub 2016 Jan 19. PMID: 26786688.
Fan	aMap	2020	hepatocellular carcinoma	Development: 0.82 (0.77-0.86) Validation: From 0.82 to 0.87 across cohorts	patients with chronic hepatitis B	Fan R, Papatheodoridis G, Sun J, Innes H, Toyoda H, Xie Q, Mo S, Sypsa V, Guha IN, Kumada T, Niu J, Dalekos G, Yasuda S, Barnes E, Lian J, Suri V, Idilman R, Barclay ST, Dou X, Berg T, Hayes PC, Flaherty JF, Zhou Y, Zhang Z, Buti M, Hutchinson SJ, Guo Y, Calleja JL, Lin L, Zhao L, Chen Y, Janssen HLA, Zhu C, Shi L, Tang X, Gaggar A, Wei L, Jia J, Irving WL, Johnson PJ, Lampertico P, Hou J. aMAP risk score predicts hepatocellular carcinoma development in patients with chronic hepatitis. J Hepatol. 2020 Dec;73(6):1368-1378. doi: 10.1016/j.jhep.2020.07.025. Epub 2020 Jul 21. PMID: 32707225.
Lee	CAMPAS Model	2020	hepatocellular carcinoma	0.874 (0.823-0.924)	patients with chronic hepatitis B and well-controlled viremia	Lee HW, Park SY, Lee M, Lee EJ, Lee J, Kim SU, Park JY, Kim DY, Ahn SH, Kim BK. An optimized hepatocellular carcinoma prediction model for chronic hepatitis B with well-controlled viremia. Liver Int. 2020 Jul;40(7):1736-1743. doi: 10.1111/liv.14451. Epub 2020 Apr 22. PMID: 32239602.
Kim	HCC-RIFLE	2023	hepatocellular carcinoma	/	/	Kim GA, Park Y, Oh SJ, Jung J, Han S, Chang HS, Park SW, Kim TH, Park HW, Choe J, Kim J, Lee HC. A risk prediction model for hepatocellular carcinoma in non-alcoholic fatty liver disease without cirrhosis: HCC prediction for non-cirrhotic NAFLD. Liver Int. 2023 Dec 18. doi: 10.1111/liv.15819. Epub ahead of print. PMID: 38110797.
Liu	NSMC-HCC Model	2023	hepatocellular carcinoma	Development: 0.960 (0.950-0.971)	High-risk populations for HCC	Liu ZJ, Xu Y, Wang WX, Guo B, Zhang GY, Luo GC, Wang Q. Development and application of hepatocellular carcinoma risk prediction model based on clinical characteristics and liver related indexes. World J Gastrointest Oncol. 2023 Aug 15;15(8):1486-1496. doi:

				Validation: 0.966 (0.945-0.986)		10.4251/wjgo.v15.i8.1486. PMID: 37663947; PMCID: PMC10473933.
Yang	Model 1	2022	hepatocellular carcinoma	0.799 (0.722-0.877)	HBsAg-cleared patients	Yang H, Bae SH, Nam H, Lee HL, Lee SW, Yoo SH, Song MJ, Kwon JH, Nam SW, Choi JY, Yoon SK, Jang JW. A risk prediction model for hepatocellular carcinoma after hepatitis B surface antigen seroclearance. J Hepatol. 2022 Sep;77(3):632-641. doi: 10.1016/j.jhep.2022.03.032. Epub 2022 Apr 7. PMID: 35398462.
Yang	Model 2	/	/	/	/	Yang H, Bae SH, Nam H, Lee HL, Lee SW, Yoo SH, Song MJ, Kwon JH, Nam SW, Choi JY, Yoon SK, Jang JW. A risk prediction model for hepatocellular carcinoma after hepatitis B surface antigen seroclearance. J Hepatol. 2022 Sep;77(3):632-641. doi: 10.1016/j.jhep.2022.03.032. Epub 2022 Apr 7. PMID: 35398462.
Yang	Model 3	/	/	/	/	Yang H, Bae SH, Nam H, Lee HL, Lee SW, Yoo SH, Song MJ, Kwon JH, Nam SW, Choi JY, Yoon SK, Jang JW. A risk prediction model for hepatocellular carcinoma after hepatitis B surface antigen seroclearance. J Hepatol. 2022 Sep;77(3):632-641. doi: 10.1016/j.jhep.2022.03.032. Epub 2022 Apr 7. PMID: 35398462.
Yang	Model 4	/	/	/	/	Yang H, Bae SH, Nam H, Lee HL, Lee SW, Yoo SH, Song MJ, Kwon JH, Nam SW, Choi JY, Yoon SK, Jang JW. A risk prediction model for hepatocellular carcinoma after hepatitis B surface antigen seroclearance. J Hepatol. 2022 Sep;77(3):632-641. doi: 10.1016/j.jhep.2022.03.032. Epub 2022 Apr 7. PMID: 35398462.
Bach	/	2003	Lung cancer	0.72	Ever smokers	Bach PB, Kattan MW, Thornquist MD, Kris MG, Tate RC, Barnett MJ, Hsieh LJ, Begg CB. Variations in lung cancer risk among smokers. J Natl Cancer Inst. 2003 Mar 19;95(6):470-8. doi: 10.1093/jnci/95.6.470. PMID: 12644540.
Bach	/	2003	Lung cancer	0.72	Ever smokers	Bach PB, Kattan MW, Thornquist MD, Kris MG, Tate RC, Barnett MJ, Hsieh LJ, Begg CB. Variations in lung cancer risk among smokers. J Natl Cancer Inst. 2003 Mar 19;95(6):470-8. doi: 10.1093/jnci/95.6.470. PMID: 12644540.
Bach	/	2003	Lung cancer	0.72	Ever smokers	Bach PB, Kattan MW, Thornquist MD, Kris MG, Tate RC, Barnett MJ, Hsieh LJ, Begg CB. Variations in lung cancer risk among smokers. J Natl Cancer Inst. 2003 Mar 19;95(6):470-8. doi: 10.1093/jnci/95.6.470. PMID: 12644540.
Cassidy	Liverpool Lung Project Model	2008	Lung cancer	0.71	General public	Cassidy A, Myles JP, van Tongeren M, Page RD, Liloglou T, Duffy SW, Field JK. The LLP risk model: an individual risk prediction model for lung cancer. Br J Cancer. 2008 Jan 29;98(2):270-6. doi: 10.1038/sj.bjc.6604158. Epub 2007 Dec 18. PMID: 18087271; PMCID: PMC2361453.

Cassidy	Liverpool Lung Project Model	2008	Lung cancer	0.71	General public	Cassidy A, Myles JP, van Tongeren M, Page RD, Liloglou T, Duffy SW, Field JK. The LLP risk model: an individual risk prediction model for lung cancer. Br J Cancer. 2008 Jan 29;98(2):270-6. doi: 10.1038/sj.bjc.6604158. Epub 2007 Dec 18. PMID: 18087271; PMCID: PMC2361453.
Etzel	/	2008	Lung cancer	0.75 (0.67−0.82) for internal data 0.63 (0.57−0.69) for external data	African-Americans	Etzel CJ, Kachroo S, Liu M, D'Amelio A, Dong Q, Cote ML, Wenzlaff AS, Hong WK, Greisinger AJ, Schwartz AG, Spitz MR. Development and validation of a lung cancer risk prediction model for African-Americans. Cancer Prev Res (Phila). 2008 Sep;1(4):255-65. doi: 10.1158/1940-6207.CAPR-08-0082. PMID: 19138969; PMCID: PMC2854402.
Tammemagi	PLCOM2011 Ever Smoker Model	2011	Lung cancer	0.809 (0.7957-0.8219) (Derivation) 0.784 (0.745-0.824) (Validation)	Ever Smokers	Tammemagi CM, Pinsky PF, Caporaso NE, Kvale PA, Hocking WG, Church TR, Riley TL, Commins J, Oken MM, Berg CD, Prorok PC. Lung cancer risk prediction: Prostate, Lung, Colorectal And Ovarian Cancer Screening Trial models and validation. J Natl Cancer Inst. 2011 Jul 6;103(13):1058-68. doi: 10.1093/jnci/djr173. Epub 2011 May 23. PMID: 21606442; PMCID: PMC3131220.
Tammemagi	PLCOM2012 Model	2013	Lung cancer	0.803 (0.782–0.813) [Derivation] [Validation]: - PLCO intervention-group smokers: 0.797 (0.782–0.813) - NLST participants: 0.701 (0.689–0.712) - PLCO intervention-group smokers who met NLST criteria: 0.710 (0.689–0.732) - PLCO intervention-group smokers who did not meet NLST criteria 0.780 (0.744–0.811)	Ever Smokers	Tammemägi MC, Katki HA, Hocking WG, Church TR, Caporaso N, Kvale PA, Chaturvedi AK, Silvestri GA, Riley TL, Commins J, Berg CD. Selection criteria for lung-cancer screening. N Engl J Med. 2013 Feb 21;368(8):728-36. doi: 10.1056/NEJMoa1211776. Erratum in: N Engl J Med. 2013 Jul 25;369(4):394. PMID: 23425165; PMCID: PMC3929969.

Park	/	2013	Lung cancer	Derivation: 0.864 (0.860–0.868) Validation: 0.871 (0.867–0.876)	General Public	Park S, Nam BH, Yang HR, Lee JA, Lim H, Han JT, Park IS, Shin HR, Lee JS. Individualized risk prediction model for lung cancer in Korean men. PLoS One. 2013;8(2):e54823. doi: 10.1371/journal.pone.0054823. Epub 2013 Feb 7. PMID: 23408946; PMCID: PMC3567090.
Maisonneuve	Recalibrated Bach Model	2011	Lung cancer	NR	Ever smokers	Maisonneuve P, Bagnardi V, Bellomi M, Spaggiari L, Pelosi G, Rampinelli C, Bertolotti R, Rotmensz N, Field JK, Decensi A, Veronesi G. Lung cancer risk prediction to select smokers for screening CT--a model based on the Italian COSMOS trial. Cancer Prev Res (Phila). 2011 Nov;4(11):1778-89. doi: 10.1158/1940-6207.CAPR-11-0026. Epub 2011 Aug 2. PMID: 21813406.
Maisonneuve	COSMOS screening model	2011	Lung cancer	0.759	Ever smokers	Maisonneuve P, Bagnardi V, Bellomi M, Spaggiari L, Pelosi G, Rampinelli C, Bertolotti R, Rotmensz N, Field JK, Decensi A, Veronesi G. Lung cancer risk prediction to select smokers for screening CT--a model based on the Italian COSMOS trial. Cancer Prev Res (Phila). 2011 Nov;4(11):1778-89. doi: 10.1158/1940-6207.CAPR-11-0026. Epub 2011 Aug 2. PMID: 21813406.
Young	/	2009	Lung cancer	0.79	Ever smokers	Young RP, Hopkins RJ, Hay BA, Epton MJ, Mills GD, Black PN, Gardner HD, Sullivan R, Gamble GD. A gene-based risk score for lung cancer susceptibility in smokers and ex-smokers. Postgrad Med J. 2009 Oct;85(1008):515-24. doi: 10.1136/pgmj.2008.077107. PMID: 19789190.
Li	wGRS (weighted genetic risk score) Model	2012	Lung cancer	Derivation: 0.639 (0.621-0.652) Bootstrap Validation: 0.637	General public	Li H, Yang L, Zhao X, Wang J, Qian J, Chen H, Fan W, Liu H, Jin L, Wang W, Lu D. Prediction of lung cancer risk in a Chinese population using a multifactorial genetic model. BMC Med Genet. 2012 Dec 10;13:118. doi: 10.1186/1471-2350-13-118. PMID: 23228068; PMCID: PMC3573944.
Markaki	HUNT Lung Cancer Model	2018	Lung cancer	Total Population 0·903 Ever-smokers 0·869 Ever-smokers (Validation): 0·879 (0·866–0·891)	Current Smokers	Markaki M, Tsamardinos I, Langhammer A, Lagani V, Hveem K, Røe OD. A Validated Clinical Risk Prediction Model for Lung Cancer in Smokers of All Ages and Exposure Types: A HUNT Study. EBioMedicine. 2018 May;31:36-46. doi: 10.1016/j.ebiom.2018.03.027. Epub 2018 Mar 30. Erratum in: EBioMedicine. 2022 Aug;82:104187. PMID: 29678673; PMCID: PMC6013755.
Wilson	Pittsburgh Predictor	2015	Lung cancer	NLST CXR: 0.688 (0.670-0.705) NLST LDCT: 0.678 (0.662-0.694)	Ever smokers	Wilson DO, Weissfeld J. A simple model for predicting lung cancer occurrence in a lung cancer screening program: The Pittsburgh Predictor. Lung Cancer. 2015 Jul;89(1):31-7. doi: 10.1016/j.lungcan.2015.03.021. Epub 2015 Mar 28. PMID: 25863905; PMCID: PMC4457558.

Marcus	Liverpool Lung Project Incidence (LLPi) Risk Model	2015	Lung cancer	Derivation: 0.852 (0.832–0.873) Bootstrap correction 0.849 (0.829–0.870)	General public	Marcus M.W., Chen Y., Raji O.Y., Duffy S.W., Field J.K. LLPi: liverpool lung project risk prediction model for lung cancer incidence. Cancer Prev. Res. (Phila.) 2015;8(6):570–575.
Guida	PLCO Risk Score	2018	Lung cancer	0.83 (0.76-0.90)	Ever smokers	Integrative Analysis of Lung Cancer Etiology and Risk (INTEGRAL) Consortium for Early Detection of Lung Cancer; Guida F, Sun N, Bantis LE, Muller DC, Li P, Taguchi A, Dhillon D, Kundnani DL, Patel NJ, Yan Q, Byrnes G, Moons KGM, Tjønneland A, Panico S, Agnoli C, Vineis P, Palli D, Bueno-de-Mesquita B, Peeters PH, Agudo A, Huerta JM, Dorronsoro M, Barranco MR, Ardanaz E, Travis RC, Byrne KS, Boeing H, Steffen A, Kaaks R, Hüsing A, Trichopoulou A, Lagiou P, La Vecchia C, Severi G, Boutron-Ruault MC, Sandanger TM, Weiderpass E, Nøst TH, Tsilidis K, Riboli E, Grankvist K, Johansson M, Goodman GE, Feng Z, Brennan P, Johansson M, Hanash SM. Assessment of Lung Cancer Risk on the Basis of a Biomarker Panel of Circulating Proteins. JAMA Oncol. 2018 Oct 1;4(10):e182078. doi: 10.1001/jamaoncol.2018.2078. Epub 2018 Oct 11. Erratum in: JAMA Oncol. 2018 Oct 1;4(10):1439. Erratum in: JAMA Oncol. 2019 Dec 1;5(12):1811. PMID: 30003238; PMCID: PMC6233784.
Choi	PLCOm2012-Update	2023	Lung cancer	Japanese American: 0.80 (0.78-0.83) Latino: 0.83 (0.79-0.86) African American: 0.72 (0.70-0.74) Native Hawaiian/Other Pacific Islander: : 0.76 (0.72-0.80)	General Public	Choi E, Ding VY, Luo SJ, Ten Haaf K, Wu JT, Aredo JV, Wilkens LR, Freedman ND, Backhus LM, Leung AN, Meza R, Lui NS, Haiman CA, Park SL, Le Marchand L, Neal JW, Cheng I, Wakelee HA, Tammemägi MC, Han SS. Risk Model-Based Lung Cancer Screening and Racial and Ethnic Disparities in the US. JAMA Oncol. 2023 Dec 1;9(12):1640-1648. doi: 10.1001/jamaoncol.2023.4447. PMID: 37883107; PMCID: PMC10603577.
Guo	Henan Lung Cancer Risk Model	2022	Lung cancer	Development: 0.766 (1 year) Validation: 0.741 (1 year)	General Public	Guo LW, Lyu ZY, Meng QC, Zheng LY, Chen Q, Liu Y, Xu HF, Kang RH, Zhang LY, Cao XQ, Liu SZ, Sun XB, Zhang JG, Zhang SK. A risk prediction model for selecting high-risk population for computed tomography lung cancer screening in China. Lung Cancer. 2022 Jan;163:27-34. doi: 10.1016/j.lungcan.2021.11.015. Epub 2021 Dec 1. PMID: 34894456.

Guo	/	2022	Lung cancer	Development: 0.753 (1-year) 0.752 (3-year) 0.755 (5-year) Validation: 0.668 (1-year) 0.678 (3-year) 0.685 (5-year)	Non-smokers	Guo LW, Lyu ZY, Meng QC, Zheng LY, Chen Q, Liu Y, Xu HF, Kang RH, Zhang LY, Cao XQ, Liu SZ, Sun XB, Zhang JG, Zhang SK. Construction and Validation of a Lung Cancer Risk Prediction Model for Non-Smokers in China. Front Oncol. 2022 Jan 4;11:766939. doi: 10.3389/fonc.2021.766939. Erratum in: Front Oncol. 2022 Mar 03;12:871848. PMID: 35059311; PMCID: PMC8764453.
Li	/	2015	Ovarian cancer	0.64 (0.57–0.70)	European women aged 45 and over	Li K, Hüsing A, Fortner RT, Tjønneland A, Hansen L, Dossus L, Chang-Claude J, Bergmann M, Steffen A, Bamia C, Trichopoulos D, Trichopoulou A, Palli D, Mattiello A, Agnoli C, Tumino R, Onland-Moret NC, Peeters PH, Bueno-de-Mesquita HB, Gram IT, Weiderpass E, Sánchez-Cantalejo E, Chirlaque MD, Duell EJ, Ardanaz E, Idahl A, Lundin E, Khaw KT, Travis RC, Merritt MA, Gunter MJ, Riboli E, Ferrari P, Terry K, Cramer D, Kaaks R. An epidemiologic risk prediction model for ovarian cancer in Europe: the EPIC study. Br J Cancer. 2015 Mar 31;112(7):1257-65. doi: 10.1038/bjc.2015.22. PMID: 25742479; PMCID: PMC4385951.
Sharma	Enriching New-onset Diabetes for Pancreatic Cancer (END-PAC)	2018	pancreatic cancer	0.87 (high-risk; score of ≥3)	/	Sharma A, Kandlakunta H, Nagpal SJS, Feng Z, Hoos W, Petersen GM, Chari ST. Model to Determine Risk of Pancreatic Cancer in Patients With New-Onset Diabetes. Gastroenterology. 2018 Sep;155(3):730-739.e3. doi: 10.1053/j.gastro.2018.05.023. Epub 2018 Jun 11. PMID: 29775599; PMCID: PMC6120785.
Boursi	/	2017	pancreatic ductal adenocarcinoma	0.82 (0.75–0.89)	patients over 35 years old with new-onset diabetes	Boursi B, Finkelman B, Giantonio BJ, Haynes K, Rustgi AK, Rhim AD, Mamtani R, Yang YX. A Clinical Prediction Model to Assess Risk for Pancreatic Cancer Among Patients With New-Onset Diabetes. Gastroenterology. 2017 Mar;152(4):840-850.e3. doi: 10.1053/j.gastro.2016.11.046. Epub 2016 Dec 5. PMID: 27923728; PMCID: PMC5337138.
Boursi	/	2022	pancreatic ductal adenocarcinoma	0.71 (95% CI, 0.67–0.75)	/	Boursi B, Finkelman B, Giantonio BJ, Haynes K, Rustgi AK, Rhim AD, Mamtani R, Yang YX. A clinical prediction model to assess risk for pancreatic cancer among patients with prediabetes. Eur J Gastroenterol Hepatol. 2022 Jan 1;34(1):33-38. doi: 10.1097/MEG.0000000000002052. PMID: 33470698; PMCID: PMC8286263.
Cai	/	2011	pancreatic cancer	multivariable analysis: 0.81 (0.70–0.91) prediction rule: 0.72 (0.60–0.83) internal validation: 0.72 (0.66–0.78)	chronic pancreatitis patients with focal pancreatic mass lesions with	Cai QC, Chen Y, Xiao Y, Zhu W, Xu QF, Zhong L, Chen SY, Zhang MM, Wang LW, Li ZS. A prediction rule for estimating pancreatic cancer risk in chronic pancreatitis patients with focal pancreatic mass lesions with prior negative EUS-FNA cytology. Scand J Gastroenterol. 2011 Apr;46(4):464-70. doi: 10.3109/00365521.2010.539256. Epub 2010 Nov 30. PMID: 21114434.

					prior negative EUS-FNA cytology	
Lu	/	2006	Pancreas cancer	0.981	General Public	Lu XH, Wang L, Li H, et al. Establishment of risk model for pancreatic cancer in Chinese Han population. World J Gastroenterol 2006;12:2229-2234.
Malhotra	/	2021	Pancreatic ductal adenocarcinoma	≤ 60 years old: 0.66 > 60 years old: 0.61	General Public	Malhotra A, Rachet B, Bonaventure A, Pereira SP, Woods LM. Can we screen for pancreatic cancer? Identifying a sub-population of patients at high risk of subsequent diagnosis using machine learning techniques applied to primary care data. PLoS One. 2021 Jun 2;16(6):e0251876. doi: 10.1371/journal.pone.0251876. PMID: 34077433; PMCID: PMC8171946.
Pang	/	2017	Pancreas cancer	/	General Public	Pang T, Ding G, Wu Z, Jiang G, Yang Y, Zhang X, Cao L. A novel scoring system to analyze combined effect of lifestyle factors on pancreatic cancer risk: a retrospective case-control study. Sci Rep. 2017 Oct 20;7(1):13657. doi: 10.1038/s41598-017-13182-w. PMID: 29057932; PMCID: PMC5651911.
Tang	/	2013	Prostate cancer	0.848	Men in the general public	Tang P, Chen H, Uhlman M, Lin YR, Deng XR, Wang B, Yang WJ, Xie KJ. A nomogram based on age, prostate-specific antigen level, prostate volume and digital rectal examination for predicting risk of prostate cancer. Asian J Androl. 2013 Jan;15(1):129-33. doi: 10.1038/aja.2012.111. Epub 2012 Dec 10. PMID: 23291910; PMCID: PMC3739110.
Huang	/	2014	Prostate cancer	0.853	Men in the general public	Huang Y, Cheng G, Liu B, Shao P, Qin C, Li J, Hua L, Yin C. A prostate biopsy strategy based on a new clinical nomogram reduces the number of biopsy cores required in high-risk patients. BMC Urol. 2014 Jan 11;14:8. doi: 10.1186/1471-2490-14-8. PMID: 24410803; PMCID: PMC3893548.
Wu	Huashan risk calculator I (RC 1) for PCa	2016	Prostate cancer	Derivation: 0.926 (0.905-0.946) Validation: 0.849 (0.815-0.882)	Men in the general public	Wu YS, Zhang N, Liu SH, Xu JF, Tong SJ, Cai YH, Zhang LM, Bai PD, Hu MB, Jiang HW, Na R, Ding Q, Sun YH. The Huashan risk calculators performed better in prediction of prostate cancer in Chinese population: a training study followed by a validation study. Asian J Androl. 2016 Nov-Dec;18(6):925-929. doi: 10.4103/1008-682X.181192. PMID: 27212127; PMCID: PMC5109890.
Wu	Huashan risk calculator II (RC 2) for PCa	2016	Prostate cancer	Derivation: 0.901 (0.877-0.925) Validation: 0.794 (0.754-0.883)	Men in the general public	Wu YS, Zhang N, Liu SH, Xu JF, Tong SJ, Cai YH, Zhang LM, Bai PD, Hu MB, Jiang HW, Na R, Ding Q, Sun YH. The Huashan risk calculators performed better in prediction of prostate cancer in Chinese population: a training study followed by a validation study. Asian J Androl. 2016 Nov-Dec;18(6):925-929. doi: 10.4103/1008-682X.181192. PMID: 27212127; PMCID: PMC5109890.

Wu	Huashan risk calculator I (RC 1) for high-grade PCa	2016	High-grade Prostate cancer (Gleason Score ≥8)	Derivation: 0.838 (0.802-0.874) Validation: 0.855 (0.809-0.900)	Men in the general public	Wu YS, Zhang N, Liu SH, Xu JF, Tong SJ, Cai YH, Zhang LM, Bai PD, Hu MB, Jiang HW, Na R, Ding Q, Sun YH. The Huashan risk calculators performed better in prediction of prostate cancer in Chinese population: a training study followed by a validation study. Asian J Androl. 2016 Nov-Dec;18(6):925-929. doi: 10.4103/1008-682X.181192. PMID: 27212127; PMCID: PMC5109890.
Wu	Huashan risk calculator II (RC 2) for high-grade PCa	2016	High-grade Prostate cancer (Gleason Score ≥8)	Derivation: 0.814 (0.772-0.856) Validation: 0.886 (0.842-0.929)	Men in the general public	Wu YS, Zhang N, Liu SH, Xu JF, Tong SJ, Cai YH, Zhang LM, Bai PD, Hu MB, Jiang HW, Na R, Ding Q, Sun YH. The Huashan risk calculators performed better in prediction of prostate cancer in Chinese population: a training study followed by a validation study. Asian J Androl. 2016 Nov-Dec;18(6):925-929. doi: 10.4103/1008-682X.181192. PMID: 27212127; PMCID: PMC5109890.
Chen	Chinese Prostate Cancer Consortium Risk Calculator (CPCC-RC)	2016	Prostate cancer	0.801 (0.771–0.831)	Men in the general public	Chen R, Xie L, Xue W, Ye Z, Ma L, Gao X, Ren S, Wang F, Zhao L, Xu C, Sun Y; Chinese Prostate Cancer Consortium. Development and external multicenter validation of Chinese Prostate Cancer Consortium prostate cancer risk calculator for initial prostate biopsy. Urol Oncol. 2016 Sep;34(9):416.e1-7. doi: 10.1016/j.urolonc.2016.04.004. Epub 2016 May 12. PMID: 27185342.
Chen	Chinese Prostate Cancer Consortium Risk Calculator (CPCC-RC)	2016	High-grade Prostate cancer (Gleason score ≥ 7)	0.826 (0.796–0.857)	Men in the general public	Chen R, Xie L, Xue W, Ye Z, Ma L, Gao X, Ren S, Wang F, Zhao L, Xu C, Sun Y; Chinese Prostate Cancer Consortium. Development and external multicenter validation of Chinese Prostate Cancer Consortium prostate cancer risk calculator for initial prostate biopsy. Urol Oncol. 2016 Sep;34(9):416.e1-7. doi: 10.1016/j.urolonc.2016.04.004. Epub 2016 May 12. PMID: 27185342.
Suzuki	Carcinoma Histological Incidence at Biopsy Assistant (CHIBA)	2006	Prostate cancer	0.8181	Men in the general public	Suzuki H, Komiya A, Kamiya N, Imamoto T, Kawamura K, Miura J, Suzuki N, Nakatsu H, Hata A, Ichikawa T. Development of a nomogram to predict probability of positive initial prostate biopsy among Japanese patients. Urology. 2006 Jan;67(1):131-6. doi: 10.1016/j.urology.2005.07.040. PMID: 16413348.
Park	Korean prostate cancer risk calculator (KPCRC)	2011	Prostate cancer	0.91 (0.88-0.93) Validation: 0.79 (0.74-0.85)	Men in the general public	Park JY, Yoon S, Park MS, Cho DY, Park HS, Moon du G, Yoon DK. Initial biopsy outcome prediction in Korean patients-comparison of a noble web-based Korean prostate cancer risk calculator versus prostate-specific antigen testing. J Korean Med Sci. 2011 Jan;26(1):85-91. doi: 10.3346/jkms.2011.26.1.85. Epub 2010 Dec 22. PMID: 21218035; PMCID: PMC3012855.
Kuo	/	2013	Prostate cancer	Derivation: 0.888 (0.861–0.914) Validation: 0.781	Men in the general public	Kuo SC, Hung SH, Wang HY, Chien CC, Lu CL, Lin HJ, Guo HR, Zou JF, Lin CS, Huang CC. Chinese nomogram to predict probability of positive initial prostate biopsy: a study in Taiwan region. Asian J Androl. 2013 Nov;15(6):780-4. doi: 10.1038/aja.2013.100. Epub 2013 Oct 14. PMID: 24121978; PMCID: PMC3854028.

Finne	LR Model	2004	Prostate cancer	0.764 (0.72–0.80)	Men with PSA concentrations between 4 –10 microg/L	Finne P, Finne R, Bangma C, Hugosson J, Hakama M, Auvinen A, Stenman UH. Algorithms based on prostate-specific antigen (PSA), free PSA, digital rectal examination and prostate volume reduce false-positive PSA results in prostate cancer screening. Int J Cancer. 2004 Aug 20;111(2):310-5. doi: 10.1002/ijc.20250. PMID: 15197788.
Karakiewicz	Basic model	2005	Prostate cancer	derivation: 0.70 (0.68-0.72) validation: 0.69 (0.68 - 0.72)	High-risk populations	Karakiewicz PI, Benayoun S, Kattan MW, Perrotte P, Valiquette L, Scardino PT, Cagiannos I, Heinzer H, Tanguay S, Aprikian AG, Huland H, Graefen M. Development and validation of a nomogram predicting the outcome of prostate biopsy based on patient age, digital rectal examination and serum prostate specific antigen. J Urol. 2005 Jun;173(6):1930-4. doi: 10.1097/01.ju.0000158039.94467.5d. PMID: 15879784; PMCID: PMC1855288.
Karakiewicz	/	2005	Prostate cancer	derivation: 0.78 (0.75-0.80) validation: 0.77 (0.72-0.81)	High-risk populations	Karakiewicz PI, Benayoun S, Kattan MW, Perrotte P, Valiquette L, Scardino PT, Cagiannos I, Heinzer H, Tanguay S, Aprikian AG, Huland H, Graefen M. Development and validation of a nomogram predicting the outcome of prostate biopsy based on patient age, digital rectal examination and serum prostate specific antigen. J Urol. 2005 Jun;173(6):1930-4. doi: 10.1097/01.ju.0000158039.94467.5d. PMID: 15879784; PMCID: PMC1855288.
Thompson	Prostate Cancer Prevention Trial Risk Calculator (PCPTRC)	2006	Prostate cancer	0.702 (0.6963-0.7077)	- healthy men - aged of 55 or more - PSA ≤ 3 ng/mL - normal DRE	Thompson IM, Ankerst DP, Chi C, Goodman PJ, Tangen CM, Lucia MS, Feng Z, Parnes HL, Coltman CA Jr. Assessing prostate cancer risk: results from the Prostate Cancer Prevention Trial. J Natl Cancer Inst. 2006 Apr 19;98(8):529-34. doi: 10.1093/jnci/djj131. PMID: 16622122.
Thompson	Prostate Cancer Prevention Trial Risk Calculator (PCPTRC)	2006	High-grade Prostate cancer (Gleason score ≥ 7)	0.698 (0.6877-0.7083)	- healthy men - aged of 55 or more - PSA ≤ 3 ng/mL - normal DRE	Thompson IM, Ankerst DP, Chi C, Goodman PJ, Tangen CM, Lucia MS, Feng Z, Parnes HL, Coltman CA Jr. Assessing prostate cancer risk: results from the Prostate Cancer Prevention Trial. J Natl Cancer Inst. 2006 Apr 19;98(8):529-34. doi: 10.1093/jnci/djj131. PMID: 16622122.
Chun	/	2007	Prostate cancer	0.767	High risk population	Chun FK, Briganti A, Graefen M, Montorsi F, Porter C, Scattoni V, Gallina A, Walz J, Haese A, Steuber T, Erbersdobler A, Schlomm T, Ahyai SA, Currlin E, Valiquette L, Heinzer H, Rigatti P, Huland H, Karakiewicz PI. Development and external validation of an extended 10-core biopsy nomogram. Eur Urol. 2007

						Aug;52(2):436-44. doi: 10.1016/j.eururo.2006.08.039. Epub 2006 Sep 11. PMID: 17010505.
Kranse	ERSPC prostate cancer risk calculator 3	2008	Prostate cancer	0.79	/	Kranse R, Roobol M, Schröder FH. A graphical device to represent the outcomes of a logistic regression analysis. Prostate. 2008 Nov 1;68(15):1674-80. doi: 10.1002/pros.20840. PMID: 18712715.
Vickers	/	2008	Prostate cancer	0.836 (0.810-0.880)	Men with elevated PSA	Vickers AJ, Cronin AM, Aus G, Pihl CG, Becker C, Pettersson K, Scardino PT, Hugosson J, Lilja H. A panel of kallikrein markers can reduce unnecessary biopsy for prostate cancer: data from the European Randomized Study of Prostate Cancer Screening in Göteborg, Sweden. BMC Med. 2008 Jul 8;6:19. doi: 10.1186/1741-7015-6-19. PMID: 18611265; PMCID: PMC2474851.
Hill	Prostate biopsy clinical decision rule (PBCDR) Model 1	2013	Prostate cancer	0.68 (0.65-0.71)	Patients with PSA above 4	Hill OT, Mason TJ, Schwartz SW, Foulis PR. Improving prostate cancer detection in veterans through the development of a clinical decision rule for prostate biopsy. BMC Urol. 2013 Jan 29;13:6. doi: 10.1186/1471-2490-13-6. PMID: 23356551; PMCID: PMC3567946.
Hill	Prostate biopsy clinical decision rule (PBCDR) Model 2	2013	Advanced stage prostate cancer ((analogous to T2 palpable PC)	0.72 (0.68-0.75)	Patients with PSA above 4	Hill OT, Mason TJ, Schwartz SW, Foulis PR. Improving prostate cancer detection in veterans through the development of a clinical decision rule for prostate biopsy. BMC Urol. 2013 Jan 29;13:6. doi: 10.1186/1471-2490-13-6. PMID: 23356551; PMCID: PMC3567946.
Nam	/	2007	Prostate cancer	0.74 (0.71 to 0.81)	Men in the general public	Nam RK, Toi A, Klotz LH, Trachtenberg J, Jewett MA, Appu S, Loblaw DA, Sugar L, Narod SA, Kattan MW. Assessing individual risk for prostate cancer. J Clin Oncol. 2007 Aug 20;25(24):3582-8. doi: 10.1200/JCO.2007.10.6450. PMID: 17704405.
Nam	/	2007	High-grade Prostate cancer	0.77 (0.74 to 0.81)	Men in the general public	Nam RK, Toi A, Klotz LH, Trachtenberg J, Jewett MA, Appu S, Loblaw DA, Sugar L, Narod SA, Kattan MW. Assessing individual risk for prostate cancer. J Clin Oncol. 2007 Aug 20;25(24):3582-8. doi: 10.1200/JCO.2007.10.6450. PMID: 17704405.
Moussa	/	2010	Prostate cancer	0.72 (development), 0.62 (validation)	Patients with a previous negative biopsy	Moussa AS, Jones JS, Yu C, Fareed K, Kattan MW. Development and validation of a nomogram for predicting a positive repeat prostate biopsy in patients with a previous negative biopsy session in the era of extended prostate sampling . BJU Int. 2010 Nov;106(9):1309-14. doi: 10.1111/j.1464-410X.2010.09362.x.
Lopez-Corona	/	2003	Prostate cancer	0.7	Patients with a previous negative biopsy	Lopez-Corona E, Ohori M, Scardino PT, Reuter VE, Gonen M, Kattan MW. A nomogram for predicting a positive repeat prostate biopsy in patients with a previous negative biopsy session. J Urol. 2003 Oct;170(4 Pt 1):1184-8; discussion 1188. doi: 10.1097/01.ju.0000087451.64657.fa.

						Erratum in: J Urol. 2004 Jan;171(1):360-1. PMID: 14501721.
Finne	LR Model	2000	Prostate cancer	/	Men with PSA 4–20 ng/ml	Finne P, Finne R, Auvinen A, et al. Predicting the outcome of prostate biopsy in screen-positive men by a multilayer perceptron network. Urology 2000;56:418–22.
Finne	/	2002	Prostate cancer	/	Men with PSA 4–20 ng/ml	Finne P, Auvinen A, Aro J, et al. Estimation of prostate cancer risk on the basis of total and free prostate-specific antigen, prostate volume and digital rectal examination. Eur Urol 2002;41:619–27.
Nam	/	2006	Prostate cancer	/	Men with PSA > 2.5 ng/ml or abnormal DRE	Nam RK, Toi A, Trachtenberg J, Klotz LH, Jewett MA, Emami M, Sugar L, Sweet J, Pond GR, Narod SA. Making sense of prostate specific antigen: improving its predictive value in patients undergoing prostate biopsy. J Urol. 2006 Feb;175(2):489-94. doi: 10.1016/S0022-5347(05)00159-X. PMID: 16406978.
Yanke	/	2006	Prostate cancer	0.75 (0.74–0.76)	Men in the general public	Yanke BV, Carver BS, Bianco FJ Jr, Simoneaux WJ, Venable DD, Powell IJ, Eastham JA. African-American race is a predictor of prostate cancer detection: incorporation into a pre-biopsy nomogram. BJU Int. 2006 Oct;98(4):783-7. doi: 10.1111/j.1464-410X.2006.06388.x. PMID: 16978273.
Garzotto	/	2003	Prostate cancer	0.73	Referred men with PSA ≤ 10 ng/mL	Garzotto M, Hudson RG, Peters L, Hsieh YC, Barrera E, Mori M, Beer TM, Klein T. Predictive modeling for the presence of prostate carcinoma using clinical, laboratory, and ultrasound parameters in patients with prostate specific antigen levels < or = 10 ng/mL. Cancer. 2003 Oct 1;98(7):1417-22. doi: 10.1002/cncr.11668. PMID: 14508828.
Eastham	Eastham Nomogram	1999	Prostate cancer	0.75	Men with abnormal DRE and PSA between 0-4 ng/mL	Eastham JA, May R, Robertson JL, Sartor O, Kattan MW. Development of a nomogram that predicts the probability of a positive prostate biopsy in men with an abnormal digital rectal examination and a prostate-specific antigen between 0 and 4 ng/mL. Urology. 1999;54::709.
Radtke	/	2017	Significant prostate cancer (= Gleason Score ≥ 3 + 4)	biopsy-naive men: 0.83 post-biopsy men: 0.81	/	Radtke JP, Wiesenfarth M, Kesch C, Freitag MT, Alt CD, Celik K, Distler F, Roth W, Wieczorek K, Stock C, Duensing S, Roethke MC, Teber D, Schlemmer HP, Hohenfellner M, Bonekamp D, Hadaschik BA. Combined Clinical Parameters and Multiparametric Magnetic Resonance Imaging for Advanced Risk Modeling of Prostate Cancer-Patient-tailored Risk Stratification Can Reduce Unnecessary Biopsies. Eur Urol. 2017 Dec;72(6):888-896. doi: 10.1016/j.eururo.2017.03.039. Epub 2017 Apr 8. PMID: 28400169.

Mehralivand	Baseline Model	2018	Significant prostate cancer (=Gleason Score ≥ 3 + 4)	0.64 (0.57-0.71)	Patients with elevated serum prostate-specific antigen (PSA) levels or abnormal results of a digital rectal examination and at least 1 lesion detected	Mehralivand S, Shih JH, Rais-Bahrami S, Oto A, Bednarova S, Nix JW, Thomas JV, Gordetsky JB, Gaur S, Harmon SA, Siddiqui MM, Merino MJ, Parnes HL, Wood BJ, Pinto PA, Choyke PL, Turkbey B. A Magnetic Resonance Imaging-Based Prediction Model for Prostate Biopsy Risk Stratification. JAMA Oncol. 2018 May 1;4(5):678-685. doi: 10.1001/jamaoncol.2017.5667. PMID: 29470570; PMCID: PMC5885194.
Mehralivand	MRI Model	2018	Significant prostate cancer (=Gleason Score ≥ 3 + 4)	0.84 (0.79-0.89)	Patients with elevated serum prostate-specific antigen (PSA) levels or abnormal results of a digital rectal examination and at least 1 lesion detected	Mehralivand S, Shih JH, Rais-Bahrami S, Oto A, Bednarova S, Nix JW, Thomas JV, Gordetsky JB, Gaur S, Harmon SA, Siddiqui MM, Merino MJ, Parnes HL, Wood BJ, Pinto PA, Choyke PL, Turkbey B. A Magnetic Resonance Imaging-Based Prediction Model for Prostate Biopsy Risk Stratification. JAMA Oncol. 2018 May 1;4(5):678-685. doi: 10.1001/jamaoncol.2017.5667. PMID: 29470570; PMCID: PMC5885194.
van Leeuwen	Multivariable model	2017	sSignificant prostate cancer (= Gleason 7 with >5% grade 4, ≥20% cores positive or ≥7 mm of cancer in any core)	0.819 (0.777–0.862)	Men with abnormal PSA/DRE	van Leeuwen PJ, Hayen A, Thompson JE, Moses D, Shnier R, Böhm M, Abuodha M, Haynes AM, Ting F, Barentsz J, Roobol M, Vass J, Rasiah K, Delprado W, Stricker PD. A multiparametric magnetic resonance imaging-based risk model to determine the risk of significant prostate cancer prior to biopsy. BJU Int. 2017 Dec;120(6):774-781. doi: 10.1111/bju.13814. Epub 2017 Mar 31. PMID: 28207981.

van Leeuwen	Advanced model	2017	sSignificant prostate cancer (= Gleason 7 with >5% grade 4, ≥20% cores positive or ≥7 mm of cancer in any core)	0.897 (0.868–0.928)	Men with abnormal PSA/DRE	van Leeuwen PJ, Hayen A, Thompson JE, Moses D, Shnier R, Böhm M, Abuodha M, Haynes AM, Ting F, Barentsz J, Roobol M, Vass J, Rasiah K, Delprado W, Stricker PD. A multiparametric magnetic resonance imaging-based risk model to determine the risk of significant prostate cancer prior to biopsy. BJU Int. 2017 Dec;120(6):774-781. doi: 10.1111/bju.13814. Epub 2017 Mar 31. PMID: 28207981.
Catalona	Prostate Health Index	2011	Prostate cancer	0.703	Men aged ≥50 years with PSA levels between 2.0 and 10.0 ng/mL and non-suspicious DRE findings	Catalona WJ, Partin AW, Sanda MG, Wei JT, Klee GG, Bangma CH, Slawin KM, Marks LS, Loeb S, Broyles DL, Shin SS, Cruz AB, Chan DW, Sokoll LJ, Roberts WL, van Schaik RH, Mizrahi IA. A multicenter study of [-2]pro-prostate specific antigen combined with prostate specific antigen and free prostate specific antigen for prostate cancer detection in the 2.0 to 10.0 ng/ml prostate specific antigen range. J Urol. 2011 May;185(5):1650-5. doi: 10.1016/j.juro.2010.12.032. Epub 2011 Mar 17. Erratum in: J Urol. 2011 Jul;186(1):354. PMID: 21419439; PMCID: PMC3140702.
Chen	/	2021	Prostate cancer	All cancers: 0.795 High-grade cancer: 0.869	/	Chen IHA, Chu CH, Lin JT, Tsai J-, Yu CC, Sridhar AN, Chand M, Sooriakumaran P. Comparing a new risk prediction model with prostate cancer risk calculator apps in a Taiwanese population. World J Urol. 2021 Mar;39(3):797-802. doi: 10.1007/s00345-020-03256-2. Epub 2020 May 20. PMID: 32436074.
Hwang	/	2023	Prostate cancer	Development: 0.911 Validation: 0.874	Men in the general public	Hwang T, Oh H, Lee JA, Kim EJ. Prostate cancer risk prediction based on clinical factors and prostate-specific antigen. BMC Urol. 2023 Jun 3;23(1):100. doi: 10.1186/s12894-023-01259-w. PMID: 37270476; PMCID: PMC10239594.
Li	/	2023	Prostate cancer	Development: 0.755 Validation: 0.756	Men in the general public	Li S, Hu X. Assessing the Risk of Prostate Cancer with Nutritional and Environmental Factors: A Cross-Sectional Study from National Health and Nutrition Examination Survey 2001-2010. Nutr Cancer. 2023;75(5):1361-1372. doi: 10.1080/01635581.2023.2197687. Epub 2023 Apr 10. PMID: 37036281.
Yeo	/	2022	Prostate cancer	0.826 (0.821–0.832)	Men in the general public	Yeo Y, Shin DW, Lee J, Han K, Park SH, Jeon KH, Shin J, Shin A, Park J. Personalized 5-Year Prostate Cancer Risk Prediction Model in Korea Based on Nationwide Representative Data. J Pers Med. 2021 Dec 21;12(1):2. doi: 10.3390/jpm12010002. PMID: 35055319; PMCID: PMC8780119.

Wu	Prostate cancer Risk calculator 1 (RC1)	2019	Prostate cancer	0.81(0.79–0.84)	Men in the general public	Wu YS, Fu XJ, Na R, Ye DW, Qi J, Lin XL, Liu F, Gong J, Zhang N, Jiang GL, Jiang HW, Ding Q, Xu J, Sun YH. Phi-based risk calculators performed better in the prediction of prostate cancer in the Chinese population. Asian J Androl. 2019 Nov-Dec;21(6):592-597. doi: 10.4103/aja.aja_125_18. PMID: 30924451; PMCID: PMC6859657.
Wu	Prostate cancer Risk calculator 2 (RC2)	2019	Prostate cancer	0.91(0.90–0.93)	Men in the general public	Wu YS, Fu XJ, Na R, Ye DW, Qi J, Lin XL, Liu F, Gong J, Zhang N, Jiang GL, Jiang HW, Ding Q, Xu J, Sun YH. Phi-based risk calculators performed better in the prediction of prostate cancer in the Chinese population. Asian J Androl. 2019 Nov-Dec;21(6):592-597. doi: 10.4103/aja.aja_125_18. PMID: 30924451; PMCID: PMC6859657.
Wu	Prostate cancer Risk calculator 3 (RC3)	2019	Prostate cancer	0.84(0.81–0.86)	Men in the general public	Wu YS, Fu XJ, Na R, Ye DW, Qi J, Lin XL, Liu F, Gong J, Zhang N, Jiang GL, Jiang HW, Ding Q, Xu J, Sun YH. Phi-based risk calculators performed better in the prediction of prostate cancer in the Chinese population. Asian J Androl. 2019 Nov-Dec;21(6):592-597. doi: 10.4103/aja.aja_125_18. PMID: 30924451; PMCID: PMC6859657.
Wu	Prostate cancer Risk calculator II (RC4)	2019	Prostate cancer	0.91(0.89–0.93)	Men in the general public	Wu YS, Fu XJ, Na R, Ye DW, Qi J, Lin XL, Liu F, Gong J, Zhang N, Jiang GL, Jiang HW, Ding Q, Xu J, Sun YH. Phi-based risk calculators performed better in the prediction of prostate cancer in the Chinese population. Asian J Androl. 2019 Nov-Dec;21(6):592-597. doi: 10.4103/aja.aja_125_18. PMID: 30924451; PMCID: PMC6859657.
Wu	High grade prostate cancer Risk calculator 1 (RC1)	2019	High grade prostate cancer (Gleason score ≥7)	0.82(0.79–0.85)	Men in the general public	Wu YS, Fu XJ, Na R, Ye DW, Qi J, Lin XL, Liu F, Gong J, Zhang N, Jiang GL, Jiang HW, Ding Q, Xu J, Sun YH. Phi-based risk calculators performed better in the prediction of prostate cancer in the Chinese population. Asian J Androl. 2019 Nov-Dec;21(6):592-597. doi: 10.4103/aja.aja_125_18. PMID: 30924451; PMCID: PMC6859657.
Wu	High grade prostate cancer Risk calculator 2 (RC2)	2019	High grade prostate cancer (Gleason score ≥7)	0.92(0.90–0.94)	Men in the general public	Wu YS, Fu XJ, Na R, Ye DW, Qi J, Lin XL, Liu F, Gong J, Zhang N, Jiang GL, Jiang HW, Ding Q, Xu J, Sun YH. Phi-based risk calculators performed better in the prediction of prostate cancer in the Chinese population. Asian J Androl. 2019 Nov-Dec;21(6):592-597. doi: 10.4103/aja.aja_125_18. PMID: 30924451; PMCID: PMC6859657.
Wu	High grade prostate Risk calculator 3 (RC3)	2019	High grade prostate cancer (Gleason score ≥7)	0.85(0.83–0.88)	Men in the general public	Wu YS, Fu XJ, Na R, Ye DW, Qi J, Lin XL, Liu F, Gong J, Zhang N, Jiang GL, Jiang HW, Ding Q, Xu J, Sun YH. Phi-based risk calculators performed better in the prediction of prostate cancer in the Chinese population. Asian J Androl. 2019 Nov-Dec;21(6):592-597. doi: 10.4103/aja.aja_125_18. PMID: 30924451; PMCID: PMC6859657.

Wu	High grade prostate Risk calculator II (RC4)	2019	High grade prostate cancer (Gleason score ≥7)	0.92(0.90–0.94)	Men in the general public	Wu YS, Fu XJ, Na R, Ye DW, Qi J, Lin XL, Liu F, Gong J, Zhang N, Jiang GL, Jiang HW, Ding Q, Xu J, Sun YH. Phi-based risk calculators performed better in the prediction of prostate cancer in the Chinese population. Asian J Androl. 2019 Nov-Dec;21(6):592-597. doi: 10.4103/aja.aja_125_18. PMID: 30924451; PMCID: PMC6859657.
Nam	/	2018	High grade prostate cancer (Gleason 7 (4+3) score)	0.74 (0.72-0.76)	Men in the general public	Nam RK, Satkunavisam R, Chin JL, Izawa J, Trachtenberg J, Rendon R, Bell D, Singal R, Sherman C, Sugar L, Chagin K, Kattan MW. Next-generation prostate cancer risk calculator for primary care physicians. Can Urol Assoc J. 2018 Feb;12(2):E64-E70. doi: 10.5489/cuaj.4696. Epub 2017 Dec 1. PMID: 29381462; PMCID: PMC5937391.
Xu	/	2021	Prostate cancer	NR	Men in the general public	Xu B, Li G, Kong C, Chen M, Hu B, Jiang Q, Li N, Zhou L. A multicenter retrospective study on evaluation of predicative factors for positive biopsy of prostate cancer in real-world setting. Curr Med Res Opin. 2021 Sep;37(9):1617-1625. doi: 10.1080/03007995.2021.1949270. Epub 2021 Jul 19. PMID: 34192993.
Guo	Logistic regression model	2021	Prostate cancer	0.963 (0.951-0.978)	Men in the general public	Guo H, Jia X, Liu H. Based on biomedical index data: Risk prediction model for prostate cancer. Medicine (Baltimore). 2021 Apr 30;100(17):e25602. doi: 10.1097/MD.0000000000025602. PMID: 33907111; PMCID: PMC8084031.
MacKie	/	1989	invasive cutaneous malignant melanoma (level 2 or deeper)	External validation: women 0·64 (0·58–0·71), men 0·64 (0·55–0·73)	General Public	MacKie RM, Freudenberger T, Aitchison TC. Personal risk-factor chart for cutaneous melanoma. Lancet. 1989 Aug 26;2(8661):487-90. doi: 10.1016/s0140-6736(89)92097-7. PMID: 2570195.
Marrett	/	1992	cutaneous malignant melanoma	NR	General Public	Marrett LD, King WD, Walter SD, From L. Use of host factors to identify people at high risk for cutaneous malignant melanoma . CMAJ. 1992 Aug 15;147(4):445-53. Erratum in: Can Med Assoc J 1992 Dec 15;147(12):1764. PMID: 1498755; PMCID: PMC1336243.
Garbe	/	1994	cutaneous malignant melanoma	NR	General Public	Garbe C, Büttner P, Weiss J, Soyer HP, Stocker U, Krüger S, Roser M, Weckbecker J, Panizzon R, Bahmer F, et al. Risk factors for developing cutaneous melanoma and criteria for identifying persons at risk: multicenter case-control study of the Central Malignant Melanoma Registry of the German Dermatological Society. J Invest Dermatol. 1994 May;102(5):695-9. doi: 10.1111/1523-1747.ep12374280. PMID: 8176250.
Landi	/	2001	cutaneous malignant melanoma	NR	Mediterranean population	Landi MT, Baccarelli A, Calista D, Pesatori A, Fears T, Tucker MA, Landi G. Combined risk factors for melanoma in a Mediterranean population. Br J Cancer. 2001 Nov 2;85(9):1304-10. doi: 10.1054/bjoc.2001.2029. PMID: 11720465; PMCID: PMC2375242.

Cho	/	2005	malignant melanoma	0·62 (0·58–0·65)	General Public	Cho E, Rosner BA, Feskanich D, Colditz GA. Risk factors and individual probabilities of melanoma for whites. J Clin Oncol. 2005 Apr 20;23(12):2669-75. doi: 10.1200/JCO.2005.11.108. PMID: 15837981.
Goldberg	HARMM Model	2007	cutaneous malignant melanoma	NR	General Public	Goldberg MS, Doucette JT, Lim HW, Spencer J, Carucci JA, Rigel DS. Risk factors for presumptive melanoma in skin cancer screening: American Academy of Dermatology National Melanoma/Skin Cancer Screening Program experience 2001-2005. J Am Acad Dermatol. 2007 Jul;57(1):60-6. doi: 10.1016/j.jaad.2007.02.010. Epub 2007 May 9. PMID: 17490783.
Quéreux	metaanalysis model	2011	invasive cutaneous melanoma cases of stage I or II	0.695	General Public	Quéreux G, Moyse D, Lequeux Y, Jumbou O, Brocard A, Antonioli D, Dréno B, Nguyen JM. Development of an individual score for melanoma risk. Eur J Cancer Prev. 2011 May;20(3):217-24. doi: 10.1097/CEJ.0b013e32834474ae. PMID: 21399503.
Quéreux	logistic regression model	2011	invasive cutaneous melanoma cases of stage I or II	0.725	General Public	Quéreux G, Moyse D, Lequeux Y, Jumbou O, Brocard A, Antonioli D, Dréno B, Nguyen JM. Development of an individual score for melanoma risk. Eur J Cancer Prev. 2011 May;20(3):217-24. doi: 10.1097/CEJ.0b013e32834474ae. PMID: 21399503.
Quéreux	combinatorial model	2011	invasive cutaneous melanoma cases of stage I or II	0.71	General Public	Quéreux G, Moyse D, Lequeux Y, Jumbou O, Brocard A, Antonioli D, Dréno B, Nguyen JM. Development of an individual score for melanoma risk. Eur J Cancer Prev. 2011 May;20(3):217-24. doi: 10.1097/CEJ.0b013e32834474ae. PMID: 21399503.
Williams	/	2011	cutaneous melanoma (only invasive)	Derivation: 0.77 (0.73-0.81) Internal validation: 0·70 (0·64–0·77)	General Public (white)	Williams LH, Shors AR, Barlow WE, Solomon C, White E. Identifying Persons at Highest Risk of Melanoma Using Self-Assessed Risk Factors. J Clin Exp Dermatol Res. 2011;2(6):1000129. doi: 10.4172/2155-9554.1000129. PMID: 22229112; PMCID: PMC3252382.
Guther	/	2012	cutaneous melanoma	0.857	General Public	Guther S, Ramrath K, Dyall-Smith D, Landthaler M, Stolz W. Development of a targeted risk-group model for skin cancer screening based on more than 100,000 total skin examinations. J Eur Acad Dermatol Venereol. 2012 Jan;26(1):86-94. doi: 10.1111/j.1468-3083.2011.04014.x. Epub 2011 Mar 4. PMID: 21371132.
Cai	/	2019	gastric cancer	0.76 0.(73-0.79) (D) 0.73 (0.68-0.77) (Validation)	Individuals at risk for GC	Cai Q, Zhu C, Yuan Y, Feng Q, Feng Y, Hao Y, Li J, Zhang K, Ye G, Ye L, Lv N, Zhang S, Liu C, Li M, Liu Q, Li R, Pan J, Yang X, Zhu X, Li Y, Lao B, Ling A, Chen H, Li X, Xu P, Zhou J, Liu B, Du Z, Du Y, Li Z; Gastrointestinal Early Cancer Prevention & Treatment Alliance of China (GECA). Development and validation of a prediction rule for estimating gastric cancer risk in the Chinese high-risk

						population: a nationwide multicentre study. Gut. 2019 Sep;68(9):1576-1587. doi: 10.1136/gutjnl-2018-317556. Epub 2019 Mar 29. PMID: 30926654; PMCID: PMC6709770.
Charvat	/	2016	gastric cancer	Derivation: 0.777 Internal validation: 0.768	General Public	Charvat H, Sasazuki S, Inoue M, Iwasaki M, Sawada N, Shimazu T, Yamaji T, Tsugane S; JPHC Study Group. Prediction of the 10-year probability of gastric cancer occurrence in the Japanese population: the JPHC study cohort II. Int J Cancer. 2016 Jan 15;138(2):320-31. doi: 10.1002/ijc.29705. Epub 2015 Aug 13. Erratum in: Int J Cancer. 2016 Aug 15;139(4):E6-7. PMID: 26219435.
Iida	/	2018	gastric cancer	Derivation: 0.79 (0.74–0.83) Validation: 0.76 (0.69–0.83)	General Public	Iida M, Ikeda F, Hata J, Hirakawa Y, Ohara T, Mukai N, Yoshida D, Yonemoto K, Esaki M, Kitazono T, Kiyohara Y, Ninomiya T. Development and validation of a risk assessment tool for gastric cancer in a general Japanese population. Gastric Cancer. 2018 May;21(3):383-390. doi: 10.1007/s10120-017-0768-8. Epub 2017 Oct 17. PMID: 29043529.
Lee	/	2009	gastric cancer	0.904 (0.876-0.932)	General Public	Lee DS, Yang HK, Kim JW, Yook JW, Jeon SH, Kang SH, Kim YJ. Identifying the risk factors through the development of a predictive model for gastric cancer in South Korea. Cancer Nurs. 2009 Mar-Apr;32(2):135-42. doi: 10.1097/NCC.0b013e3181982c2e. PMID: 19258828.
Tu	/	2017	gastric cancer	0.803 (0.789–0.816)	General Public	Tu H, Sun L, Dong X, Gong Y, Xu Q, Jing J, Bostick RM, Wu X, Yuan Y. A Serological Biopsy Using Five Stomach-Specific Circulating Biomarkers for Gastric Cancer Risk Assessment: A Multi-Phase Study. Am J Gastroenterol. 2017 May;112(5):704-715. doi: 10.1038/ajg.2017.55. Epub 2017 Mar 21. PMID: 28323271.
Kunzmann	/	2018	Gastric cancer	0.72 (0.69–0.76)	General Public	Kunzmann AT, Thrift AP, Cardwell CR, Lagergren J, Xie S, Johnston BT, Anderson LA, Busby J, McMenamin ÚC, Spence AD, Coleman HG. Model for Identifying Individuals at Risk for Esophageal Adenocarcinoma. Clin Gastroenterol Hepatol. 2018 Aug;16(8):1229-1236.e4. doi: 10.1016/j.cgh.2018.03.014. Epub 2018 Mar 17. PMID: 29559360.
Hüsing	/	2016	Endometrial cancer	0.77 (0.68–0.85)	Women in the general public	Hüsing A, Dossus L, Ferrari P, Tjønneland A, Hansen L, Fagherazzi G, Baglietto L, Schock H, Chang-Claude J, Boeing H, Steffen A, Trichopoulou A, Bamia C, Katsoulis M, Krogh V, Palli D, Panico S, Onland-Moret NC, Peeters PH, Bueno-de-Mesquita HB, Weiderpass E, Gram IT, Ardanaz E, Obón-Santacana M, Navarro C, Sánchez-Cantalejo E, Etxezarreta N, Allen NE, Khaw KT, Wareham N, Rinaldi S, Romieu I, Merritt MA, Gunter M, Riboli E, Kaaks R. An epidemiological model for prediction of endometrial cancer risk in Europe. Eur J Epidemiol. 2016 Jan;31(1):51-60. doi: 10.1007/s10654-015-0030-9. Epub 2015 May 13. PMID: 25968175.

Kitson	PRECISION Full Model	2023	Endometrial cancer	Development: 0.741 (0.74–0.76) Validation: 0.70 (0.69–0.70)	Women in the general public	Kitson SJ, Crosbie EJ, Evans DG, Lophatananon A, Muir KR, Ashcroft D, Kontopantelis E, Martin GP. Predicting risk of endometrial cancer in asymptomatic women (PRECISION): Model development and external validation. BJOG. 2023 Dec 10. doi: 10.1111/1471-0528.17729. Epub ahead of print. PMID: 38073256.
Kitson	PRECISION Basic Model	2023	Endometrial cancer	Development: 0.71 Validation: 0.69 (0.68–0.69)	Women in the general public	Kitson SJ, Crosbie EJ, Evans DG, Lophatananon A, Muir KR, Ashcroft D, Kontopantelis E, Martin GP. Predicting risk of endometrial cancer in asymptomatic women (PRECISION): Model development and external validation. BJOG. 2023 Dec 10. doi: 10.1111/1471-0528.17729. Epub ahead of print. PMID: 38073256.
Kitson	/	2016	Endometrial cancer	NR	General Public	Kitson SJ, Evans DG, Crosbie EJ. Identifying High-Risk Women for Endometrial Cancer Prevention Strategies: Proposal of an Endometrial Cancer Risk Prediction Model. Cancer Prev Res (Phila). 2017 Jan;10(1):1-13. doi: 10.1158/1940-6207.CAPR-16-0224. Epub 2016 Dec 13. PMID: 27965288.
Jayawickrama	/	2022	Endometrial cancer	0.92 (0.88-0.95)	Postmenopausal women	Jayawickrama IU, Abeysena C. Development of a Risk Prediction Model for endometrial carcinoma among postmenopausal women in the Western province of Sri Lanka. Ceylon Med J. 2022 Dec 31;67(4):169-176. doi: 10.4038/cmj.v67i4.9746. PMID: 38421317.
Guther	/	2012	SCC	0.9	General Public	Guther S, Ramrath K, Dyall-Smith D, Landthaler M, Stolz W. Development of a targeted risk-group model for skin cancer screening based on more than 100,000 total skin examinations. J Eur Acad Dermatol Venereol. 2012 Jan;26(1):86-94. doi: 10.1111/j.1468-3083.2011.04014.x. Epub 2011 Mar 4. PMID: 21371132.
Guther	/	2012	BCC	NA (derivation was based on melanome and SCC patients)	General Public	Guther S, Ramrath K, Dyall-Smith D, Landthaler M, Stolz W. Development of a targeted risk-group model for skin cancer screening based on more than 100,000 total skin examinations. J Eur Acad Dermatol Venereol. 2012 Jan;26(1):86-94. doi: 10.1111/j.1468-3083.2011.04014.x. Epub 2011 Mar 4. PMID: 21371132.
Guther	/	2012	Melanoma	0.857	General Public	Guther S, Ramrath K, Dyall-Smith D, Landthaler M, Stolz W. Development of a targeted risk-group model for skin cancer screening based on more than 100,000 total skin examinations. J Eur Acad Dermatol Venereol. 2012 Jan;26(1):86-94. doi: 10.1111/j.1468-3083.2011.04014.x. Epub 2011 Mar 4. PMID: 21371132.
Nair	/	2021	SCC	Derivation: 0.79, 0.78, 0.77 (for 5, 8, and 10 years respectively) Validation: 0.80, 0.78, 0.77 (for 5, 8,	Heart transplant recipients	Nair N, Hu Z, Du D, Gongora E. Risk prediction model for cutaneous squamous cell carcinoma in adult cardiac allograft recipients. World J Transplant. 2021 Mar 18;11(3):54-69. doi: 10.5500/wjt.v11.i3.54. PMID: 33816146; PMCID: PMC8009060.

				and 10 years respectively)		
Nair	/	2021	BCC	Derivation: 0.77, 0.76, 0.76 (for 5, 8, and 10 years respectively) Validation: 0.75, 0.74, 0.74 (for 5, 8, and 10 years respectively)	Heart transplant recipients	Nair N, Hu Z, Du D, Gongora E. Risk Prediction Model for Basal Cell Carcinoma in Cardiac Allograft Recipients. Transplant Proc. 2021 Jul-Aug;53(6):1981-1988. doi: 10.1016/j.transproceed.2021.02.022. Epub 2021 Apr 27. PMID: 33931248.
Zabor	/	2022	choroidal melanoma	Derivation: 0.880 Internal Validation:0.849 External Validation: 0.861	Patients with choroidal lesions	Zabor EC, Raval V, Luo S, Pelayes DE, Singh AD. A Prediction Model to Discriminate Small Choroidal Melanoma from Choroidal Nevus. Ocul Oncol Pathol. 2022 Feb;8(1):71-78. doi: 10.1159/000521541. Epub 2021 Dec 22. PMID: 35356604; PMCID: PMC8914269.
Boekstegers	Enhanced Model I	2023	Gallbladder cancer	0.85 (0.83-0.88)	General public	Boekstegers F, Scherer D, Barahona Ponce C, Marcelain K, Gárate-Calderón V, Waldenberger M, Morales E, Rojas A, Munoz C, Retamales J, de Toro G, Barajas O, Rivera MT, Cortés A, Loader D, Saavedra J, Gutiérrez L, Ortega A, Bertrán ME, Bartolotti L, Gabler F, Campos M, Alvarado J, Moisán F, Spencer L, Nervi B, Carvajal-Hausdorf D, Losada H, Almau M, Fernández P, Olloquequi J, Fuentes-Guajardo M, Gonzalez-Jose R, Bortolini MC, Acuña-Alonzo V, Gallo C, Linares AR, Rothhammer F, Lorenzo Bermejo J. Development and internal validation of a multifactorial risk prediction model for gallbladder cancer in a high-incidence country. Int J Cancer. 2023 Sep 15;153(6):1151-1161. doi: 10.1002/ijc.34607. Epub 2023 Jun 1. PMID: 37260300.
Boekstegers	Enhanced Model II	2023	Gallbladder cancer	0.87 (0.85-0.89)	General public	Boekstegers F, Scherer D, Barahona Ponce C, Marcelain K, Gárate-Calderón V, Waldenberger M, Morales E, Rojas A, Munoz C, Retamales J, de Toro G, Barajas O, Rivera MT, Cortés A, Loader D, Saavedra J, Gutiérrez L, Ortega A, Bertrán ME, Bartolotti L, Gabler F, Campos M, Alvarado J, Moisán F, Spencer L, Nervi B, Carvajal-Hausdorf D, Losada H, Almau M, Fernández P, Olloquequi J, Fuentes-Guajardo M, Gonzalez-Jose R, Bortolini MC, Acuña-Alonzo V, Gallo C, Linares AR, Rothhammer F, Lorenzo Bermejo J. Development and internal validation of a multifactorial risk prediction model for gallbladder cancer in a high-incidence country. Int J Cancer. 2023 Sep 15;153(6):1151-1161. doi: 10.1002/ijc.34607. Epub 2023 Jun 1. PMID: 37260300.