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SOURCE (OR PART OF THE FOLLOWING SOURCE):

Type	PhD thesis
Title	Risk profiling and screening for colorectal cancer
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Year	2013

FULL BIBLIOGRAPHIC DETAILS:
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Systematic Review Cancer Risk models and preselection for screening

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Cancer Epidemiology 2012;36:461–9

Abstract

Objective

The invitation to population screening is based on age criteria in many countries. Screening is not offered to younger or older participants, because the benefits in these age groups do not outweigh the harms. One could argue that it is not so much age that determines the benefits but the risk of developing preclinical and treatable cancer. Cancer risk varies with age but is also affected by other factors.

Methods

We performed a systematic review for risk models for the three types of cancer for which population screening programs exist: breast, cervical and colon cancer. We used an evaluation scheme that distinguishes three phases of model development: model derivation, validation and impact analysis. Data were collected in August 2010.

Results

We identified two colorectal, four breast and three cervix cancer risk models. One colorectal, four breast and none of the cervix cancer models have been externally validated. We could not identify evaluations of the impact on population screening effectiveness.

Conclusion

We conclude that risk models for the pre-selection of screening have been developed. These models could improve the pre-selection for screening, help in making personal decisions about participation, and reduce adverse effects of population screening. The validity of this hypothesis, as well as practicalities and issues of equity and reliability, have to be tested in further studies.

Introduction

Several countries in the world have organized cancer screening programs, but screening also has its downsides. Although most screening methods are minimally or not invasive, some carry a risk of sometimes serious complications. Screening may lead to false positives, or can detect conditions that would not have become clinically significant had they not been detected by screening. Given the relatively low prevalence of undetected cancer, these downsides must be taken seriously. Unlike the benefits of screening, which may be large but happen in the future, the downsides occur soon after screening and can apply to many, if not all invitees.
Because of these downsides, screening programs usually do not target the whole population. Cancer screening is usually not offered to young people because the benefits for them are considered too small to outweigh the harms and burden of screening. Analogously, screening is not offered to the elderly, because the burden of screening is considered too large relative to the health gains.

One could argue that it is not so much age that determines the benefits from screening but, more general, the risk of having or developing preclinical and treatable cancer. Age is a major determinant of risk, yet cancer risk is also affected by other known variables. Based on these risk factors, several multivariable cancer risk models have been introduced.[1,2]

If one accepts that risk is the major factor for limiting access to screening, one could explore whether it is feasible and reasonable to replace the age criterion by a more general risk criterion. Inviting persons at increased risk, not just those in the target age range, may change the benefits-harms ratio of screening.[3,4]

We performed a systematic review of the literature was performed to assess to what extent models have been developed for calculating cancer risk for the three forms of cancer for which population screening programs have been introduced in the Netherlands and elsewhere: breast cancer, cervical cancer, and colon cancer. We focused our search was on models with risk factors that do not need additional testing; all the models in our review include information obtained via questionnaires. We examined to what extent the validity and performance of these cancer risk models have been evaluated, and whether they have been used and evaluated in defining inclusion criteria for risk-based cancer screening programs.

Methods

Inclusion criteria

Eligible for this review were published papers that presented or evaluated multivariable risk models for breast cancer, cervical cancer or colon cancer. No limitations were set to the type of study. Models had to contain variables that were available without additional testing. Models that contained laboratory measurements were excluded. The development or evaluation of the model had to be based on empirical data collected in a series of screenees or in some other group of study participants.

Search strategy

We systematically searched for papers in the Medline and Embase database. No restrictions were made concerning date of publication or language. Our search strategy was based on Medical Subject Headings and text words. The search terms used are described in full detail in the appendix.

Both authors screened the titles and abstracts and identified potentially eligible papers in the search findings. Data were collected in August 2010. Full text versions of all potentially eligible papers were then obtained for detailed evaluation and examined by the two authors. Any disagreements during the selection process were resolved by discussion.

Data extraction and analysis

From each included paper, we extracted data on type of cancer, study authors, country, setting, year of data collection, study design, and study participants. We characterized the development of the risk models using an evaluation scheme that was originally proposed for the assessment of clinical decision rules[5,6] (see Figure 1). Reilly and Evans[6] distinguished five levels of evidence, which represent a series of phases in the evaluation of risk models.

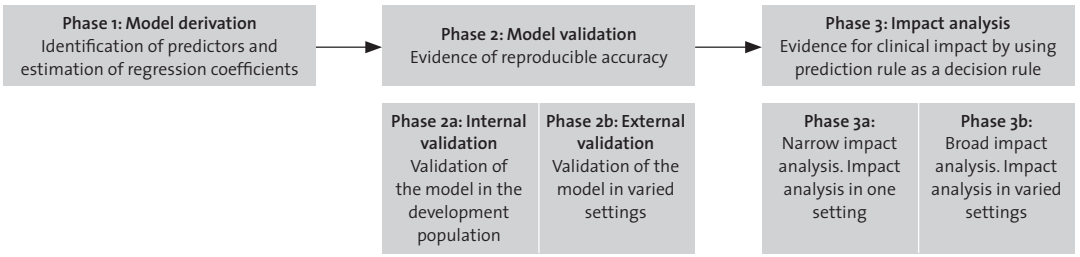

Figure 1 Phases of model development.

We summarize these as model derivation, model validation, and impact analysis. In the model derivation phase, risk factors are selected and the weight of these factors is calculated.

In the model validation phase, the performance of the model is evaluated. We distinguished between internal and an external validation, with external validation defined as validation in fully independent data[2]. For expressing model performance, we distinguished between discrimination, calibration, and the distribution of risk. Discrimination refers to the ability of the model to give higher risk values to patients that have cancer or will develop cancer than those who do not[2]. The concordance or c-statistic is the most commonly used statistic to express discriminatory power. Calibration refers to the level of agreement between the observed and predicted number of patients with cancer.[2] The distribution of risk in the target population is relevant for evaluating the potential usefulness of the model. Ideally, risk modeling should result in a relatively wide risk distribution[7]. In an impact analysis, the effects of introducing calculated risk as a screening selection criterion are evaluated.

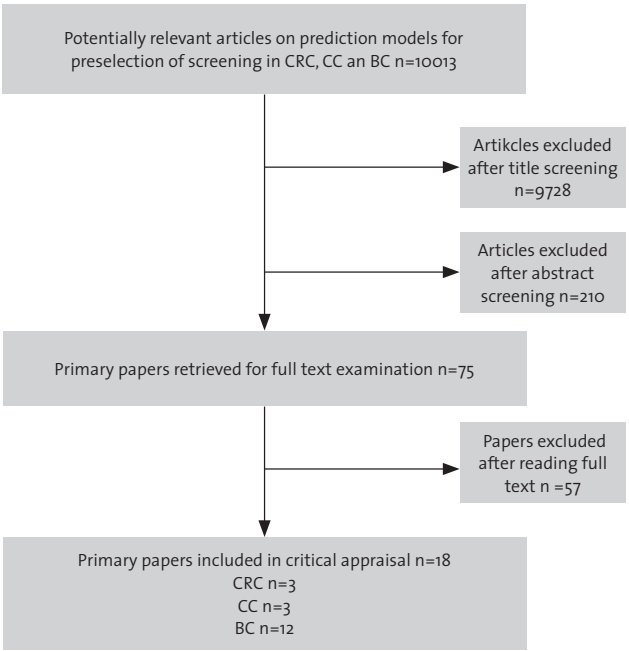

Figure 2 Process from Initial Search to Final Inclusions for Papers on Prediction models in Cancer.

Table 1 Phases of Development and Performance of the Models

				Specification of model performance in the case of external validation			
First author	**Model**	**Phase of the model**	**External validation in**	**Calibration**	**Range**	**Discrimination**	**Impact study**
				Result as reported in the paper			
Colorectal cancer							
Freedman[9]	Freedman	2b	[10]	O/E ratio: Well	Men: 0.16% (lowest 10 y risk)- 19.4%(highest 20 y risk) Women: 0.09% (lowest 10 y risk) – 17.49 % (highest 20 y risk)	0.61 (men) 0.61 (women)	
Driver[8]	Driver	2a		Goodness of fit test: Good (p=.91)	1% (lowest risk 20 y risk) – 6% (highest 20 y risk)	0.695	
Breast Cancer							
Gail [11]	Gail model 1	3a	[19],[24],[12], [25],[26],[13], [14]	[19] sensitivity: 17.9% [24] O/E: 0.93 [14] E/O 0.84 [25] no data [26] O/E: 1.2 [13] O/E: 1.6-2.43	[19]: 0.2% - 15.4% [24]: 0%-6.12% [14]: 2.32%-4.73% (pred. 5 y risk) [25]: Breast cancer: 1%-8.729% Control: 1.099%-4.903% [26]no data [13]0.0016 -0.0907 [14]risk score gm 1-10	[19]: limited, close to 0.50 [24]: c-statistic 59% [14]: no data [25]: no data [26]: auc: 0.58 [13]: no data	[14]Potentially usefully in clinical setting.

Costantino [12]	Gail model 2	2b	[15] [12]	[15]E/O well, 0.93 [12]E/O1.03	[15] 0.56-10.14 (predicted 5 y risk) [12] no data	[15] c- statistic: 0.58 [12] no data	
Gail[18]	Care model	2a		[18]O/E: 1.08	0.10-43.7 (10 y risk)	[18]0.555, modest	
Rosner [21]	Log incidence	2b	[23]	[21]Chi square: adequate [23] E/O 1.00	[21] no data [23] 0,49%- 5.42%	[21] no data [23] modest	
Colditz[22]	Colditz	2b		[22] not reported [23]E/O 1.01	[23] 0,06%-13,72%	[22]not reported [23] modest	
Cervix cancer							
Sengupta[27]	Sengupta	2a		[27]E/O: 74.5% p 0.9	No data		
Patil [29]	Patil	2a		[29]No data	No data	Wilkinson statistic: 0.7432	
Wilkinson[28]	Wilkinson	2a		[28]E/O:75%	No data	No data	

Results

Our search resulted in 10,013 papers, of which 18 could be included in our analysis. The process of paper selection is summarized in Figure 2. As some papers described the validation or the implementation of previously developed models, the actual number of models is lower than the number of included papers. Most papers were excluded because they did not contain a prediction model, others because they addressed practical issues in using models. Two colorectal cancer risk models, four breast cancer models and three cervix cancer models were identified. A report on each of these three classes of models in more detail is written below. The phase of development and the performance of the models are summarized in table 1.

Colorectal Cancer

Driver and colleagues

Driver and colleagues developed risk models for the development of colorectal cancer and colon cancer in men, based on data collected in the Physician's Health Study,[8] a prospective cohort of 21,581 US male physicians who were free of cancer at the start of the study, as summarized in table 2. The cohort was followed up for 20 years, during which 381 cases of colon cancer and 104 cases of rectal cancer developed. In addition to age, the model includes smoking history, body mass index, and weekly or daily alcohol use. The point scores were used to define 10 risk groups.

Table 2 Study Characteristics of Colon and Colorectal Cancer Risk Models

Model	First author	Population	Inclusion criteria	n	Study design
Freedman	Freedman, 2009[9]	2 studies: *Cases with a first primary crc. *Patients with a first primary tumor in the rectosigmoid.	White men and women Age: 50 years and older	2073 primary cases 2466 matched controls Rectal study: 952 intervention 1205 controls	Case control
	Park, 2009[10]	Men and women	50-71 years of age	567169 participants NIH Observed: 2092 man 832 women	Case control
Driver	Driver, 2007[8]	Male physicians	40-81 years of age No cancer	21581	Cohort

Internal validation was done by bootstrap validation, using 200 repetitions. This internal validation revealed an expected AUC of 0.686 in other data sets for the colorectal cancer risk model. [8] Goodness of fit test showed that the model fitted the data well (p=0.91). Discrimination by the final model was fair (AUC 0.695). The authors also developed a risk model for colon cancer, which had an AUC of 0.717, with a goodness of fit of 0.43 with the Hosmer Lemershow test, which indicates moderate calibration.

The authors used the risk variables in the colon cancer risk model to identify 10 risk groups. The odds developing colorectal cancer for the group with the highest risk were 15.9 higher than for those in the lowest risk group, although only 10 percent of the study group was in the highest four risk groups. All evaluations were done in the data in which the model was developed.

Freedman and colleagues

Freedman and colleagues[9] developed separate risk models for men and women, based on data from two population-based case-control studies, one for colon cancer and one for rectal cancer. In total, 1,599 colon cancer cases, 1,974 controls and 664 rectal cancer cases with 859 controls were included. Table 3 summarizes the variables in these models. Freedman et al. then combined the risk factor data with age-specific cancer hazard rates and competing risks to estimate the probability of developing cancer over a pre-specified time interval given a person's age and risk factors. Given the nature of their study, Freedman and colleagues[9] could not perform an internal evaluation of their model.

Park and colleagues[10] performed an external validation study of this Freedman model using data from a prospective cohort study. Men and women between 50 and 71 years at baseline were asked to answer a self-administrated questionnaire, including risk factors. Expected numbers of CRC were compared with observed cases. They obtained a c-statistic of 0.610 in men and 0.605 in women. When comparing the expected and the observed numbers of CRC cases overall, the ratio was 0.99 in men and 1.05 in women. Agreement was found to be good in most risk factor categories, except for screening and polyp history and family history of CRC. No impact analysis of either the Driver or the Freedman model were found.

Breast cancer

We identified four breast cancer risk models. These models are summarized in Table 4. A summary of the variables in these models can be found in Table 5.

Table 3 Overview of variables used in the risk models for colon and rectal cancer

	Freedman, 2009 [9] distal , men	Freedman, 2009 [9] Proximal, men	Freedaman ,2009 [9] Rectal, men	Freedman , 2009 [9] Distal Women	Freedmanl, 2009 [9] Proximal, women	Freedman , 2009 Rectal, women	Driver , 2007 [8]
Gastro history							
Prior neg sigmo/colo	+	+	+	+	+	+	
Polyp history	+	+	+	+	+	+	
Number of relatives with crc	+	+	+	+	+	+	
One or more relatives with crc			+				
Medication							
Aspirin/nsaid use	+	+	+	+	+	+	
Lifestyle factors							
Usual number of cigarettes smoked per day		+					+
Years of smoking in current and former smokers		+					+
Servings of vegetables per day		+			+		
Current vigorous leisure time activity			+		+	+	
Alcohol use							+
Hormone status							
Estrogen status within last 2 yr				+	+	+	
Interaction BMI and estrogen status				+			
Demographic data							
+65 years				+			
Age							+
BMI	+	+		+		+	+

Table 4 Study Characteristics Breast Cancer Risk Models

Model	First author	Population	Inclusion criteria	n	Study design
Gail model	Gail MH, 1989[11]	BCDDP (artikel in amc)	Women who's breast cancer was incident (not prevalent at the first screening). In situ and invasive carcinoma.	2852 intervention 3146 controls	Case control
	Adams-Campbell, 2007[19]	Black women	35 years and older No history of cancer	725 intervention 725 controls	Nested case control
	Decarli A, 2006[24]	Women	20-74 years of age No history of cancer	2569 intervention 2588 control	Case control
	J.P. Costantino, 1999[12]	White women	35 years and older Life expectancy of at least 10 y Neg. mammography within 180 days Women under 60 a predicted 5 year risk, no less than 60	5969	Case control
	Mac Karem, 2001[25]		Ductal carcinoma in situ or invasive carcinoma	124 intervention 107 controle randomly selected 129 nurses	Case control
	Chlewbowski,2007 [26]	Postmenopausal women	50-79 years of age No history of breast cancer	3236 cases	Observational study
	Spiegelman,1994[13]	Women	No cancer at beginning of the study 20-81 years of age	115172	
Gail model 2	Rockhill,2001[15]	Women	45-71 years of age	82109	
	Costantino,1999[12]	Women	35 years and older Life expectancy of at least 10 y Neg. mammography within 180 days Women under 60 a predicted 5 year risk, no less than 60	5969	Case control
Care model	Gail et al 2007[18]	African American women	35-64 years of age. Newly diagnosed with breast cancer.	1607 cases 1647 control	Case control
	Adams-Campbell,2009[20]	African American women	35 years and older	883	Case control
Log incidence	Rockhill, 2003[23]	Women	45-73 No previous diagnsosis of cancer	45210	Cohort
	Rosner, 1996[21]		No previous diagnosis of cancer	2249	Cohort
Colditz	Colditz, 2000[22]	Women	Women aged 30-55	58520	cohort

Gail model 1

The Gail model was presented in 1989[11] and calculates invasive and in situ breast cancer risk. To develop the model, the authors retrospectively obtained risk factor information in a case-control study embedded in the Breast Cancer Detection Demonstration Project. The model included age at menarche, number of previous breast biopsies, age at first live birth and number of first-degree relatives with breast cancer. A model of relative risks for various combinations of these factors was developed from the case control data. The baseline age-specific hazard rate was computed as the product of the observed age-specific composite hazard rate minus the attributable risk. Individualized breast cancer probabilities can be calculated from information on relative risks and the baseline hazard rate.[11]

The Gail model has been externally validated, with good performance in predicting the incidence of breast cancer in groups of women. Costantino et al,[12] and Spiegelman et al[13] compared the observed number of breast cancers with the predicted number from the model. Costantino et al validated the model in a prospective cohort study of 5969 women. The overall expected versus observed ratio was 0.84 (95 %CI: 0.73 to 0.97). Spiegelman et al[13] compared the number of cancer cases predicted by the model to the actual number of cases observed in the Nurses health study. Questionnaires on risk factors and diagnosis of cancer were sent to participants every two years. In this validation study the model over-predicted absolute breast cancer risk by 33% (95% CI: 28% to 39%). The observed versus predicted ratio was 0.67. The Gail models' ability to predict which individual women will develop breast cancer appeared to be relatively poor in these two studies.

Bondy and colleagues invited 38,000 women to complete a self-administered breast cancer risk factor questionnaire, in order to evaluate the Gail model's ability for assigning women to risk groups for counseling and follow up.[14] They first identified 3165 women with one or more first degree relatives affected with breast cancer, these women had a threefold elevated risk. Risk perception was found to be a motivator for participation in mammography screening. The authors concluded that an estimate of relative risk of breast cancer could be made in a short period of time in screening settings and that the model had clinical utility, by identifying a large proportion of women with increased risk of breast cancer.

Gail model 2

A second Gail model was developed later; it projects invasive breast cancer risk. This second model was a modification of the first one, in which age specific invasive breast cancer rates and attributable risk estimates form the Surveillance, Epidemiology, and End Results Program of the National Cancer Institute replaced the original estimates.

Rockhill et al[15] evaluated both the goodness of fit of model 2 and its discriminatory accuracy at the individual level. A prospective cohort study was done in 82,109 white women aged 45 to 47. The model fitted well in the total sample with an expected versus observed ratio of 0.94 (95% CI: 0.89 to 0.99). The discriminatory performance of the model was evaluated, with an AUC of 0.58. The distribution of risk was not very wide: women in the top decile of calculated risk had a relative risk of 2.83 relative to those in the bottom decile.

Gail and Rimer[16] applied a version of the breast cancer risk model to a large population-based sample of women who did not have breast cancer. They estimated that the percentage of white women in their 40s who would be recommended for screening based on the calculated risk ranged from 10% of 40-year-old women to 95% of 49-year-old women. The threshold for screening was set at an expected one-year breast cancer incidence rate greater or as great as that of a 50-year–old woman with no risk factors.
In another form of impact analysis McPherson and Nissen applied Gail and Rimer's algorithms retrospectively in a group of 404 women diagnosed with breast cancer in their 40s.[17] Using risk factors that existed before the breast cancer diagnosis, they estimated the percentage of these women who would have been referred for mammography screening by the two models made by Gail and Rimer. Of these women, between 70 and 75 percent would have been recommended for screening, while the model would have recommended screening for approximately one half of the women who had no conventional risk factors.

CARE model

The Contraceptive and Reproductive Experience (CARE) model was developed to replace the Gail model in expressing breast cancer risk in African-American women.[18] The CARE model contains fewer variables than the Gail models; age at first birth and its interaction with the number of affected first degree relatives were omitted and age at menarche was dichotomized in before or after the age of 13.[19] To develop the model data of 1607 African American women with invasive breast cancer and of 1647 controls were used to compute relative and attributable risks. These were based on age at menarche, number of affected mother or sisters, and number of previous benign biopsy examinations. Absolute risks were obtained by combining this information with data on invasive breast cancer incidence in African American women. The unweighted average age-adjusted AUC was 0.555 and the observed/expected ratio was 1.08.

Adams-Campbell and colleagues compared 5-year breast cancer incidence among African-American women participating in the Black Women's Health Study with the risks determined

using the original Gail Model and the CARE model.[19,20] They used a nested case-control study design and evaluated the diagnostic accuracy of both models. Risk profiles were derived via a questionnaire. Here also, the ROC curves were close to the chance diagonal.

Table 5 Overview of Variables Used in the Risk Models for Breast Cancer

	Gai model 1; gail ,1989 [11]	Gail model 2; Costantino, 1999[12]	Care model; gail et al, 2007[18]	Log incidence model; Rockhill, 2003[23]	Colditz, 2000 [35]
Demographic data					
Age >50	+	+	+		
Age				+	+
Number of biopsies	+	+	+		
Hormone status					
Age at menopause				+	+
Age at menarche	+	+	+	+	+
Oral estrogen					+
Post menopausal hormones (other than estrogen)					+
Age first birth	+	+		+	+
Other					
Number of affected first degree relatives			+		
Parousity				+	
Benign breast disease					+
Family history of breast cancer					+
BMI					+
Alcohol consumption					+

*difference between gail model 1 en 2: model 2 contains age specific breast cancerrates.

No AUC's were reported, which probably indicates that the CARE model had a disappointing discriminatory performance.[18] Sensitivity was 4.1% for the CARE model.

Rosner and Colditz

The Rosner and Colditz log-incidence model of breast cancer is based on the analytic approach to breast cancer incidence modeling originally proposed by Pike and colleagues.[21,22] The initial version of the Rosner and Colditz log-incidence model was built on data from the Nurses Health Study, obtained between 1976 and 1990. Subjects were followed until the development of cancer or until death. Participants completed questionnaires on risk factors. The log incidence models were fitted using iteratively reweighted least squares analysis. This version was subsequently expanded in 2000, using data from 1980 through 1994.

Rockhill et al. compared the discriminatory capacity of this model with that of the Gail model in a prospective cohort in 82,109 white women aged 45 to 47.[23] Both versions fitted the data well, with a ratio of expected to observed number of cases of 1.00 for the first version and 1.01 for the extended version.The average age-adjusted c-statistic was 0.57 for the first model and 0.63 for the extended one.

Cervical cancer

We identified three cervical cancer risk models, as summarized in table 6. The variables included in the cervix cancer models are shown in table 7.

Table 6 Study Characteristics Cervix Cancer Risk Models

Model	First author	Population	Inclusion	n	Study design
Sengupta	Sengupta, 2001 [27]	Women in mass screening programs in India.	No history of cancer	398	Case control
Patil	Patil,2006[29]	Female patients admitted to the hospital for other reasons than gynecologic cancer	Female patients admitted to the hospital for other reasons than gynecologic cancer	230 intervention 230 control	Case control
Wilkinson	Wilkinson, 1992[28]	Consecutive attendees for cervical smear tests	No previous dyskaryosis	3661	cohort study

Sengupta and colleagues

Sengupta and colleagues tried to identify women with a high probability of transformation of cervical dysplasia to a higher stage of cervical intraepithelial neoplasia (CIN).[27] They used a case-control approach in 398 samples taken from taken from screening programs in eastern India and reported three variables that were associated with CIN: age, education, and parity. Sengupta et al. evaluated the model in a small additional sample and found good overall accuracy. The model was not additionally internally or externally validated. A follow up study was done, in which the model was fitted to 85 subsequent observations. This analysis showed that, with a probability of 0.90 as the cutoff point, 18 CIN values out of 85 were different from those obtained from the model.

Wilkinson and colleagues

In the United Kingdom, Wilkinson and colleagues searched the literature and identified the following four factors as being independently associated with cervical dysplasia or carcinoma in situ: the woman's educational level, current smoking habit, years of oral contraceptive use, and lifetime number of sexual partners.[28] Based on the reported odds ratios, they developed a multivariable scoring system. This system was subsequently evaluated using data from a number of practices. The relative risk in the highest risk category was 11 compared to the lowest category. A ROC was shown in the paper but the AUC was not reported; 75% of the women with CIN 2 or 3 were correctly identified. No internal or external validation was done.

Patil

Patil and colleagues[29] discussed a risk based model for cervical cancer. In a case control study they used data from 230 cervical cancer cases and 230 matched controls, and evaluated risk factors for cervix cancer. They reported a cutoff point but did not made clear how it was chosen, no AUC was reported. No additional external validations or any impact analysis studies of these models for cervical cancer risk were found.

Table 7 Overview of Variables Used in the Risk Models for Cervix Cancer

	Senbupta ,1999 [27]	Patil, 2006 [29]	Wilkinson, 1994 [28]
Demographic data			
Age	+		
Education	+		+
SES			
Illiteracy		+	
Age at menarche		+	
Parity	+	+	
Lifestyle factors			
Current smoking habit			+
Years of oral contraceptive use			+
Number of sexual partners			+
Poor genital hygiene		+	
Long duration of married life		+	

Discussion

This systematic review synthesizes the available evidence on the development and evaluation of multivariable risk models in cancer screening programs. Two colorectal cancer, four breast cancer and three cervix cancer models were identified. Five of these nine models have been externally validated. Only one of the risk models has reached the phase of impact analysis, in which actual implementation in screening was assessed.

The performance of the models was moderate at best for most. Overall observed and expected rates corresponded well, but discrimination was rather poor. Information on the distribution of risk was fairly limited for the colorectal and cervical cancer models.

Advances in the identification and understanding of risk factors for colorectal cancer[30-42] could lead to better risk models, although skepticism may persist about the ability of such models to stratify individuals into clearly distinguished risk categories.

A number of limitations of our review have to be acknowledged. Risk models are not indexed as such in literature databases, and papers reporting on risk models are difficult to find. We restricted our search to models with variables that could be measured in potential screening participants without substantial additional effort. For that reason we excluded models with genetic variables, and breast cancer risk models with data on breast density. Several such models have been presented.[43-45]

Apart from using personal information and data on history, one could use a different approach in triaging population screening participants. A simple test, for example, can precede more invasive procedures, as in colorectal cancer screening programs that rely on fecal occult blood testing. Another example is cervical cancer screening. A small number of risk factors have been identified as contributing to the development of invasive cervix carcinoma,[46] of which a prior infection with a human papillomavirus (HPV) is now known to be the primary risk factor [46] for developing cervix cancer. Several studies have been conducted to assess the use of HPV testing in cervical cancer screening.[47,48]Despite its promising abilities, HPV screening has not yet been adequately studied to be recommended for screening. Perhaps risk models could be used to indicate who should get HPV testing.

One could hypothesize that a population screening program based on personal risk will lead to higher participation rates and better informed decision-making, compared to screening programs based on age criteria only. Communication on the basis of risk factors has been suggested to increase the uptake in and adherence to screening programs.[14,49] A balance should be found between supplying transparent information and providing the desired refinement in risk communication. If the message becomes to complex, mistakes will be made, or participants will not be able to fully understand the message. Risk based models may give more accurate information about the personal risk of disease, which could help decision making.[50] In general, personal perceptions of susceptibility to a disease may translate into behavior and lifestyle changes designed to reduce risk or to prevent an illness. Yet it is not immediately clear whether this hypothesis will survive empirical testing. Risk perception and health behavior are complex processes. Daly and colleagues, for example, did a survey of almost 1,000 women with a positive family history of breast cancer eligible for participation in a randomized trial comparing personalized breast cancer risk counselling with general health education.[51]

The majority of women overestimated their risk of breast cancer, as calculated by the Gail model.

In principle, a screening program based on risk profiling and pre-selection could be more ethical and definitely less burdensome to the individual.[52] Inviting people at increased risk could help in addressing the problem of false positive results. In breast cancer screening, for example, women who had a false-positive result at first screen have been shown to be less likely to re-attend for subsequent screens than non-assessed women.[53]

This review was based on the premise that a more fine grained risk assessment could replace age-based criteria for invitations to screening. One could argue that it is not so much risk but, more general, anticipated benefit that should guide invitations to screening. The expected health gains from screening are not just determined by the risk of having or developing cancer, but also by other factors, such as the life expectancy of screenees, their comorbidity and competing causes of death and disease. Calculating the personal anticipated benefit from screening, however, could turn out to be even more challenging and far more difficult to implement. At this stage, risk is a concept that already permeates cancer screening, where a number of more intensive programs and more demanding procedures are being reserved for people at increased risk. For this reason, we believe a general risk based approach, rather than a benefits based approach, is more likely to replace age based preselection.

Before risk based replaces age as the basis for preselection, a number of issues have to be dealt with. In the past, the use of risk-based mammographic recommendations for breast cancer has been criticized by the American College of Radiology Task Force on Breast Cancer[54]. The group was concerned that the model would overlook the large number of women who develop breast cancer despite having none of the identifiable risk factors. Despite claims about increased effectiveness, issues of equity and practicality should not be ignored easily. Another potential drawback of the use of prediction models in pre-selection for screening is the limited generalizability of these models. Cancer incidence is different for the several subtypes of cancers and baseline risks can vary with other variables than those on which the model is based. In several models, these are included as a determinant of the model. Other models are solely based on one specific population or cancer type. Depending on these characteristics models can be extrapolated to several populations or cancer types. These issues could return strongly when age-based criteria would be replaced by risk-based criteria.

In conclusion, this review shows that there are a number of cancer risk models for colorectal, breast and cervical cancer, of which the ones for breast cancer have been more

extensively validated and the ones for cervical cancer the least. More research needs to be done in assessing the impact of using prediction models in colorectal and breast cancer screening. If additional impact studies demonstrated the effectiveness of these models then the breast and colorectal cancer risk models can be used as pre-selection tools in screening programs, thereby increasing the effectiveness and efficiency of population screening programs by targeting more exclusively those at increased cancer risk.

Appendix

("Models, Statistical"[Mesh] or model*[tiab] OR "Mass Screening"[Majr]) and ("Risk Assessment"[MeSH Terms] OR risk assessment*[tiab] OR risk[mh] or risk factors[mh]) and ("Predictive Value of Tests"[MeSH Terms] OR predict*[tiab] OR "Probability"[Mesh:NoExp] OR "Risk"[Mesh]) and (Colorectal cancer[ti] or "Uterine Cervical Neoplasms"[Majr] or cervix cancer[ti] or "Colorectal Neoplasms"[Majr] or "Breast Neoplasms"[Majr] or breast cancer[ti])

chapter
3

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