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ERASMUS MC (PROSTATE)

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We recommend you let your interests guide you through this document, using the navigation tree as a general guide to the content available.

The intent of this document is to provide the interested reader with insight into ongoing research. Model parameters, structure, and results contained herein should be considered representative but preliminary in nature.

We encourage interested readers to contact the contributors for further information.

Go directly to the: Reader's Guide.

READERS GUIDE

Core Profile Documentation

These topics will provide an overview of the model without the burden of detail. Each can be read in about 5-10 minutes. Each contains links to more detailed information if required.

Model Purpose

This document describes the primary purpose of the model.

Model Overview

This document describes the primary aims and general purposes of this modeling effort.

Assumption Overview

An overview of the basic assumptions inherent in this model.

Parameter Overview

Describes the basic parameter set used to inform the model, more detailed information is available for each specific parameter.

Component Overview

A description of the basic computational building blocks (components) of the model.

Output Overview

Definitions and methodologies for the basic model outputs.

Results Overview

A guide to the results obtained from the model.

Key References

MODEL PURPOSE

SUMMARY

The MISCAN micro-simulation model is used to analyze the effect of PSA screening on prostate cancer incidence and mortality. This document summarizes the objectives in developing a prostate cancer simulation model.

PURPOSE

The MISCAN computer simulation model has been developed for estimating the effect of cancer screening in a dynamic population, to explain results of cancer screening trials, to predict and compare the (cost-) effectiveness of different screening policies, and to monitor the results of population screening programs.

The objective of the prostate cancer model is to quantify the role of PSA screening in prostate cancer incidence and mortality. The prostate cancer screening model is used to simulate the results of the Rotterdam section of the ERSPC trial as the incidence and mortality in the US population. By calibrating the model to the trial data and baseline incidence, parameters for the natural history have been estimated. Using the MISCAN model, based on the results of ERSPC Rotterdam, we try to understand the trends in the US and how they differ from European or Dutch conditions.

The models are used to determine optimal screening ages and test intervals and to calculate cost-effectiveness of various screening policies, compared with a situation without screening. Also, the models are used to estimate unobservable processes and variables (natural history of the disease, the amount of overdiagnosis and lead time) in the ERSPC trial as well as the US population.

Model Overview

Summary

This document provides an overview of the modeling effort, and describes the model in general terms.

Purpose

In the Miscan model knowledge on natural history of prostate cancer, screening and treatment obtained from randomized controlled trials and observational studies are integrated. In this way Miscan can be helpful in analyzing and explaining results of cancer screening trials, predicting the (cost-) effectiveness of different screening policies and predicting the potential of present and new interventions on future national trends. See also Model Purpose.

Background

The MISCAN computer program has been used for building screening models for cancers of breast, prostate, cervix, colon and lung[1234]. The MISCAN prostate cancer model has been used to model trends of prostate cancer incidence and mortality in the ERSPC-trial Rotterdam, and in the ERSPC-trial Sweden, the Dutch population and in the US population. With these models it is possible to compare trends of prostate cancer with and without treatment and screening.
The ERSPC model has been used to predict mean lead times and overdetection rates, associated with different screening programs[15]. It has also been used to provide epidemiological evidence of dedifferentiation as a mechanism of progression in prostate cancer[6].

Model Description

MISCAN model is a micro-simulation model. Using the model inputs, independent life histories are generated including a possible cancer history, the effects of treatment and the effects of early detection by screening. The MISCAN-prostate model contains four primary components:

1. Demography component
2. Natural History component
3. Treatment component
4. Screening component

First the demography component simulates a population of individual life histories, according to the demography parameters. Each individual in the population consists of a date of birth and age of death.

Subsequently the Natural history component simulates prostate cancer histories for each individual life history separately. Some individuals will have no prostate cancer in their life and others will have prostate cancer in their life. Once the individual has prostate cancer the cancer can progress to different preclinical states. In the preclinical phase the tumor is asymptomatic, but can be detected by screening. In this definition,

the preclinical phase does not only depend on biological processes, but also on the state of medical technology. Eighteen preclinical detectable states are defined in combinations of clinical T-stage (T1, T2 and T3), Gleason grade (well, moderately, and poorly differentiated) and metastatic stage (local-regional and distant). From each preclinical detectable state the cancer can progress to the clinical disease state, which implies that cancer is diagnosed because of symptoms.

In the third part the treatment component simulates the life history after clinical diagnosis. Detection with cancer is followed by treatment and possibly prostate cancer death. Different treatments have their treatment-specific survival of prostate cancer death.

The screening component super-imposes screening on the life histories in the absence of screening. Screening tests applied to a person in a preclinical disease state may result in detection and alter the life history of this individual. We assume that the consequences of early detection by screening are that a part of the screen-detected men is cured of prostate cancer and will die from other causes. For the other part of the screen-detected men early detection does not alter the life history.

See Component Overview for a more elaborated description of these components.

CONTRIBUTORS

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1 Draisma, G, Boer, R, Otto, SJ, van der Cruijsen, IW, Damhuis, RA, Schröder, FH, de Koning, HJ. “Lead times and overdetection due to prostate-specific antigen screening: estimates from the European Randomized Study of Screening for Prostate Cancer” in J Natl Cancer Inst 2003; 95: : 868-878

2 Tan, SYGL, van Oortmarssen, GJ, Piersma, N. “Estimating Parameters of a Microsimulation Model for Breast Cancer Screening” in Annals of Operations Research 2003; 119: : 43-61

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5 Draisma, G, Etzioni, R, Tsodikov, A, Mariotto, A, Wever, E, Gulati, R, Feuer, E, de Koning, HJ “Lead time and overdiagnosis in prostate-specific antigen screening: importance of methods and context” in J Natl Cancer Inst 2009; 101: : 374-383

6 Draisma, G, Postma, R, Schröder, FH, van der Kwast, TH, de Koning, HJ. “Gleason score, age and screening: modeling dedifferentiation in prostate cancer” in Int J Cancer 2006; 119: : 2366-2371

ASSUMPTION OVERVIEW

SUMMARY

The assumptions made for the MISCAN model are described in this section.

BACKGROUND

The MISCAN prostate cancer model can be used to simulate prostate cancer screening and treatment policies in a dynamic population (see Model Purpose), based on assumptions on demography, natural history of prostate cancer, treatment and screening. Most of the assumptions arise from the unobservable part in the screening and treatment of prostate cancer, the natural history of the disease and the effect of screening on improvement of survival

ASSUMPTION LISTING

The MISCAN ERSPC and US population model use the following assumptions, categorized by model component (see Component Overview):

Demography

a. The (country specific) life table is the same for all men in the same birth cohort
b. Death from prostate cancer and death from other causes are independent
c. The life time prostate cancer risk is the same for all men in a the same birth cohort

Natural history

a. Tumor onset:

Tumors are assumed to initiate with the same age specific initiation rate for all men.

b. Progression of disease:

The tumor starts in the preclinical phase. Progression is defined by a matrix of transition probabilities between states, and dwelling time distributions for the time spent in each state. The dwelling times are determined by Weibull distributions. Transition probabilities and dwelling time distributions are age-dependent. A correlation between duration in subsequent states is assumed.
In the preclinical phase the cancer can be detected by screening. There are eighteen preclinical detectable states which are derived from combinations of clinical T-stage (T1, T2 and T3), Gleason grade (well, moderately, and poorly differentiated) and metastatic stage (local-regional and distant).

c. Clinical detection:

From each preclinical detectable state the cancer can progress to the clinical disease state, which implies that cancer is diagnosed because of symptoms. The progression to the clinical state is defined by the matrix of transition probabilities between states, and dwelling time distributions determined by Weibull distributions. To explain a higher incidence and a more favorable stage distribution in the control arm of the trial compared to the base population, the population in 1991, it is assumed that in the trial population (during trial period) prostate cancer was clinically diagnosed earlier than in the baseline situation in 1991. Specifically, it is assumed that the hazard of being clinically diagnosed given that you are in the preclinical disease state in the trial population compared to the baseline situation is larger. This difference can for instance be attributed to contamination (screening in the control arm) or to changes in clinical practice leading to earlier diagnosis e.g to the use of PSA testing for symptomatic disease in a clinical setting.

Treatment

After prostate cancer diagnosis the treatments radical prostatectomy, radiation therapy and active surveillance can be assigned.

a. Treatment dissemination:

ERSPC model: treatment is modeled as a multinomial logit model with covariates age, T-stage and Gleason score at diagnosis. The categories of the multinomial model are radical prostatectomy, radiation therapy and active surveillance. The parameter estimates are based on data of the ERSPC trial section Rotterdam from the year 2000.
US model: treatment is modeled as a multinomial logit model with covariates age, year and grade at diagnosis. The categories of the multinomial model are radical prostatectomy, radiation therapy and active surveillance. The parameter estimates are based on SEER and Ca PSURE data. Conditional on patient's characteristics available at diagnosis and primary therapy hormone therapy is assigned by a logistic model.

b. Survival after treatment:

Baseline survival:
The baseline survival has been estimated from SEER (Surveillance, Epidemiology and

End Results) data in the pre-PSA era, specifically of cases diagnosed between 1983 and 1986. The survival curves were modeled using Poisson regression with grade, stage, age and treatment type as explanatory variables. To assign the survival curves in our model we assumed that Gleason score 7 or less than 7 corresponds to grade well/ moderately differentiated and that Gleason score more than 7 corresponds to grade poor/undifferentiated.

Treatment effect:
The time of death of prostate cancer is defined by the survival curve of the corresponding treatment. Bill-Axelson et al.[1] showed for men with clinically diagnosed localized prostate cancer a relative risk of 0.65 for the efficacy of radical prostatectomy compared to the efficacy of watchful waiting. Considering this result, we assume that men receiving watchful waiting have the baseline survival and that those men receiving radical prostatectomy and radiation therapy have a relative risk of 0.65 compared to watchful waiting for local-regional cancers. For distant prostate cancer it is assumed that treatment has no effect on the survival, implying that irrespective of the treatment type all men diagnosed with prostate cancer in the distant stage have a survival generated from the corresponding baseline survival curve.

Screening

a. Attendance to screening:

In the model, men can only be screened when they are still alive at the moment of the screen and when they have not already been diagnosed with prostate cancer.
ERSPC model: Data of the Rotterdam section of the ERSPC trial have been used to simulate the age and year specific attendance rate. Also, the attendance to the screening is dependent on whether or not the person attended the last screening.
US model: For the dissemination of PSA screening, we used the results of Mariotto et al.[2], who retrospectively constructed PSA screening histories in the population by use of survey data from the 2000 National Health Interview Survey and claims data from the linked SEER-Medicare database (http://healthservices.cancer.gov/seermedicare/).

b. Sensitivity of the test:

PSA screening and subsequent biopsy are modeled as one single test. The test has a T-stage-dependent sensitivity. These parameters are estimated using data of the ERSPC trial Rotterdam and the US population. We do not model digital rectal exam (DRE) explicitly.

c. Effect on survival because of early detection by screening:

We assume that a part of the screen-detected men is cured from cancer and that for the other part detection does not alter the life history. The cure rate is estimated by assuming a mortality reduction of 27% in the ERSPC model after a follow-up of 9 years for men who were actually screened. The mortality reduction of 27 % was observed in

the ERSPC-trial[3].

Parameter estimation

Model parameters for the natural history component and the test-sensitivity are estimated as follows: A model is constructed for a specific situation, such as prostate cancer incidence in the US or both arms of the ERSPC trial Rotterdam. Parameters are then estimated by numerical minimization of the deviance between observed numbers of cases and the corresponding numbers predicted by the model. Deviances are calculated assuming Poisson likelihood for incidence data or a multinomial likelihood for stage distribution data. For the minimization an adapted version of the simplex optimization method of Nelder and Mead is used[4]. Optimization is initiated with small sample sizes and repeated with larger sample sizes (up to 1 million) when optimization progress is no longer statistically significant.

ERSPC model: Estimates of natural history parameters and test sensitivities were obtained using observed detection rates and interval cancer rates and stage distributions in the ERSPC-trial Rotterdam.

US model: US-specific estimates of test-sensitivities were obtained using observed age-specific incidence and age-specific stage distribution (local/regional vs distant). For parameter estimation data of men 50 to 84 years old diagnosed in 1975 to 2000 from the SEER registry were used.

REFERENCES:

1 Bill-Axelson A, Holmberg L, Filen F, Ruutu M, Garmo H, Busch C, et al. “Radical prostatectomy versus watchful waiting in localized prostate cancer: the Scandinavian prostate cancer group-4 randomized trial” in J Natl Cancer Inst 2008; 100: : 1144-1154

2 Mariotto, AB, Etzioni, R, Krapcho, M, Feuer, EJ. “Reconstructing PSA testing patterns between black and white men in the US from Medicare claims and the National Health Interview Survey” in Cancer 2007; 109: : 1877-1886

3 Schröder, FH, Hugosson, J, Roobol, MJ, et al “Screening and prostate-cancer mortality in a randomized European study” in N Engl J Med 2009; 360: : 1320-1328

4 Bazaraa, MS, Sherali, HD, Shetty, CM. “Nonlinear programming: theory and algorithms” 1993; : 353

PARAMETER OVERVIEW

SUMMARY

Provides a complete overview of the parameters used to quantify the MISCAN-Prostate model.

BACKGROUND

The MISCAN-Prostate model consists of for basic components: The demography component, the natural history component, the treatment component and the screening component. Each component has its own set of parameters.

PARAMETER LISTING OVERVIEW

Demography Parameters

1. number of birth cohorts
2. proportion of the population in each birth cohort
3. for each birth cohort parameters of its birth table
4. for each birth cohort the parameters of its life table

Natural history Parameters

1. parameters for the age specific distribution of onset of the first screen detectable state
2. for each birth cohort the life time prostate cancer risk
3. parameters for the duration distribution in each preclinical state
4. parameters for the transition probability in each preclinical state
5. parameters for additional clinical diagnosis
6. correlation between duration in subsequent states
7. parameters for survival after clinical diagnosis by age at diagnosis, year of diagnosis, grade and stage of disease at diagnosis

Screening Test Parameters

1. parameters for the dissemination of PSA screening by age and year
2. test-sensitivity parameters
3. cure rate parameters defining the benefit because of early detection

Treatment parameters

1. parameters for the dissemination of treatment by age at diagnosis, year of diagnosis, grade and stage of disease at diagnosis
2. hazard ratios associated with initial treatments i.e. radical prostatectomy, radiation therapy and radiation therapy combined with hormones

COMPONENT OVERVIEW

SUMMARY

An overview of the major components in the MISCAN-Prostate model.

OVERVIEW

As described in the Model overview document, the MISCAN-prostate model contains four primary components: Demography, Natural History, Treatment and Screening.

COMPONENT LISTING

Demography Component

The demography component simulates a population of individual life histories, according to the demography parameters. The demography parameters are:

1. birth table parameters
2. life table parameters

Each individual in the population consists of a date of birth and age of death. It is possible to define a dynamic population of all ages, which can be adjusted for different countries. Also it is possible to define a cohort of people with the same age or age range.

Natural History Component

The cancer related event history is defined by a sequence of disease states and the ages at which these states are entered. The life histories are generated by a semi-Markov process, defined by a matrix of transition probabilities between states, and dwelling

time distributions for the time spent in each state. The disease history is divided in a preclinical phase and a clinical phase. The preclinical phase corresponds to the asymptomatic states, that do not lead to clinical diagnosis, but can be detected by screening. In this definition, the preclinical phase does not only depend on biological processes, but also on the state of medical technology. Its parameters have to be estimated from indirect evidence. In the Miscan prostate cancers model there are eighteen preclinical detectable states which are derived from combinations of clinical T-stage (T1, T2 and T3), Gleason grade (well, moderately, and poorly differentiated) and metastatic stage (local-regional and distant). The progression through these states is illustrated in Figure 1. From each preclinical detectable state the cancer can progress to the clinical disease state, which implies that cancer is diagnosed because of symptoms.

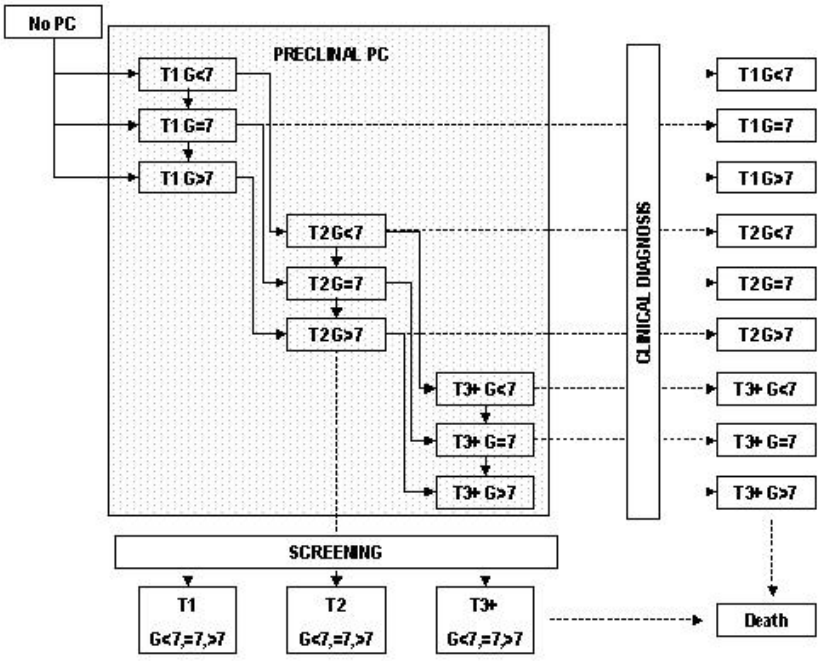

Figure 1: The MISCAN prostate cancer model. Prostate cancer develops from no prostate cancer via 1 or more screen-detectable preclinical stages to a clinically diagnosed cancer. There is also a distinction between local en metastatic stage, but for simplicity not illustrated. Screening is superimposed on the life histories in the absence of screening. Screening may detect cancers earlier in one of the preclinical screen-detectable states.

Screening Component

Screening is super-imposed on the life histories in the absence of screening. Screening tests applied to a person in a preclinical disease state may result in detection and alter his life history. A screening test is defined by its stage-specific sensitivity. A screening policy, is defined by the tests used, attendance rate and screening ages. Screening ages may be selected at regular intervals, or stochastically, allowing the modeling of both regular screening as in trials or screening programs and opportunistic screening. Screen detection may alter the cause of events. We assume that the consequences of early detection by screening is that a part of the screen-detected men is cured of prostate cancer and that for the other part detection does not alter the life history.

Treatment Component

The life history after clinical diagnosis is defined by stage-specific survival functions. Detection with cancer is followed by treatment and a survival of prostate cancer death. Different treatments can be assigned and the different treatments have their treatment-specific survival of prostate cancer death.

OUTPUT OVERVIEW

SUMMARY

This document describes the main outputs of the Miscan microsimulation model.

OUTPUT LISTING

The main outputs of the model are:

1. Projected incidence by age, year, clinical T-stage, Gleason score, metastatic state and mode of detection.
2. Treatment assignment by age, year, clinical T-stage, Gleason score, metastatic state and mode of detection.
3. Five-, 10-, 15-, and 20-year survival by age and stage at diagnosis and by treatment.
4. Mortality by age and year at death and cause of death and by clinical T-stage, Gleason score, metastatic state and mode of detection.
5. Number of PSA tests performed by age and year and total number of men screened.
6. Detection rate by age, year and screen round (first screen or subsequent screen). Detection rate is defined as cancers detected / # of men screened.
7. Overdiagnosis rates by age, year of diagnosis, clinical T-stage, Gleason score. An individual is overdiagnosed if he is screen detected but would not have been diagnosed in his lifetime in the absence of screening.
8. Mean lead time. Lead time is defined as the amount of time, in years, between prostate cancer detection and either clinical diagnosis in the absence of screening or death by other causes. Lead time is calculated for all screen-detected cancers and for the screen-detected relevant (non-overdiagnosed) cases only.
9. Mean sojourn time: Time from disease onset to clinical diagnosis.
10. Total life years of the population and total life years in a particular interval (e.g. from birth to diagnosis, from diagnosis till death)

All outputs (except for overdiagnosis and lead time) are projected in the presence and in the absence of screening.

Results Overview

Summary

This document lists various results generated by the model.

Overview

First a model was made for the screen arm and control arm of the European Randomized Study of Screening for Prostate Cancer (ERSPC) trial section Rotterdam. This model was adjusted to project the US population, by adjusting some input parameters and fitting the model to the US incidence and stage distribution. With both models lead time and overdiagnosis were estimated.

Results List

MODEL ERSPC

Model for ERSPC trial Rotterdam

Summary

This document describes the model made for the European Randomized Study of Screening for Prostate Cancer (ERSPC) trial.

Overview

A prostate cancer model has been made and validated using the results of the ERSPC trial Rotterdam and baseline incidence and stage distribution data of the Netherlands.

Methods

Based on the results of the Rotterdam section of the ERSPC trial and baseline incidence and stage distribution a model was made which could accurately predict the results of the first two screening rounds[1,2]. The trial started in Rotterdam in 1994 and included 21166 men aged 55-74 in the control arm and 21210 men in the screen arm. In the first years a PSA cut-off of 4 ng / ml was used as an indication for biopsy, later this was changed to 3 ng / ml. The model was also validated with the baseline incidence in the Netherlands (1991) and the stage distribution of clinically diagnosed cancers (1991-1993), of the Rotterdam Cancer Registry.

Results

After fitting the parameters (transition probabilities, dwelling times, test sensitivities), the model could predict the observed baseline values accurately (Table 1):

Table 1: Baseline incidence in the Netherlands 1991 and stage distribution 1991-1993, compared with the model predictions.

Incidence per 1000 men years		
Age group	Observed	Model prediction
50-55	0.14	0.16
55-60	0.36	0.46
60-65	1.19	1.13
65-70	2.59	2.45
70-75	4.50	4.49
75-80	6.57	6.68
80-85	7.98	8.33
85+	8.52	7.71
55-75 (trial population)	1.86	1.91

Stage distribution (%)		
Stage	Observed	Model prediction
Localized	58.03	57.75
Regional	18.81	19.44
Distant	23.15	22.85

The detection rate in the screen arm per round is compared with the model predictions (Figure 1)

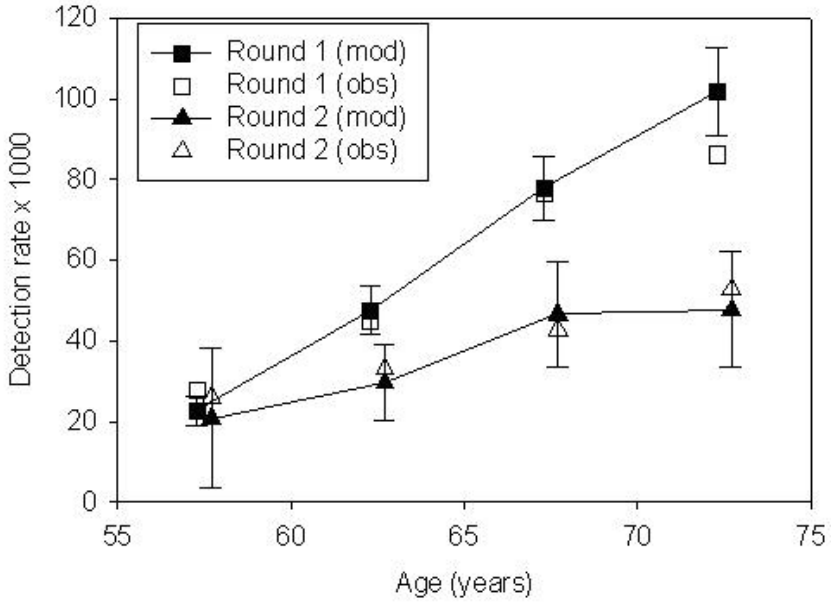

Figure 1: Detection rate in the screen arm, observed and predicted by the model.

The stage distribution and Gleason score compared with the model are presented in Figure 2.

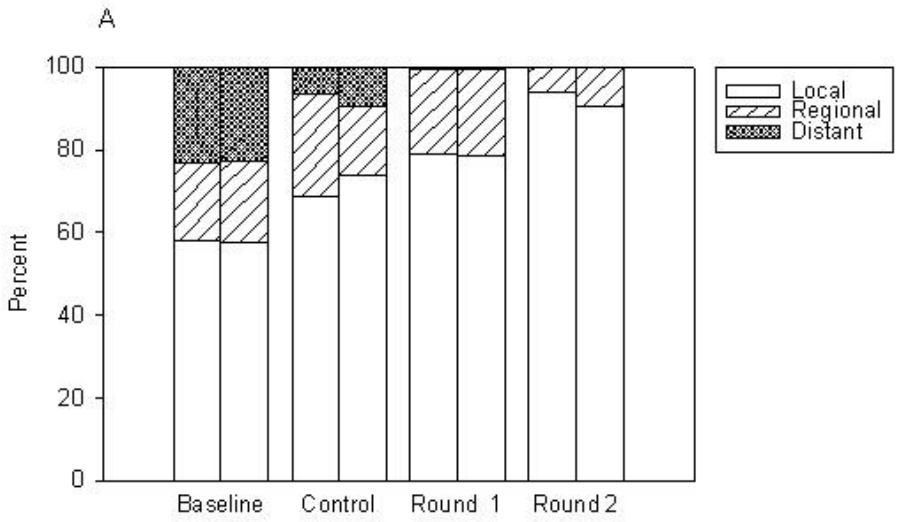

Figure 2A: Stage distribution of baseline (1991) level, in the control arm and in the first and second round of the trial. Left bar of each pair is the observed value, right bar the model prediction.

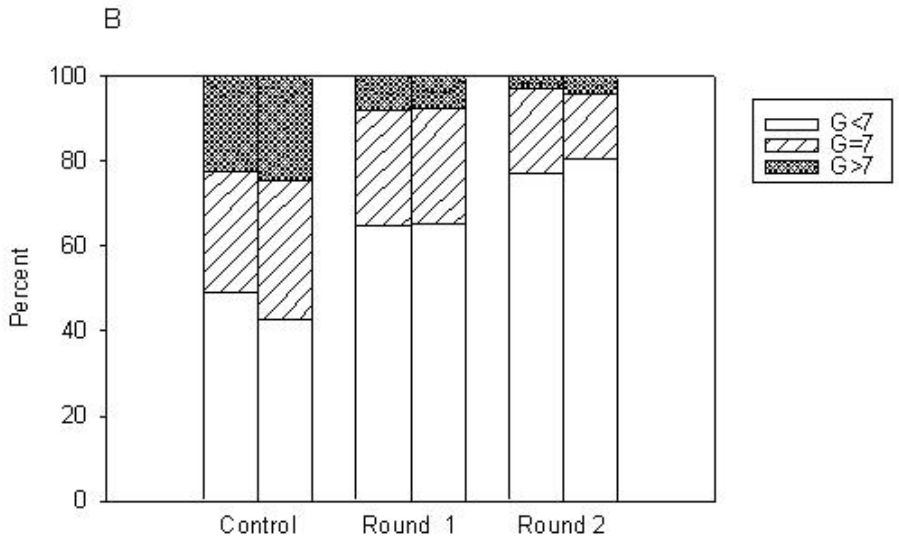

Figure 2B: Gleason score distribution in the control arm and in the first and second round of the trial. Left bar of each pair is the observed value, right bar the model prediction.

Discussion

The model, fitted to the baseline and trial data reproduced the essential characteristics of the observed data on clinical incidence, detection rates and tumor stage and Gleason score distributions. However, observed incidence and detection rates in the older age groups in the trial were significantly lower than predicted by the model. These results suggest a selection effect in the older age groups (older participants in the trial could be healthier than average).

Conclusion

The model could acceptably well project the observed baseline incidence and stage distribution and the results of the first two rounds of the ERSPC trial section Rotterdam.

REFERENCES:

[1] Draisma, G, Boer, R, Otto, SJ, van der Cruijsen, IW, Damhuis, RA, Schröder, FH, de Koning, HJ. "Lead times and overdetection due to prostate-specific antigen screening: estimates from the European Randomized Study of Screening for Prostate Cancer" in J Natl Cancer Inst 2003; 95: : 868-878

[2] Draisma, G, Postma, R, Schröder, FH, van der Kwast, TH, de Koning, HJ. "Gleason score, age and screening: modeling dedifferentiation in prostate cancer" in Int J Cancer 2006; 119: : 2366-2371

MODEL US

Summary
This document describes the model made for the US population.

Overview
The model of the ERSPC trial has been modified to a model for the US population.

Methods
The validated MISCAN-model developed for the progression of prostate cancer and screening in the ERSPC-trial Rotterdam is adjusted for the US situation by adapting the population and the PSA testing practice[1]. Also, an estimated extra stage-specific risk of clinical diagnosis has been added, implying an earlier diagnosis of prostate cancer in the absence of screening in the United States. The model is calibrated to the SEER 9 incidence from 1985 to 2000, as well as stage distribution data.

Results

REFERENCES:

[1] Draisma, G, Etzioni, R, Tsodikov, A, Mariotto, A, Wever, E, Gulati, R, Feuer, E, de Koning, HJ "Lead time and overdiagnosis in prostate-specific antigen screening: importance of methods and context" in J Natl Cancer Inst 2009; 101: : 374-383

LEAD TIME

Lead time

Summary
This document describes the estimates of lead time using the model based on the ERSPC Rotterdam trial and the model for the US population.

Overview
Lead time, the time that screening advances cancer diagnosis, is estimated with the use of the validated models for the ERSPC trial and the US population.

Methods
For this study lead time is defined as the amount of time, in years, between prostate cancer detection and either clinical diagnosis in the absence of screening or death by other causes[1,2]. The model for the ERSPC trial as well as the model for the US population has been used to estimate lead time. The lead time was calculated for various screen programs, for all screen detected cancers and for screen-detected relevant (non-overdiagnosed) cancers only.

Results
The lead time is dependent on the screening program (Table 1).

Table 1. Mean lead time for various screening programs using the ERSPC model.

screen program	**mean lead time (years)**		
age	all cases	relevant cases	
single	55	12.3	12.8
60	11.0	11.5	
65	9.5	10.0	
70	7.7	8.1	
75	6.0	6.2	
interval	every year, 55-67	12.3	13.7
every year, 55-75	11.6	13.4	
every 4 years, 55-67	11.2	12.3	
every 4 years, 55-75	10.3	11.7	

For the US population, the estimated lead times were lower: 6.9 years for all cases and 7.8 years for the relevant cases.

Discussion
The results suggest that regular screening as in the ERSPC trial for prostate cancer may advance diagnosis by approximately 10 years when assuming 100% attendance.
For screening in the US population, the estimated lead times were lower.

Conclusion
Due to differences in PSA testing between US and the ERSPC trial, there is a small difference in estimated lead time. However, the lead time is long in comparison with other cancers.

REFERENCES:

[1] Draisma, G, Boer, R, Otto, SJ, van der Cruijsen, IW, Damhuis, RA, Schröder, FH, de Koning, HJ. "Lead times and overdetection due to prostate-specific antigen screening: estimates from the European Randomized Study of Screening for Prostate Cancer" in J Natl Cancer Inst 2003; 95: : 868-878

[2] Draisma, G, Etzioni, R, Tsodikov, A, Mariotto, A, Wever, E, Gulati, R, Feuer, E, de Koning, HJ "Lead time and overdiagnosis in prostate-specific antigen screening: importance of methods and context" in J Natl Cancer Inst 2009; 101: : 374-383

OVERDIAGNOSIS

Overdiagnosis

Summary
This document describes the estimates of overdiagnosis using the model based on the ERSPC Rotterdam trial and the model for the US population.

Overview
Overdiagnosis, the detection by screening of cancers that would not be detected in the absence of screening, is estimated with the use of the validated models for the ERSPC trial and the US population.

Methods
For this study overdiagnosis is defined as cancers that would not have been diagnosed within the person's life time in the absence of screening[1,2]. The model for the ERSPC trial as well as the model for the US population has been used to estimate overdiagnosis. In the ERSPC model 100% attendance to screening is assumed. Overdiagnosis was calculated for various screen programs and expressed as percentage irrelevant cancers of screen detected cancers.

Results
The amount of overdiagnosis is dependent on the screening program (Table 1).

Table 1. Percentage of overdiagnosis for various screening programs using the ERSPC model.

screen program	age	% overdiagnosis
single	55	27
60	38	
65	47	
70	53	
75	56	
interval	every year, 55-67	50
every year, 55-75	56	
every 4 years, 55-67	48	
every 4 years, 55-75	54	

For the US situation the estimated overdiagnosis is 44%.

Discussion
The introduction of regular PSA screening in the Netherlands would lead to a substantial increase in prostate cancer incidence. In the model prediction, approximately half of the screen-detected cancers would not have been diagnosed in the absence of screening.

Conclusion
Screening is associated with a considerable amount of overdiagnosis.

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