THE LANCET

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Schröder FH, Hugosson J, Roobol MJ, et al for the ERSPC Investigators. Screening and prostate cancer mortality: results of the European Randomised Study of Screening for Prostate Cancer (ERSPC) at 13 years of follow-up. *Lancet* 2014; published online Aug 7. http://dx.doi.org/10.1016/S0140-6736(14)60525-0.

Web extra material

Appendix 1 – Acknowledgements

The following people are being acknowledged for their contribution to the ERSPC study.

The Netherlands:
Erasmus Medical Centre, Departments of Urology, Clinical Chemistry, Pathology, Public Health and statistics Netherlands (CBS)
Dr. W.J. Kirkels, urologist; COD committee
Dr. J.B.W Rietbergen, urologist
Dr. I.W. van der Cruijsen, urologist
Dr. R. Raaijmakers, urologist
Dr. S.H. de Vries, urologist
Dr. S. Roemeling, urologist
Dr. C. Gosselaar, general practicioner
Dr. T. Wolters, urologist in training
Dr. R.C.N. van den Bergh, urologist in training
Dr. P.J. van Leeuwen, urologist in training
Dr. M. Bul, urologist in training
Dr. X. Zhu, urologist in training
Dr. H.A. van Vugt, postdoc
Drs. L.P. Bokhorst, PhD student
Drs. J.W. Salman, PhD student
Drs. L.D.F. Venderbos, PhD student
Drs. G. Yurdakul, urologist
Drs. A. Boeken-Kruger, urologist
Drs. C. Wijburg, urologist
Drs. M. Forouzanfor, urologist
Drs. M. de Boer, urologist
Dr. R. Postma, pathologist
Dr. A.N. Vis, urologist
Dr. R. Hoedemaeker, pathologist
Dr. A. van Leenders, pathologist
Dr. B. Blijenberg, clinical chemistry
Prof. Dr. P.J. van der Maas, epidemiologist
Dr. S. Otto, epidemiologist
Dr. G. Draisma, statistician
Dr. P. Beemsterboer, epidemiologist
Dr. M. Essink-Bot, epidemiologist

Dr. I. Korfage, epidemiologist
Dr. R. Boer, informatician/mathematician
Dr. M. Wildhagen, statistician
Dr. E. Heijnsdijk, epidemiologist
Drs. W. Merkelbach, COD committee
Dr. W. Hoekstra, COD committee
Dr. J. Blom, COD committee
Drs. RAM Damhuis, epidemiologist, cancer registry
Drs. A. Reedijk, epidemiologist, cancer registry
Dr. R. Kranse, statistician, cancer registry
Mrs. D.W. Roobol, data management
Mr. W. Roobol, website management
Mrs. E. van den Berg, administrative support
Mr. G-J de Zwart, echografist
Mrs. C.G.A.M. Franken-Raab, data management
Mrs. M. van Slooten-Midderig, data management
Mrs. A. Smit, medical assistant
Mrs. V van der Drift, data management
Mrs. E. de Bilde, data management
Mrs. L. Mani, medical assistant
Mrs. M. Visser-van Dongen, data management
Mrs. H. Versteeg-Leenheer, data management
Mrs. B. Zoutendijk, data management
Mrs. N. Vink, data management
Mrs. H. van Meurs, echografist
Mrs. A E. de Bruijn, secretary

Belgium:
H. Devriendt Dr.Sc, director, Provincial Institute Hygiene
G. Thijs, Data Manager, Provincial Institute Hygiene
A. Hermans, Data Manager, Provincial Institute Hygiene
K. D'Hooge, Data Manager, Provincial Institute Hygiene
Dr. H. Neels, lab Biochemistry, ZNA Antwerp City Hospitals
Dr. A. Wauters, lab Biochemistry, ZNA Antwerp City Hospitals
Dr. I. Neetens, lab Pathology, ZNA Antwerp City Hospitals
Dr. M. Kockx, lab pathology, ZNA Antwerp City Hospitals
Prof. F. Keuppens, University Hospital Brussels Urology
Dr. J. Braeckman, University Hospital BrusselsUrology
Dr. F. Govaerts, General Practice Associations, WVVH, UHAK, DOMUS, HAVAC

Dr. B. Spinnewijn, General Practice Associations, WVVH, UHAK, DOMUS, HAVAC
Dr. M. Van Hoey, General Practice Associations, WVVH, UHAK, DOMUS, HAVAC
Dr. T. Putzeys, General Practice Associations, WVVH, UHAK, DOMUS, HAVAC
M. De Coninck, chair, Oncologic Centre Antwerp
B. Dourcy-Belle-Rose, Coordinator, Oncologic Centre Antwerp
A. Vancauwenbergh, Secretary, Oncologic Centre Antwerp
Prof. J.W. Coebergh, COD committee
Prof. H. Verhaegen, COD committee
Dr. Van Vliet, COD committee
Dr. B. Standaert
Mr. L. Van Herck

Sweden:
Maria Nyberg, study nurse
Svante Bergdahl, Urologist
Pär Lodding, Urologist
Ali Khatami, Urologist, former PhD-student
Johan Stranne, Urologist
Helén Ahlgren, data manager, study secretary
Gun-Britt Eriksson, Laboratory technician
Mona Hassan Al-Battat, Laboratory technician
AnnaPeri Erlandsson, Laboratory technicianCharlotte Becker, MD, PhD, Clinical chemistry
Sigrid Carlsson, MD, PhD, Postdoc
Anna Grenabo, MD, PhD-student
Rebecka Godtman, MD, PhD-student
Silas Pettersson, COD committee
Eberhard Varenhorst. COD committee
Bo-Johan Norlén, COD committee
Björn Zackrisson, Urologist, former PhD-student
Erik Holmberg, Statistician and database manager
Roland Frösing, Urologist
Erik Pileblad, Urologist
Carl-Gustaf Pihl, pathologist, pathology committee

Finland:
Marita Laurila, pathologist, pathology committee, Dept. of Pathology, Centre for Laboratory Medicine, Tampere University Hospital, Tampere, Finland
Jussi Aro, Dept. of Urology, Helsinki University Central Hospital, Helsinki
Harri Juusela, Helsinki University Central Hospital, Jorvi Hospital, Espoo
Markus Mildh, Helsinki University Central Hospital, Peijas-Rekola Hospital, Vantaa

Jorma Lahtela, Dept. of Internal Medicine, Tampere University Hospital, Tampere
Pekka J Karhunen, Dept. of Forensic Medicine and Research Unit of Clinical Chemistry, University of Tampere, Tampere
Tuukka Mäkinen, Dept. of Urology, Sinäjoki Central Hospital, Seinäjoki
Antti Rannikko MD, PhD, Department of Urology, Helsinki University Hospital, Helsinki
Prof. Nea Malila, Finnish Cancer Registry
Tuomas Kilpeläinen, MD, PhD, Department of Urology, Helsinki University Hospital, Helsinki, School of Health Sciences, University of Tampere and Tampere University Hospital
Teemu Murtola MD, PhD, School of Medicine, University of Tampere and Department of Urology, Tampere University Hospital
Professor Sakari Rannikko, MD, PhD, Department of Urology, Helsinki University Hospital, Helsinki
Professor Mirja Ruutu, MD, PhD, Department of Urology, Helsinki University Hospital, Helsinki
Martti Ala-Opas, MD, PhD, Department of Urology, Helsinki University Hospital, Helsinki
Sanna Kuivalainen, research nurse, Finnish Cancer Registry
Tiina Karhunen, research nurse, Finnish Cancer Registry
Maarit Leinimaa, research nurse, Department of Clinical Chemistry, Helsinki University Hospital, Helsinki
Jaana Saarinen, study nurse, Department of Urology, Tampere University Hospital

Italy:
Mario Cappellini, COD Committee
Simonetta Bianchi, COD Committee
Claudio Lombardi, COD Committee
Alessandro Bussotti, COD Committee
Paolo Bastiani, COD Committee
Simonetta Di Lollo, Pathology Committee

Co-operators:
Gianfranco Manneschi, Cancer Research and Prevention Institute (ISPO)
Emanuele Crocetti, Cancer Research and Prevention Institute (ISPO)
Rita Bonardi, Cancer Research and Prevention Institute (ISPO)
Tiziana Rubeca, Cancer Research and Prevention Institute (ISPO)
Beatrice Detti, AOU Careggi

Spain:
Antonio Berenguer. Servicio de Urologia. Hospital de Madrid Norte Sanchinarro. Madrid, Spain.
Jose A. Rodriguez. Instituto Nacional de Estadistica. Madrid, Spain.
Benita Aybar. Instituto Nacional de Estadistica. Madrid, Spain.
Javier C. Angulo. Department of Urology, Hospital Universitario de Getafe, Getafe, Madrid, Spain, Universidad Europea de Madrid, Madrid, Spain.
Rosario Granados. Department of Pathology, Hospital Universitario de Getafe, Getafe, Madrid, Spain, Universidad Europea de Madrid, Madrid, Spain.

Switzerland:
Kantonsspital Aarau, Aarau, Switzerland:
Dr. med. Daniel Seiler, Urologist, Department of Urology
Dr. med. Martin Baumgartner, Urologist, Department of Urology
Dr. med. Marco Randazzo, resident, Department of Urology
† Prof. Dr. Reto Tscholl, previous Chairman of local COD Committee, Professor emeritus, Department of Urology
Mrs. Elsbeth Woodtli, study nurse/ data management, Department of Urology
Mrs. Lydia Schärer, study nurse/ data management, Department of Urology
Dipl. Pharm. Roberto Herklotz, Centre of Laboratory Medicine
Prof. Dr. Bernhard Stamm, Pathologist, histopathological evaluation and pathological review, Professor emeritus, Institute for Pathology
Dr. med. Martin Wernli, Oncologist, care for patients, Department of Oncology and Hematology
Prof. Dr. Stephan Bodis, Radiooncologist, care for patients, Department of Radiooncology
Prof. Dr. Rainer Grobholz, Pathologist, Institute for Pathology

Kantonsspital Baden, Baden:
Dr. med. Kurt Lehmann, Urologist, Department of Urology
Dr. Hans-Ruedi Schmid, Central Laboratory
Aargau Association of Medical Doctors, Baden:
Dr. med. Hans-Ulrich Iselin, General Practitioner, cooperation with general practitioners in Aargau

University Hospital Basel, Basel:
Prof. Dr. Lukas Bubendorf, Review Pathologist, Pathology Committee, Institute for Pathology, Division of Cytology
Prof. Dr. Stephen Wyler, Chairman of local COD Committee, Department of Urology
Department of Medicine, University Hospital Zürich, Zürich:
Prof. Dr. Johann Steurer, Internist, Member of local COD Committee
Group Practice for Pathology, Zürich:
PD Dr. Michael Kurrer, Pathologist, Member of local COD Committee

France:
Bernard Malavaud, urologist
François Iborra, urologist
Sandra Malavaud, epidemiologist
Pascale Grosclaude, epidemiologist
Brigitte Tretarre, epidemiologist
Vincent Bataille, data manager
Faiza Bessaoud, dara manager

The United Kingdom:
Datamanager of the ERSPC central database:
M. Neville

Appendix 2 – Grants received per centre

The Netherlands:
The Dutch Cancer Society (KWF 94-869, 98-1657, 2002-277, 2006-3518, 2010-4800); The Netherlands Organisation for Health Research and Development (ZonMW-002822820, 22000106, 50-50110-98-311, 62300035).

Belgium:
Europe against Cancer, Flemish Ministry of Welfare, Public Health and Family, Province and City of Antwerp, Public Centre for Social Welfare Antwerp

Sweden:
Abbott Pharmaceuticals, Sweden, Af Jochnick's foundation, Catarina and Sven Hagstroms family foundation, Gunvor and Ivan Svensson's foundation, Johanniterorden, King Gustav V Jubilée Clinic Cancer Research Foundation, Sahlgrenska University Hospital, Schering Plough, Sweden, Swedish Cancer Society, Wallac Oy, Turkku, Finland. Dr. Lilja moved to the US during the cause of the study. He requests the following acknowledgements for his personal contribution:National Cancer Institute grants: R01CA160816 and P50-CA92629; Swedish Cancer Society 11-0624; The Sidney Kimmel centre for prostate and Urological cancers; David H. Koch trough the Prostate Cancer Foundation; the National Institute for Health Research (NIHR) Oxford Biomedical Research Centre Program; Fundacion Federico SA; and FiDiPro grant support from TEKES, Finland. Conflicts of interest: Dr. Hans Lilja holds patents for free PSA, intact PSA and hK2 assays.

Finland:
Academy of Finland (Grant no. 123054, 261205), Competitive Research Funding of the Tampere University Hospital (Grant no. 9K131, 9L103, 9M102, 9N078 and 9P053), Nordic Cancer Union, The Cancer Society of Finland

Italy:
Italian League for the Fight aganist Cancer - LILT Lega Italiana per la Lotta contro i Tumori, Italian Association for Cancer Research - AIRC Associazione Italiana Ricerca sul Cancro, National Reasrch Council - CNR Consiglio Nazionale delle Ricerche, Tuscany Region - Regione Toscana

Spain:
The Spanish "Fondo de Investigación Sanitaria": 96/0248, 99/0245, 02/0732, 06/0831.

Switzerland:
The Horten Foundation, Aargau Cancer League, Swiss Cancer League (Grant Nr KFS 787-2-1999 and 01112-02-2001), Health Department of Canton Aargau, Prostate Cancer Research Foundation, Baugarten Foundation and the Messerli Foundation.

France:
Institut National du Cancer convention 12-2008 Convention : 07/3D1616/SPC-111-13/NG-NC Appel à projets 2007 : Santé publique et Cancers
Ligue Nationale Contre le cancer PROJET N° PRE08/AV – CONV. DRC 2009/119

International coordination:
European Union Grants SOC 95 35109, SOC 96 201869 05F022, SOC 97 201329, SOC 98 32241, the 6th Framework Program of the EU: PMark:LSHC-CT-2004-503011;

Unconditional grants:
Beckman-Coulter-Hybritech Inc

Appendix 3: Pathology review

The Pathology Committee of ERSPC.
Composition and mandate: the Pathology Committee of the ERSPC is composed of the reference pathologists representing one of each ERSPC screening center (see below for list of members). Their mandate is to enhance the application of the guidelines on reporting of prostate biopsies of participants of the screening arm of the ERSPC trial (see documentation 1, below).

Objectives of the Pathology Committee:
1) To guard the uniformity in tissue processing and nomenclature of diagnosis and staging terms in the histopathological reporting of sextant needle biopsies taken from participants of the screening arm of the ERSPC trial.
2) To enhance the quality of histopathological diagnosis of prostate biopsies.
3) To reduce the inter-observer variation among screening centers particularly with regard to Gleason score of prostatic adenocarcinomas.

Duties of the members of the Pathology Committee
1) Supervision of the pathology reporting of the prostate biopsies obtained from participants in the ERSPC screening centers. In most centers the reference pathologists reviewed all needle biopsies of patients with a diagnosis of adenocarcinoma or a lesion suspicious for carcinoma. They further provide low threshold (intradepartmental) inter-collegial consultations for prostate biopsy diagnostics. In a few centers the reference pathologists examines and reports all prostate biopsies of the participants of the screening arm of the ERSPC trial.
2) Attendance of the annual Pathology Committee used for discussion of issues regarding quality assurance, uniform reporting and Gleason scoring.
3) Participation in slide reviews and educational sessions, designed for reduction of inter-observer variation of Gleason score and diagnosis.

Actions to reduce inter-observer variation for Gleason score on prostate biopsies:
1) Educational sessions using multiheader microscope.
2) Inter-observer studies using virtual microscopy (see Helin H, Lundin M, Lundin J, Martikainen P, Tammela T, Helin H, Van der Kwast TH. Web-based virtual microscopy in teaching and standardizing Gleason grading. Hum Pathol. 2005; 36: 381-386).
3) On site review of prostate biopsies of the Finnish ERSPC trial by two members of the pathology committee (Van der Kwast, Hoedemaeker) in order to improve grading consistency (see document 2 for details).

Documents / publications produced by the Pathology Committee of the ERSPC:
1. Guideline documents accepted at the Consensus Workshop on Prostatic Screening held in Antwerp (see Denis L, Murphy GP, Schröder FH. Cancer 1995; 75: 1178-1207): van der Kwast TH, Lopes C, Santonja C, Pihl C-G, Martikainen P, Di Lollo S, Bubendorf L, Hoedemaeker RF, and members of the pathology committee of the ERSPC. Guidelines for processing and reporting of prostatic needle biopsies. J. Clin Path 2003: 56:336-40.
2. Van der Kwast TH, Roobol MJ, Wildhagen MF, Martikainen PM, Määttänen L, Pihl C-G, Santonja C, Bubendorf L, Neetens I, Di Lollo S and Hoedemaeker RF. Consistency of prostate cancer grading results in screened populations across Europe. BJUI 2003; 92 (S2): 88-91.
3. Van der Kwast TH, Lopes C, Martikainen PM, Pihl CG, Santonja C, Neetens I, Di Lollo S, Hoedemaeker RF. Report of the Pathology Committee: false-positive and false-negative diagnoses of prostate cancer. BJU Int. 2003 Dec;92 Suppl 2:62-5.
4. Van der Kwast TH, Ciatto S, Martikainen PM, Hoedemaeker R, Laurila M, Pihl C-G, Hugosson J, Neetens I, Nelen V, Di Lollo S, Roobol MJ, Maattanen L, Santonja C, Moss S and Schröder FH. Detection rates of high-grade prostate cancer during subsequent screening visits. Results of the European Randomized Screening Study for Prostate Cancer. Int J Cancer 2006; 118: 2538-2542.

Members of the Pathology Committee
Th. Van der Kwast ERSPC section Rotterdam (chair)
G.J. van Leenders ERSPC section Rotterdam (2004-)
R.F. Hoedemaeker ERSPC section Rotterdam (1997-2002)
C-G. Pihl ERSPC section Goteborg
P.M. Martikainen ERSPC section Tampere/Helsinki
M. Laurila ERSPC section Tampere/Helsinki
L. Bubendorf ERSPC section Aarau
C. Santonja ERSPC section Getafe (-2007)
I. Neetens ERSPC section Antwerp
S. DiLollo ERSPC section Florence
C. Mazerolles ERSPC section Toulouse

Appendix 4 – Medical ethical approvals per centre

The Netherlands		
Institution	Date of issue	Record number
Health Council of the Netherlands	29-03-1996	1996/02
Health Council of the Netherlands	15-12-2000	2000/05
Health Council of the Netherlands	24-07-2007	2007/03

Belgium		
Institution	Date of issue	Record number
Ministry of the Flemish Community, the minister of welfare, national health and family	1999	ZG/PET/ERSPC 06031
Ministry of the Flemish Community, the minister of welfare, national health and family	2002	ZG/PET/ERSPC 06031
Ministry of the Flemish Community, the minister of welfare, national health and family	2004	ZG/PET/ERSPC 06031

Sweden		
Institution	Date of issue	Record number
University of Goteborg	02-02-1994	463-93
University of Goteborg	31-05-1995	180-95

Finland		
Institution	Date of issue	Record number
Population Register Centre	15-12-1995	1058/40/95
City of Helsinki, Office for Health Care	04-06-1996	6/96
City of Vantaa	02-02-1996	6/96
Ministry of Social Affairs and Health in Finland	01-10-1999	51/07/1999
City of Tampere	13-12-2000	7649/403/2000
Hospital District of Helsinki and Uusimaa	29-01-2001	55/2000
Helsinki University Hospital	28-05-2001	249/2001
The National Authority for Medico legal Affairs	27-02-2002	601/32/300/02
Statistics Finland	19-12-2003	TK-53-1610-03
National Institute of Health and Welfare	2010	THL/1752/5.05.00/2010
Pirkanmaa Hospital District (Tampere University Hospital)	07-12-2010	R10617/13/2010

Italy		
Institution	Date of issue	Record number
Centro per lo Studio e la Prevenzione Oncologica Firenze	03-06-1996	1996/06/03

Spain		
Institution	Date of issue	Record number
Hospital Universitario de Getafe	22-03-2006	Acta -3/06

Switzerland		
Institution	Date of issue	Record number
Kantonsspital Aarau	09-09-1998	1998-09-09/RK

France		
Institution	Date of issue	Record number
Le Comite Consultatif de Protection des Personnes dans la Recherche Biomedicale de Toulouse I	17-07-2000	

Appendix Table 1: ERSPC – Randomization, participants and results of screening per center (all ages, cut-off date December 31- 2010, data truncated at 13 years of follow-up.

Period of randomization	Netherlands Nov 1993 – March 2000	Belgium June 1991- Dec 2003	Sweden 31-Dec-04	Finland Jan 1996-Jan 1999	Italy Oct 1996 – Oct 2000	Spain Feb 1996 – June 1999	Switzerland Sep 1998 - Aug-03	Total Excluding France	Herault June 2003 – Mar 2005	Tarn Dec 2000 – June 2004	Total
Median age at randomisation (yrs)	63.2	64.1	56.4	58.7	62.0	56.6	61.0	60.1	62.6	61.7	61.2
Randomized – N	42,368	10,359	19,911	80,379	14,971	3,702	10,309	181,999	62039	22473	266,511
- screening	21,206	5,188	9,957	31,970	7,497	1,840	5,158	82,816	31,024	11,423	125,263
	50.1%	50.1%	50.0%	39.8%	50.1%	49.7%	50.0%	45.5%	50.0%	50.8%	47.0%
- control	21,162	5,171	9,954	48,409	7,474	1,862	5,151	99,183	31,015	11,050	141,248
	49.9%	49.9%	50.0%	60.2%	49.9%	50.3%	50.0%	54.5%	50.0%	49.2%	53.0%
Screened at least once N	19970	4682	7558	23771	5896	1840	5015	68,732	7587	4352	80,671
(%)	(94.2)	(90.2)	(75.9)	(74.4)	(78.6)	(100.0)	(97.2)	(83.0)	(24.5)	(38.1)	(64.4)
Screen tests done – N	43491	7280	31152	52142	13022	3317	12561	162,965	7587	5646	176,198
Mean no of screens / man screened	2.2	1.6	4.1	2.2	2.2	1.8	2.5	2.4	1.0	1.3	2.2
Positive tests – N	10671	1213	5042	5925	1491	543	2678	27,563	1183	847	29,593
(%)	(24.5)	(16.7)	(16.2)	(11.4)	(11.4)	(16.4)	(21.3)	(16.9)	(15.6)	(15.0)	(16.8)
Biopsies – N	9499	849	4393	5404	923	394	2088	23,550	342	430	24,322
(% of screen positive)	(89.0)	(70.0)	(87.1)	(91.2)	(61.9)	(72.6)	(78.0)	(85.4)	(28.9)	(50.8)	(82.2)
Prostate cancers											
Screening cohort total – N	2643	500	1082	3018	417	115	596	8371	1320	573	10264
Screen detected N	2120	214	861	1631	202	78	447	5553	174	123	5850
Interval and Non attender N	523	286	221	1387	215	37	149	2818	1146	450	4414
PPV (S det cancers/biopsy, %)	22.3	25.2	19.6	30.2	21.9	19.8	21.4	23.6	50.9	28.6	24.1
Cumulative incidence (total cancers / all rand. To S arm, %)	12.5	9.6	10.9	9.4	5.6	6.3	11.6	10.1	4.3	5.0	8.2
Prostate cancers											
Control group – N	1353	414	654	3609	301	66	310	6707	1204	522	8433
Cumulative incidence (%)	(6.4)	(8.0)	(6.6)	(7.5)	(4.0)	(3.5)	(6.0)	(6.8)	(3.9)	(4.7)	(6.0)
Mean Follow up (years)	11.2 (3.1)	10.7 (3.3)	12.0 (2.7)	11.4 (3.0)	11.3	12.0	9.8 (2.0)	11.3 (2.9)	6.2 (1.1)	7.3 (1.5)	9.8 (3.4)
Median follow-up (years)	12.8 (1.8)	13.0 (4.2)	13.0 (0)	13.0 (1.0)	12.6	12.6	10.2 (2.5)	13.0 (1.8)	6.4 (0.6)	7.5 (0)	11.4 (6.4)

Appendix tables 2a and 2b: Prostate cancer incidence and mortality in the intervention and control arms during 3 time periods – All ages, France excluded except for Years 1-9

a) Prostate cancer incidence

	Intervention			Control			Rate Ratio[1] (95% CI)	Rate difference per 1000 persons year (95% CI)	Rate difference per 1000 men
	Prostate Cancer N	Person years	Rate per 1000 person years	Prostate Cancer N	Person years	Rate per 1000 person years			
Year 1-9 inc France	8777	929592	9.44	6258	1080759	5.79	1.64 (1.59-1.70)	3.69 (3.44-3.94)	26.5
Years 1-9	6884	663471	10.38	4533	816211	5.55	1.91 (1.83- 1.98)	4.92 (4.62-5.22)	38.3
Years 1-11	7643	784291	9.75	5779	967490	5.97	1.66 (1.60 - 1.73)	3.88 (3.60 -4.15)	35.2
Years 1-13	8371	879450	9.52	6707	1086705	6.17	1.57 (1.52 – 1.63)	3.46 (3.20 – 3.72)	34.9

[1] Adjusted by centre

B: Prostate cancer mortality (France included years 1 – 9)										
	Intervention			**Control**			**Rate Ratio[1] (95% CI)**	**Rate difference per 1000 persons year (95% CI)**	**Rate difference per 1000 men**	**Adjusted rate ratio in attenders**
	Prostate Cancer deaths N	**Person years**	**Rate per 1000 person years**	**Prostate Cancer deaths N**	**Person years**	**Rate per 1000 person years**				
Years 1-9	226	696395	0.32	313	832917	0.38	0.86 (0.72-1.03) p=0.10	-0.05 (-0.11 - +0.01)	-0.43	
Years 1-11	314	829341	0.38	465	992742	0.47	0.80 (0.69 – 0.93) P=0.004	-0.09 (-0.15 - -0.03)	-0.92	0.75 (0.62 -0.91)
Years 1-13	427	935185	0.46	610	1120432	0.54	0.83 (0.73- 0.94) p = 0.004	-0.09 (-0.16 - -0.03)	-1.05	0.78 (0.66-0.92)

1 Adjusted by centre

Appendix table 3: Numbers needed to be invited (NNI) and numbers needed to be detected (NND)

Follow-up periods 11 and 13 years, all ages, France excluded.

	11 years of follow-up		13 years of follow-up	
	NNI (95% CI)	NND	NNI (95% CI)	NND
Excl. France	1091 (647 - 3462)	37	953 (563 – 3093)	33

Appendix table 4: Prostate cancer mortality for individual centres – core age group, FU truncated at 13 years.

	Intervention arm			Control arm			
Center	Deaths	Person years	Rate p.1000 p.years	Deaths	Person years	Rate p.1000 p.years	Rate ratio (95% CI)
Netherlands	85	199958	0.43	126	199165	0.63	0.67 (0.51 – 0.88)
Belgium	18	46939	0.38	23	45932	0.50	0.77 (0.41 – 1.42)
Sweden	38	69152	0.55	62	69498	0.89	0.62 (0.41 – 0.92)
Finland	170	365529	0.47	284	553046	0.51	0.91 (0.75 – 1.10)
Italy	26	82457	0.32	32	81715	0.39	0.81 (0.48– 1.35)
Spain	2	12594	0.16	4	13583	0.29	0.54 (0.10 – 2.94)
Switzerland	16	48388	0.33	14	48253	0.29	1.14 (0.56 – 2.33)

The result of the heterogeneity test is $\chi^2_6 = 5.95$ (p = 0.43).

Appendix table 5: T1c cancers, core age group, excluding France (n = number of T1c cancers)

	Year			
Arm	1	4	8	12
Intervention (n)	733	136	186	117
Follow-up (years)	71089.84	67121.73	60179.52	47279.88
Rate per 1.000 person years	10.31	2.03	3.09	2.47
Control (n)	75	159	282	218
Follow-up (years)	88282.97	83738.10	76035.44	60903.35
Rate per 1.000 person years	0.85	1.90	3.71	3.58

Appendix Figure 1: Flow diagram of the ERSPC trial; all ages. Excluding France

Appendix Figure 2: Nelson Aalen estimates of cumulative PCa mortality: all ages

Fig 1

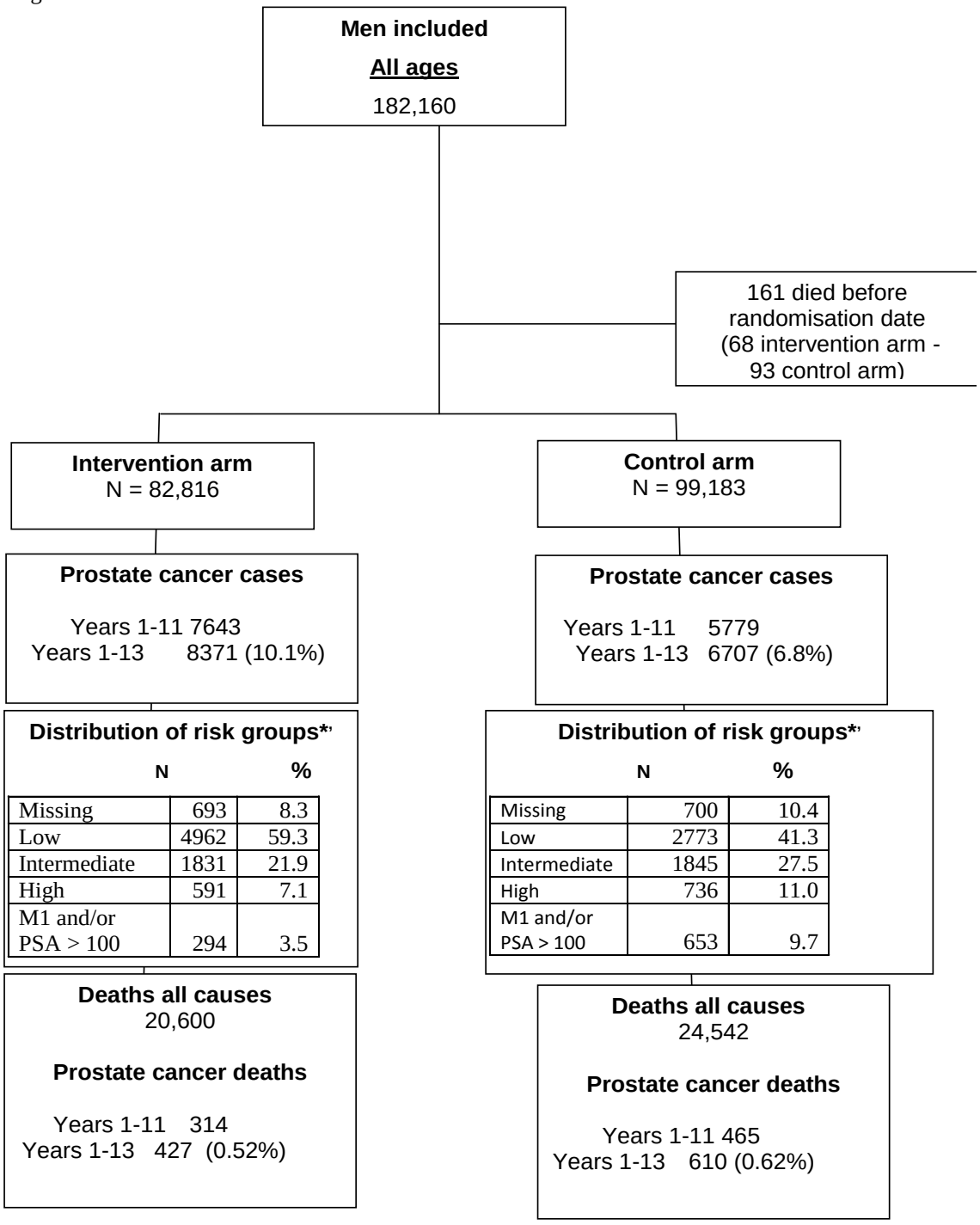
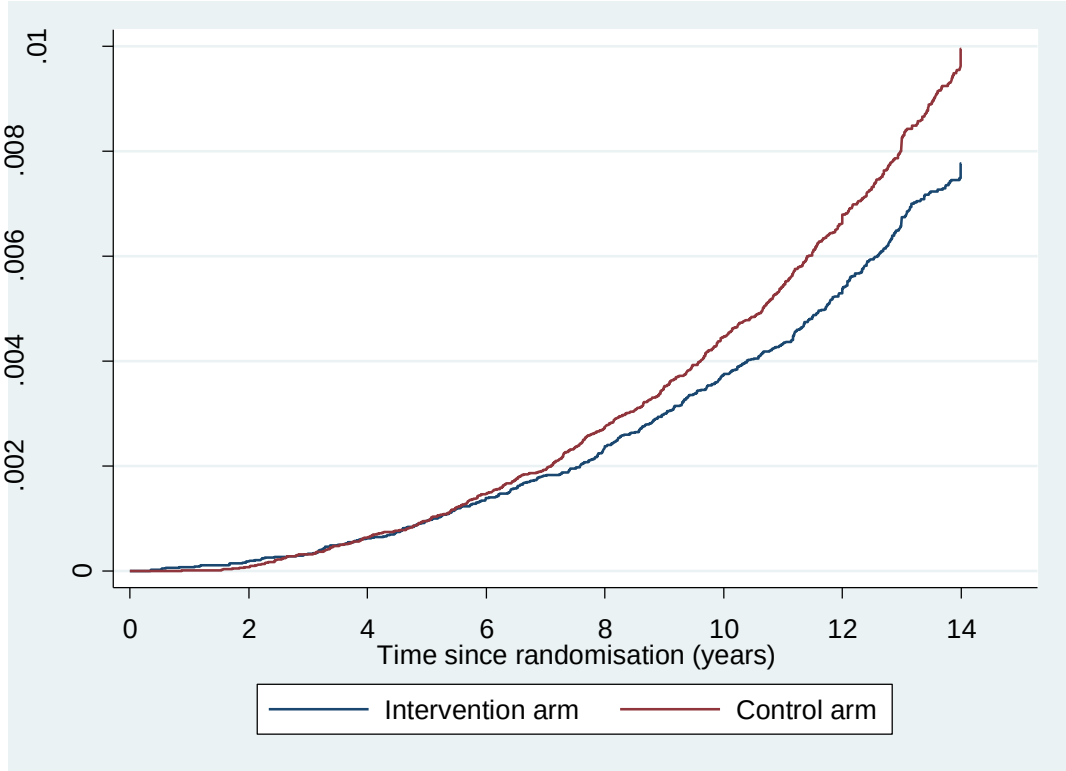


Figure 1

* Low risk= T1,T2 with Gleason score (GS) <= 6; Intermediate risk = T1,T2 with GS 7 and T3 with GS <=7; High risk = T1,T2,T3 with GS 8-10 and T4 with any GS; M1 and/or PSA > 100 = any T stage or GS with M1 and/or PSA > 100

Figure 2


0
.002
.004
.006
.008
.01
0
2
4
6
8
10
12
14
Time since randomisation (years)
Intervention arm
Control arm