

Diabetes Register(s)

Register collaboration

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Danish Registers, University of Copenhagen,
November 2017

<http://BendixCarstensen.com>

Background for the NDR

Population surveillance

- ▶ Monitor and describe:
 - ▶ Prevalence (no. and %)
 - ▶ Incidence (no. and rates)
 - ▶ Mortality and SMR

Health care surveillance

- ▶ Keep track of diabetes patients
- ▶ Predictions of likely future developments
- ▶ Match patients to treatment indicators (GPs)
- ▶ ... improve accuracy of treatment information

Results up to 31.12.2006 reported in:

Carstensen *et al.*: The Danish National Diabetes Register: Trends in incidence, prevalence and mortality. *Diabetologia* 2008

Construction of the register

- ▶ Based on existing registers in Denmark:
 - ▶ National Patient Register
 - all hospital and outpatient clinic contacts.
 - ▶ National Health Insurance Service Registry
 - all services provided in the NHS.
 - ▶ Register of Medicinal Product Statistics
 - all prescriptions taken out at pharmacies.
- ▶ Linked to mortality and migration data from the Central Person Register.
- ▶ All records are CPR-identified, for linkage purposes.
- ▶ Inclusion start at 1.1.1990.

Inclusion criteria for the register

- ▶ Diagnosis of DM in NPR.
- ▶ Gestational diabetes excluded. A diagnosis of GDM precludes inclusion for a period of 1 year.
- ▶ Foot-therapy for diabetics recorded in NHISR.
- ▶ 5 blood-glucose measurements within 1 year recorded in Register of Medicinal Product Statistics.
- ▶ 2 blood-glucose measurements per year in 5 consecutive years recorded in NHISR.
- ▶ Prescription on insulin or oral antidiabetic medicine. Metformin alone in women aged 20–39 excluded (PCOS).

Variables in the NDR (scrambeled)

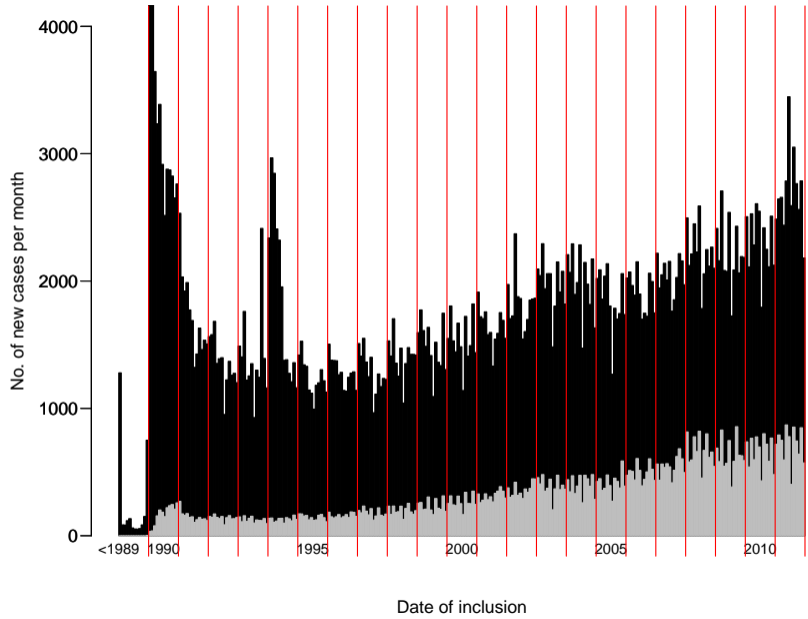
- ▶ D_FODD0 - date of birth
- ▶ C_SEX - sex
- ▶ D_INKLD0 - date of inclusion
- ▶ C_INKLAARSAG - criterion first met
- ▶ D_DODSD0 - date of death
- ▶ D_LPR - first DM diagnosis in LPR
- ▶ D_FODT - first date of chiropody
- ▶ D_BLOD2I5 - first date of 2 BG / 5y
- ▶ D_BLOD5I1 - first date of 5 BG / 1y
- ▶ D_OAD - date of 2nd OAD purchase
- ▶ D_INS - date of 2nd insulin purchase
- ▶ V_PID - person-id

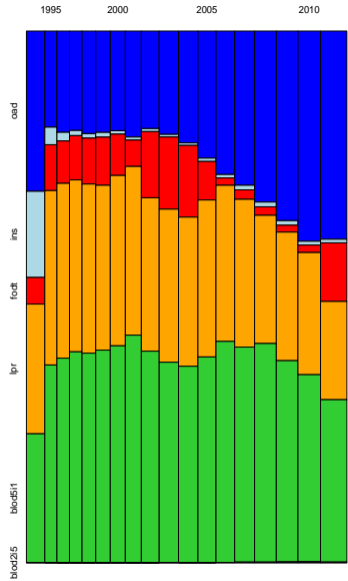
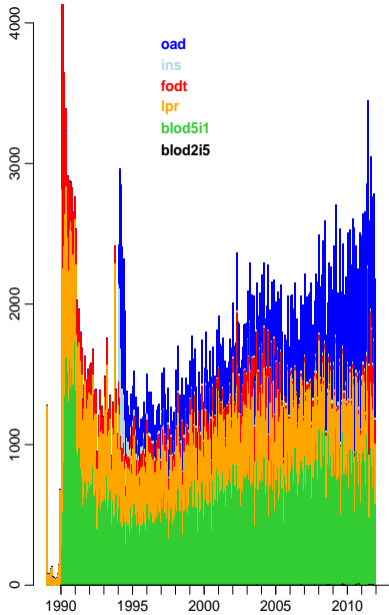
Random sample from NDR

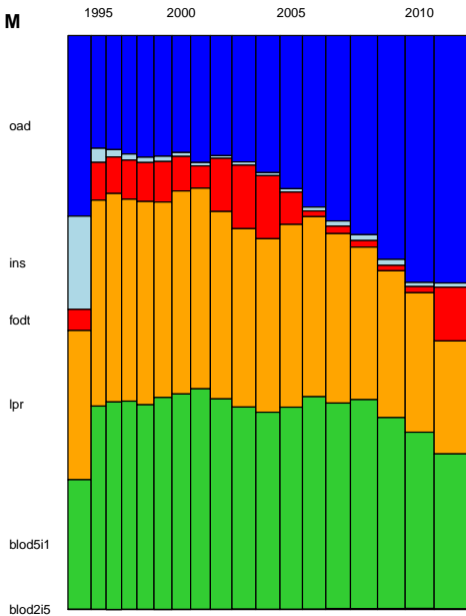
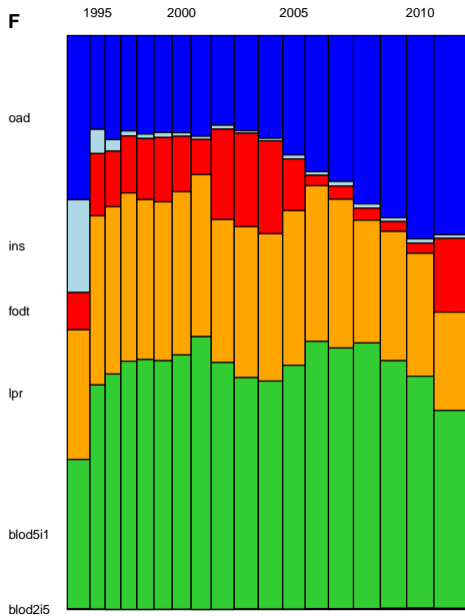
D_FODDTP	C_SEX	D_INKLDTP	C_INKLAAR	D_DODSDTP	D_LPR	D_FODT	D_BLOD2I5	D_BLOD5I1	D_OAD
09NOV1935	K	12OCT2009	oad	12OCT2009
11SEP1919	M	19APR1990	lpr	22MAY1992	19APR1990	.	.	04JUL1990	.
12JUN1923	K	03JUN1998	blod5i1	22FEB2008	.	.	.	03JUN1998	.
18MAR1936	M	18APR2001	blod5i1	.	06JUN2007	23MAY2007	.	18APR2001	01JUN2001
12AUG1959	K	08OCT2008	blod5i1	08OCT2008	.
24DEC1941	M	16MAR2005	blod5i1	24FEB2007	.	.	.	16MAR2005	.
03JUL1944	M	09JAN2003	oad	12DEC2007	09JAN2003
22JAN1964	K	22JAN1997	blod5i1	22JAN1997	.
29MAR1941	K	01OCT2009	lpr	.	01OCT2009	.	.	.	22OCT2009
01JUN1949	M	06OCT2005	oad	11JAN2006	06OCT2005
15AUG1962	M	29SEP2009	oad	29SEP2009
02APR1949	K	18AUG2004	blod5i1	.	21JAN2009	19MAR2008	23APR2008	18AUG2004	08SEP2007
21JUL1931	K	14MAY2003	blod5i1	14MAY2003	.
08OCT1901	K	08AUG1992	lpr	20DEC1993	08AUG1992
19APR1913	K	23JAN1991	fodt	29AUG1992	.	23JAN1991	.	.	.
09MAR1913	K	03APR1998	oad	20MAY1999	03APR1998
15APR1947	M	24APR2001	oad	.	21MAY2001	.	.	.	24APR2001
12DEC1940	K	16JUL2002	lpr	.	16JUL2002	.	.	.	13JAN2006
31DEC1916	M	24MAY1991	lpr	28JUN1991	24MAY1991
21JUN1919	K	16FEB1992	lpr	15NOV1993	16FEB1992	20JAN1993	.	17JUN1992	.
31DEC1944	K	05OCT1993	lpr	.	05OCT1993	21APR2004	.	.	05NOV1994
30JUN1916	K	01FEB2006	blod5i1	18MAR2009	.	.	.	01FEB2006	.
16OCT1971	K	08DEC2004	blod5i1	08DEC2004	.
16MAY1965	K	25MAY2005	blod5i1	.	22MAY2006	.	.	25MAY2005	23NOV2005
06AUG1923	K	28OCT1998	blod5i1	01APR2004	.	.	.	28OCT1998	.
26JAN1932	M	20FEB2008	blod5i1	.	.	21MAY2008	.	20FEB2008	05MAR2008
16JUN1932	M	25FEB1998	lpr	24APR2006	25FEB1998	18NOV1998	04AUG2004	27SEP2000	03MAR2000
15FEB1914	M	22JUL1992	blod5i1	17FEB1993	.	.	.	22JUL1992	.
05MAR1957	M	11AUG2004	blod5i1	.	07AUG2004	.	.	11AUG2004	11SEP2004

Random sample from NDR

D_INKLDTO	C_INKLAAR	D_LPR	D_FODT	D_BLOD2I5	D_BLOD5I1	D_OAD	D_INS	V_PID
12OCT2009	oad	12OCT2009	.	OC25D
19APR1990	lpr	19APR1990	.	.	04JUL1990	.	.	OCEC1
03JUN1998	blod5i1	.	.	.	03JUN1998	.	.	OCAF5
18APR2001	blod5i1	06JUN2007	23MAY2007	.	18APR2001	01JUN2001	.	OCCE3
08OCT2008	blod5i1	.	.	.	08OCT2008	.	.	OC2CD
16MAR2005	blod5i1	.	.	.	16MAR2005	.	.	OC47B
09JAN2003	oad	.	.	.	12DEC2007	09JAN2003	.	OC619
22JAN1997	blod5i1	.	.	.	22JAN1997	.	.	OC6F9
01OCT2009	lpr	01OCT2009	.	.	.	22OCT2009	.	QCD42
06OCT2005	oad	.	.	.	11JAN2006	06OCT2005	.	OC42B
29SEP2009	oad	29SEP2009	.	OCBE4
18AUG2004	blod5i1	21JAN2009	19MAR2008	23APR2008	18AUG2004	08SEP2007	.	OC2ED
14MAY2003	blod5i1	.	.	.	14MAY2003	.	.	OC2CD
08AUG1992	lpr	08AUG1992	OC5FA
23JAN1991	fodt	.	23JAN1991	OCFBO
03APR1998	oad	03APR1998	.	OC976
24APR2001	oad	21MAY2001	.	.	.	24APR2001	.	OCB64
16JUL2002	lpr	16JUL2002	.	.	.	13JAN2006	17JAN2006	OCEE1
24MAY1991	lpr	24MAY1991	OCB84
16FEB1992	lpr	16FEB1992	20JAN1993	.	17JUN1992	.	.	OCF20
05OCT1993	lpr	05OCT1993	21APR2004	.	.	05NOV1994	.	OCCE3
01FEB2006	blod5i1	.	.	.	01FEB2006	.	.	OC867
08DEC2004	blod5i1	.	.	.	08DEC2004	.	.	OCB44
25MAY2005	blod5i1	22MAY2006	.	.	25MAY2005	23NOV2005	.	OC52A
28OCT1998	blod5i1	.	.	.	28OCT1998	.	.	OCE21
20FEB2008	blod5i1	.	21MAY2008	.	20FEB2008	05MAR2008	.	OC758
25FEB1998	lpr	25FEB1998	18NOV1998	04AUG2004	27SEP2000	03MAR2000	30JUL2002	OCBB4
22JUL1992	blod5i1	.	.	.	22JUL1992	.	.	OC709
11AUG2004	blod5i1	27AUG2004	.	.	11AUG2004	11SEP2004	.	OC485

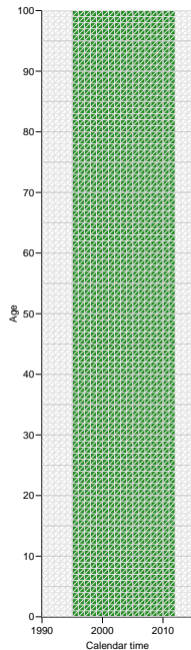




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Methods: Incidence

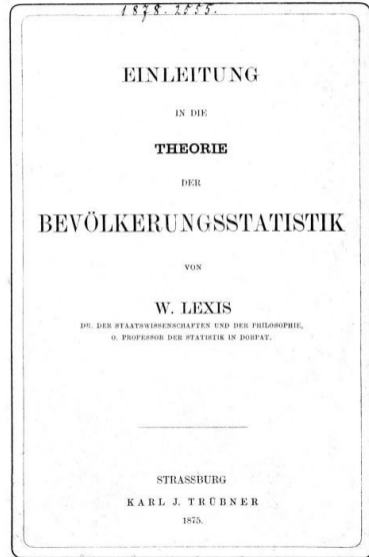
- ▶ New cases tabulated by age and date of diagnosis (1995-2007) and date of birth, in 1-year classes.
- ▶ Corresponding person-years figures from Statistics Denmark — person-years in the diabetes register subtracted.
- ▶ Incidence rates analysed by Poisson-regression with smooth parametric terms in age and date of diagnosis, using log-person-years as offset.



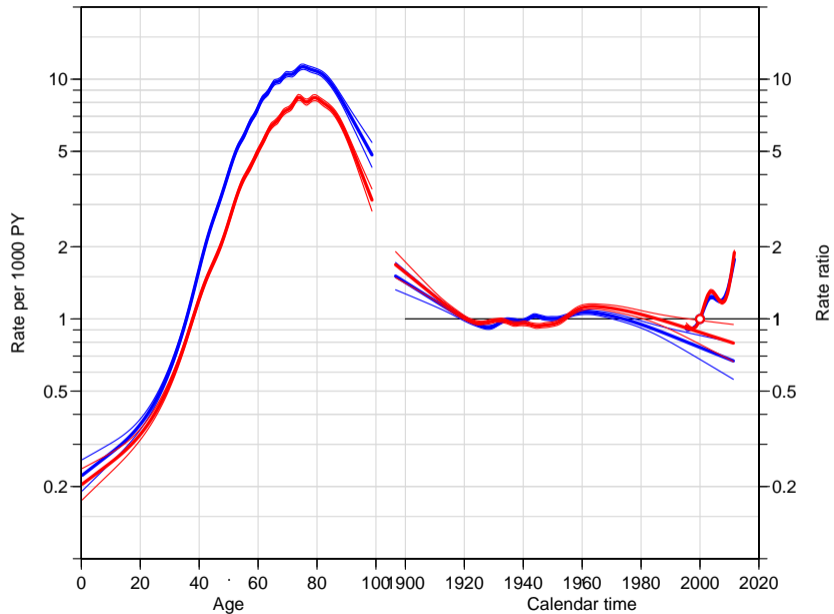
Digression: Lexis diagram



Wilhelm Lexis (1837–1914)
German demographer, statistician and
economist.



New cases in NDR		2006			2011		
Year	M	F	All	M	F	All	
≤ 1989	1,480	1,310	2,790	1,514	1,330	2,844	
1990	21,347	24,738	46,085	21,434	24,775	46,209	
1991	10,681	9,987	20,668	10,763	10,055	20,818	
1992	8,554	7,855	16,409	8,463	7,786	16,249	
1993	9,165	7,639	16,804	9,196	7,642	16,838	
1994	12,103	10,733	22,836	11,993	10,688	22,681	
1995	7,745	7,148	14,893	7,756	7,150	14,906	
1996	8,015	7,388	15,403	8,016	7,388	15,404	
1997	7,923	7,528	15,451	7,928	7,533	15,461	
1998	8,800	8,039	16,839	8,819	8,048	16,867	
1999	9,295	8,537	17,832	9,314	8,565	17,879	
2000	9,614	8,881	18,495	9,620	8,883	18,503	
2001	10,181	9,468	19,649	10,215	9,481	19,696	
2002	11,123	10,745	21,868	11,178	10,790	21,968	
2003	12,385	11,378	23,763	12,370	11,361	23,731	
2004	12,465	11,465	23,930	12,472	11,477	23,949	
2005	11,607	10,535	22,142	11,619	10,582	22,201	
2006	12,007	10,865	22,872	12,094	10,920	23,014	
2007				12,719	11,783	24,502	
2008				14,005	12,663	26,668	
2009				14,298	12,360	26,658	
2010				14,974	12,818	27,792	
2011				17,080	15,314	32,394	
1995–2006	121,160	111,977	233,137	121,401	112,178	233,579	
1995–2011				194,477	177,116	371,593	
Total	184,490	174,239	358,729	257,840	239,392	497,232	

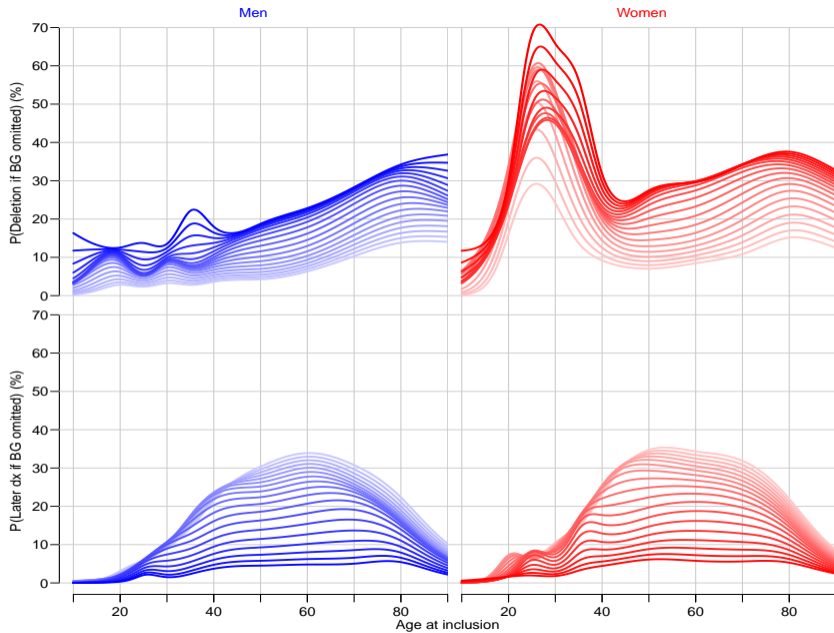


Incidence summary

- ▶ Women with gestational diabetes are closer monitored (?), hence the increased incidence rates in ages 20–35 (RR \approx 1.5).
- ▶ Incidence rates peak in ages 70–85: 1.2%/year for men, 1.2%/year for women in 2005.
- ▶ Annual increase in incidence rates over the period 1995–2004 was 5.6%, after 2004 almost flat

Glucose criteria

- ▶ Women who have a glucose tolerance test triggers typically 6 blood glucose measurements.
- ▶ Omitting the glucose criteria:
 - ▶ Some are removed from the register
 - ▶ Some have a later diagnosis (meeting a different criterion).
- ▶ The new diagnostic criteria based on HbA1c makes the blood glucose criteria even more uncertain.
- ▶ No consensus on how to proceed.



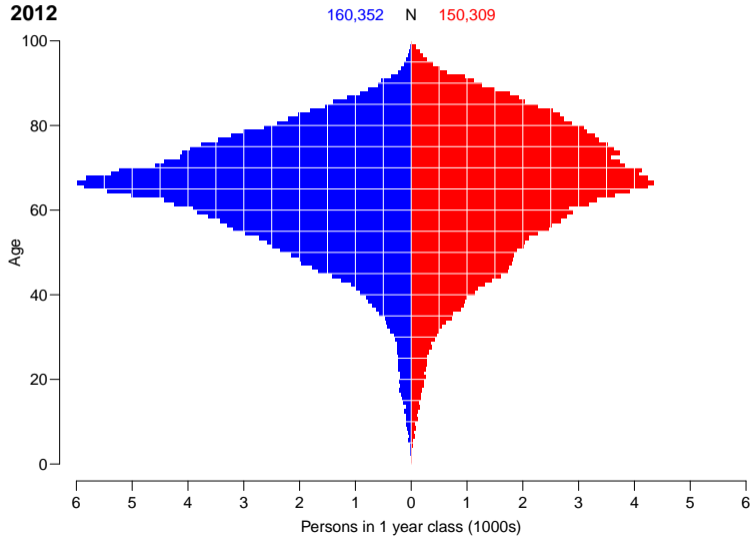
Methods: Prevalence

- ▶ Prevalent cases by 1 Jan 1995, . . . , 2010 tabulated by sex and 1-year age.
- ▶ Corresponding population figures from Statistics Denmark.
- ▶ Prevalence analysed by a binomial model with log-link and the population size as denominator. Separate parametric terms used for each sex and date.

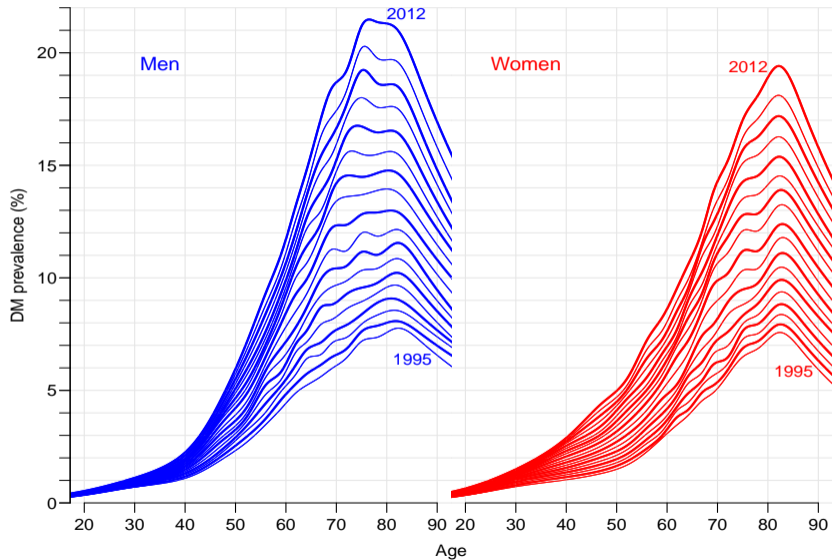
Prevalence of diabetes

1 January	No. patients			Prevalence (%)		
	M	F	All	M	F	All
1995	49,438	49,126	98,564	1.92	1.86	1.89
1996	53,443	52,631	106,074	2.06	1.98	2.02
1997	57,739	56,551	114,290	2.22	2.12	2.17
1998	61,832	60,522	122,354	2.36	2.26	2.31
1999	66,746	64,974	131,720	2.54	2.42	2.48
2000	71,798	69,692	141,490	2.73	2.59	2.65
2001	77,120	74,570	151,690	2.92	2.76	2.84
2002	82,914	79,895	162,809	3.12	2.94	3.03
2003	89,291	86,364	175,655	3.35	3.17	3.26
2004	96,706	93,199	189,905	3.62	3.42	3.52
2005	104,149	100,227	204,376	3.89	3.67	3.78
2006	110,581	106,028	216,609	4.12	3.87	3.99
2007	117,328	112,018	229,346	4.35	4.07	4.21
2008	124,501	118,726	243,227	4.59	4.30	4.44
2009	132,847	126,295	259,142	4.86	4.54	4.70
2010	140,940	133,318	274,258	5.14	4.78	4.96
2011	149,702	140,507	290,209	5.43	5.01	5.22
2012	160,352	150,309	310,661	5.80	5.34	5.57

Prevalence of diabetes — age distribution



Prevalence of diabetes — % by age



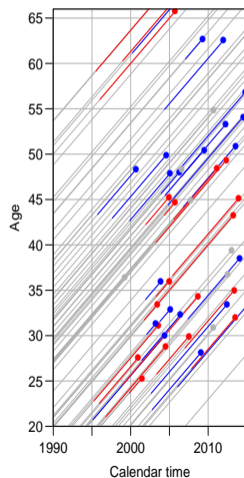
Methods: Mortality and SMR

- ▶ Deaths and person-years of follow-up among diabetics tabulated by age and period at follow-up in 1-year classes.
- ▶ Corresponding mortality figures from Statistics Denmark. Deaths and person-years from the diabetes cohort subtracted.
- ▶ Mortality analysed by Poisson-regression of deaths with smooth parametric terms for current age, current date and current disease duration, using log-person-years as offset.
- ▶ SMR analysed using dataset amended by mortality among non-DM persons, using interaction between DM / non-DM and age / duration.

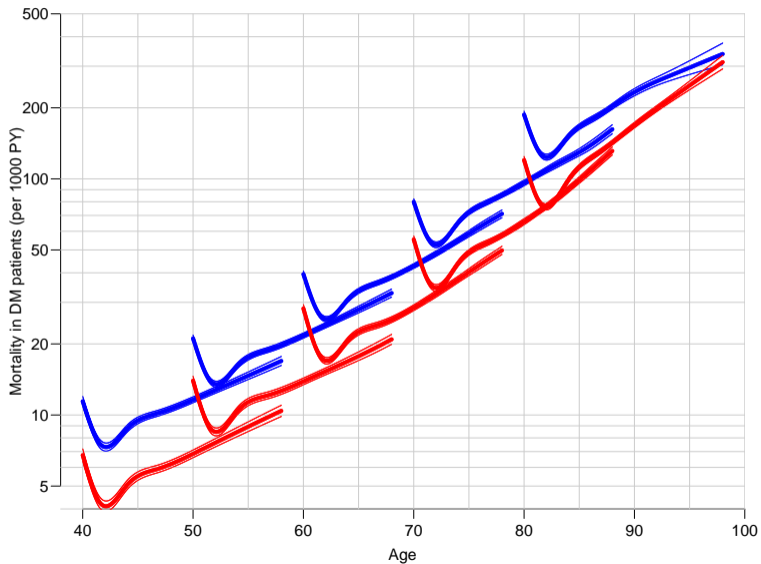
Number of deaths — imbalance

Year	New cases	Deaths	Surplus
1995	14,874	7,377	7,497
1996	15,385	7,147	8,238
1997	15,438	7,366	8,072
1998	16,842	7,457	9,385
1999	17,853	8,058	9,795
2000	18,480	8,242	10,238
2001	19,675	8,521	11,154
2002	21,948	9,072	12,876
2003	23,712	9,427	14,285
2004	23,927	9,421	14,506
2005	22,186	9,879	12,307
2006	23,001	10,227	12,774
2007	24,477	10,544	13,933
2008	26,648	10,647	16,001
2009	26,639	11,455	15,184
2010	27,770	11,767	16,003
2011	32,374	11,782	20,592

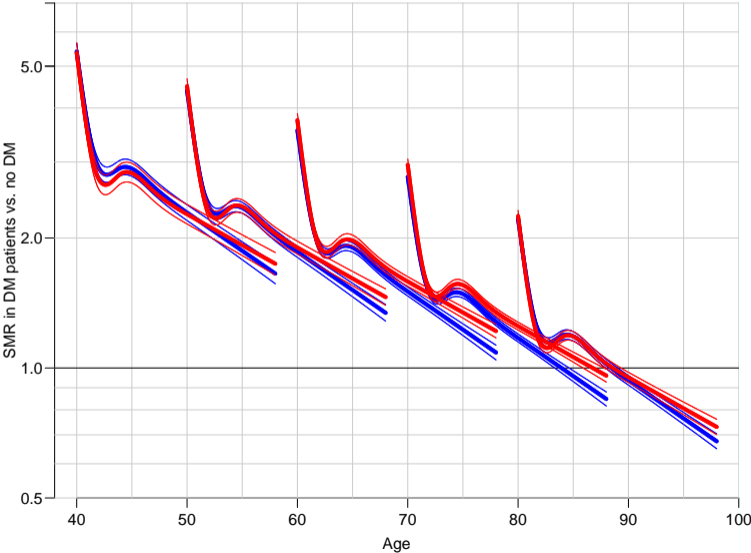
Incident cases Mortality



Mortality among DM patients



SMR relative to persons without DM



Mortality summary

- ▶ Mortality in DM patients increases exponentially by age.
- ▶ Decreasing by time: 4.0/3.8%/year
(non-DM: 2.8/2.4)
- ▶ SMR is the same for men and women.
- ▶ SMR is 3 at age 45, 1 at 85

Summary: Danish Diabetes Register

Note: a register of “administrative” diabetes:

- ▶ Population based 1995–2012 (18 years)
- ▶ Coverage 100%
- ▶ No selection bias at individual level
- ▶ Imprecise diagnostic criteria
- ▶ Incidence rates increasing in general
- ▶ Mortality and SMR decrease
- ▶ Prevalence increases
- ▶ Discontinued . . .

RUKS — Register for Udvalgte Kroniske Sygdomme

- ▶ NDR only updated until 2012 — discontinued
- ▶ RUKS comprises:
 - ▶ Asthma
 - ▶ Dementia
 - ▶ COPD
 - ▶ Arthritis
 - ▶ Osteoporosis
 - ▶ Schizophrenia
 - ▶ Diabetes, type 1
 - ▶ Diabetes, type 2

RUKS definition of T2 DM

- ▶ Two purchases of OAD (A10B)
- ▶ Latest NPR diagnosis is E10 / E11
- ▶ Women with PCOS excluded
- ▶ Date of T1D debut is the first of:
 - ▶ date of first (!) insulin/OAD purchase
 - ▶ date of first NPR recording

RUKS definition of T1 DM

- ▶ Two purchases of insulin (A10A)
- ▶ NPR diagnosis E10
- ▶ Purchase of insulin ± 280 days from GDM diagnosis not counted
- ▶ Persons classified as T2D excluded
- ▶ Date of T1D debut is the first of:
 - ▶ date of first (!) insulin purchase
 - ▶ date of first NPR recording

RUKS definition of T1/T2 DM

- ▶ If a person have no recording of insulin/OAD purchase or diagnosis E10 / E11 in NPR, in a period of 10 years, the person is excluded from RUKS.
- ▶ Not specified whether the person is excluded from registrations earlier than the 10 year limit.
- ▶ The register is not currently (end 2017) available as individual records for research purposes.
- ▶ Work in progress to update the criteria for RUKS.
- ▶ — and make it available for research.

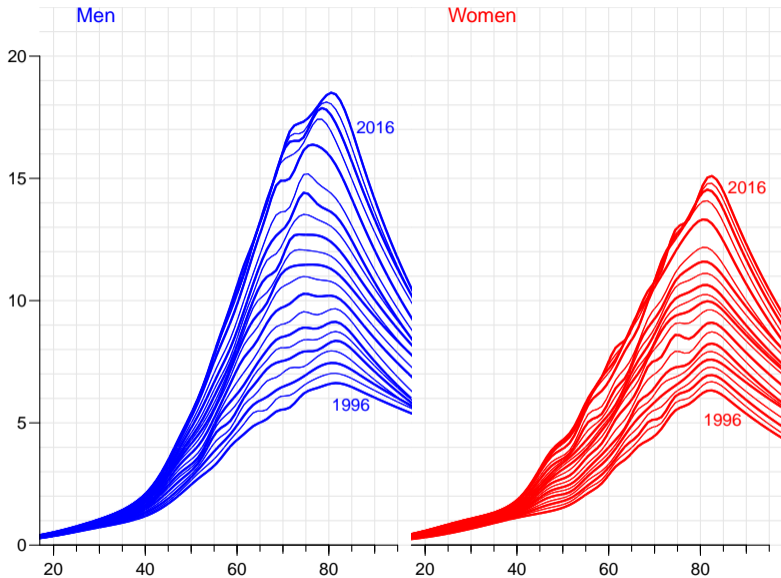
“Private” update of NDR

A side effect of a project at Statistics Denmark

Only available inside the project, though.

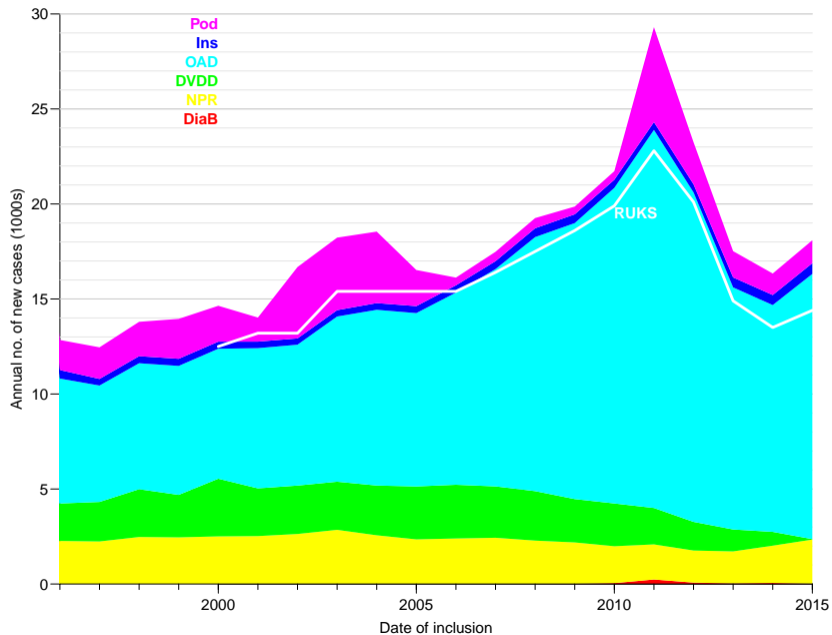
- ▶ No blood glucose criteria used
- ▶ Podiatry (foot therapy) for DM patients
- ▶ GDM window –30 to 365 days
- ▶ PCOS: –30 days from NPR diagnosis
or only metformin in the age-range 20–40 years — excluded
- ▶ T1/T2:
 - ▶ Based on DVDD (Danish Adult Diabetes Database)
 - ▶ Subsequently on NPR
 - ▶ Any OAD before age 15 → T1D
 - ▶ Any insulin before age 30 → T1D
 - ▶ Non-classifiable coded as T2D

Age-specific prevalences of DM according to the reconstructed register.



Annual number of cases by the reconstructed algorithm, according to first criterion met.

White line is the RUKS annual number included



Cancer among diabetes patients

- ▶ Merge the Diabetes Register with the Danish Cancer Register.
- ▶ Compute the RR of cancer between persons with and without diabetes.
- ▶ 25 cancer sites, 2 sexes, age-interaction, duration.

Aims

- ▶ Describe cancer incidence rates among diabetes patients in Denmark.
- ▶ and how rates vary relative to the non-DM population with:
 - ▶ duration of diabetes
 - ▶ duration of insulin use
- ▶ for all types of cancer
- ▶ and for specific sites of cancer

Cancer occurrence in Danish diabetic patients: duration and insulin effects

B. Carstensen · D. R. Witte · S. Friis

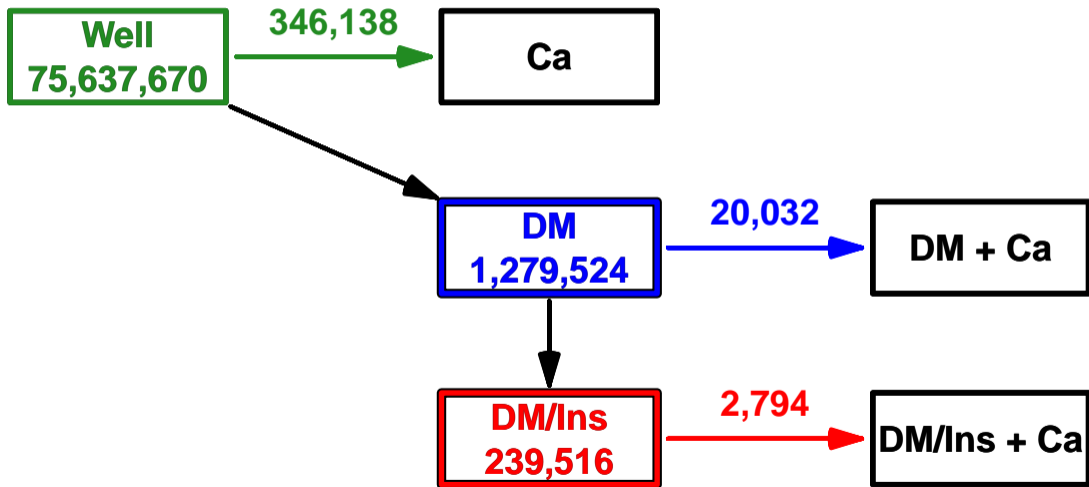
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Abstract

Aims/hypothesis Cancer is more frequent among diabetes patients, but it is unknown how this cancer excess with

population decreased from over 2 at diagnosis to 1.15 after 2 years of diabetes duration. The cancer incidence rate ratio

Follow-up of the Danish population



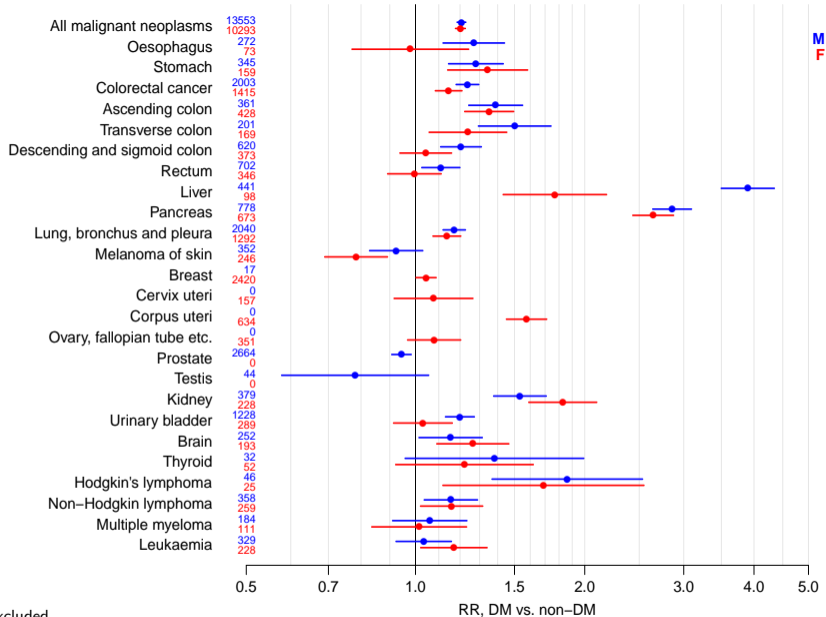
Follow-up in the population

Persons are followed 1 Jan 1995 to:

event: first primary cancer of a given type

censoring:

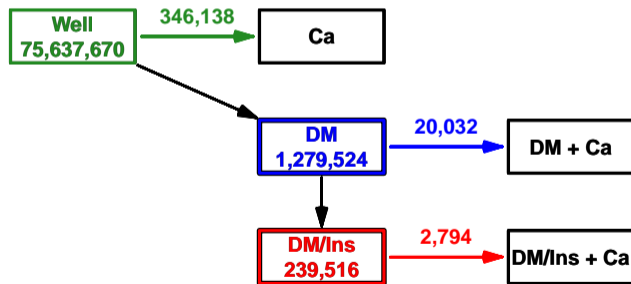
- ▶ diagnosis of any other primary cancer
- ▶ death
- ▶ 31 Dec 2009



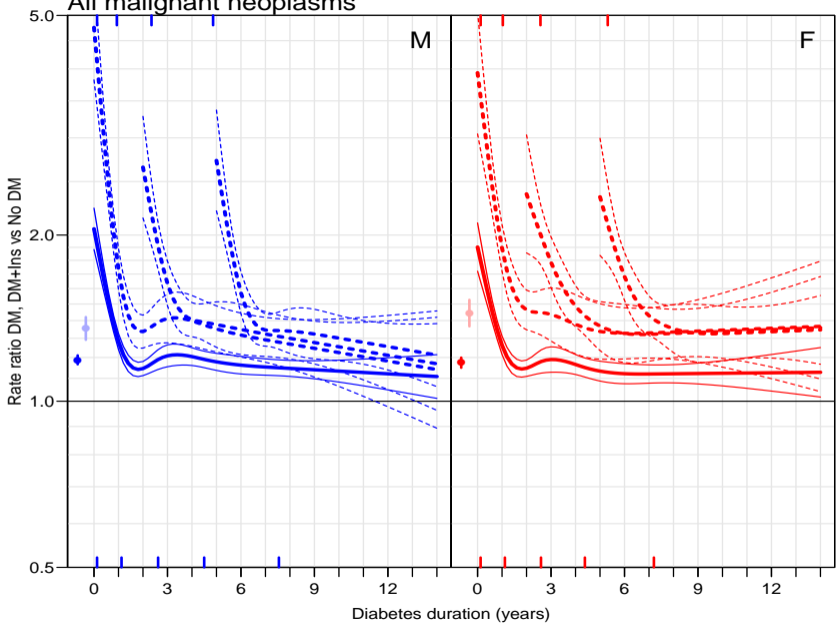
DM prevalent at 1.1.1995 excluded

Duration model

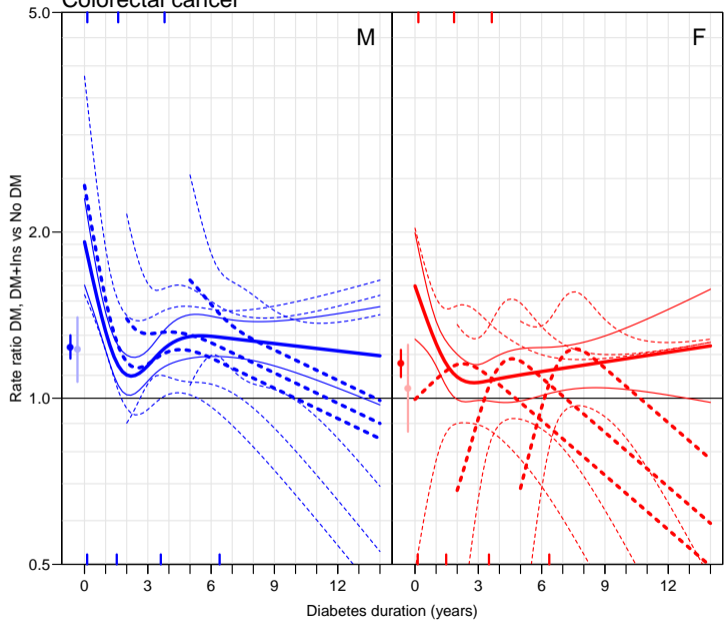
$$\begin{aligned} \text{rate} = & f(\text{age}) \times g(\text{date of FU}) \times h(\text{date of birth}) \\ & \times t(\text{DM-duration}) \\ & \times s(\text{Ins-duration}) \end{aligned}$$



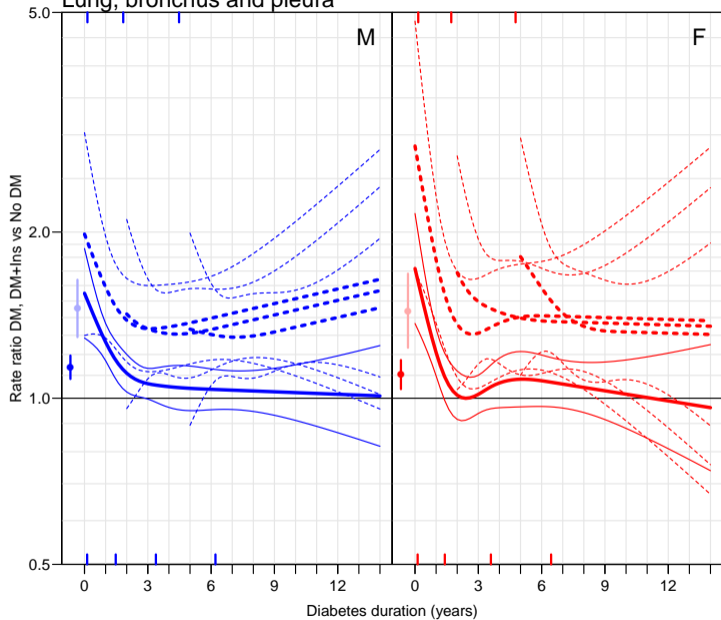
All malignant neoplasms

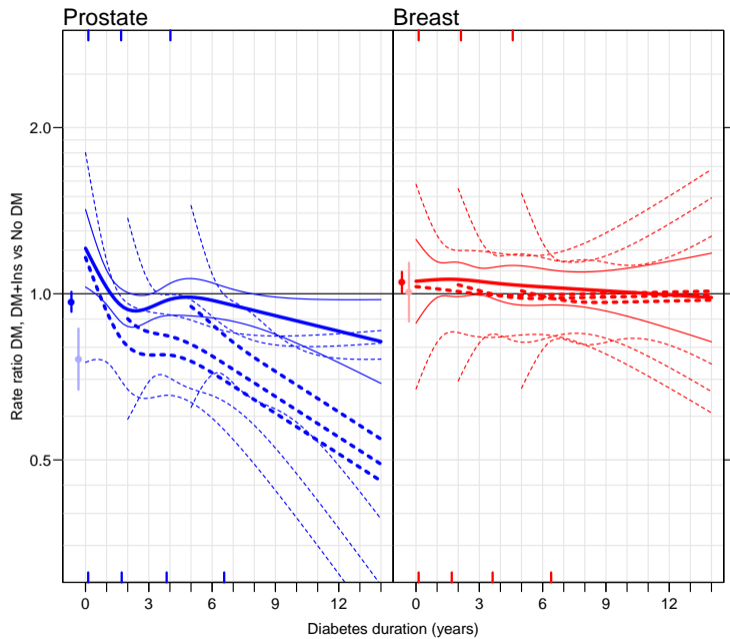


Colorectal cancer



Lung, bronchus and pleura





The Epidemiology of Diabetes and Cancer

Bendix Carstensen · Marit Eika Jørgensen · Søren Friis

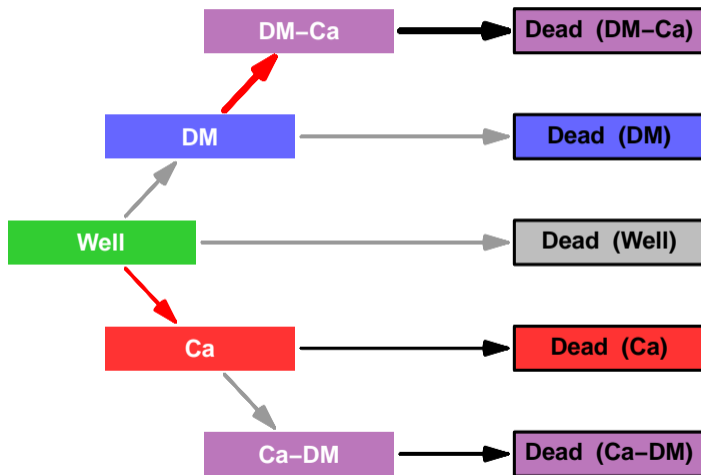
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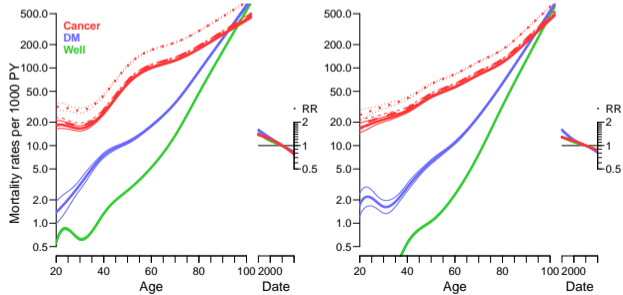
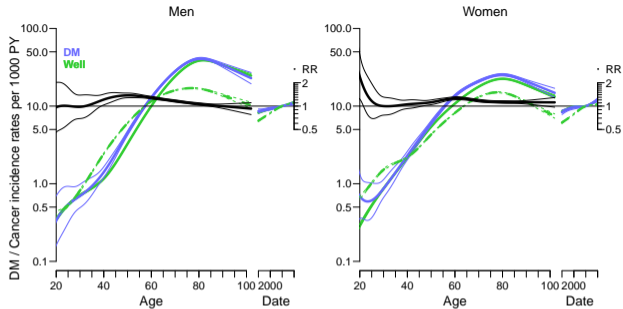
Abstract The literature on cancer occurrence in persons with diabetes has almost invariably been concerned with relative measures. In this paper, we briefly review this, but the aim is to quantify the absolute occurrence of diabetes and cancer in the population in order to give a fuller picture, which also includes the population at large. Overall, we find that

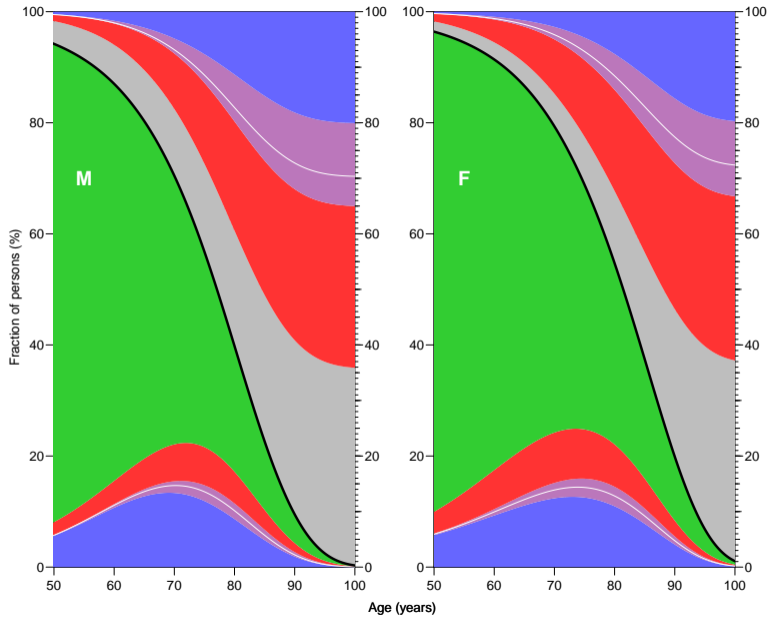
Introduction

The link between diabetes and cancer occurrence is well established, and comprehensive population-based studies have demonstrated that the association relates to both cancer incidence and mortality [1, 2]. Because the association is

Demography: Life time risk







Demography: Cumulative risk

