

Diabetes Register(s)

Register collaboration

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Danish Registers, University of Copenhagen, December 2019

Background for a diabetes register

Population surveillance

Health care surveillance

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

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Results up to 31.12.2006 reported in:

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- ▶ ... improve accuracy of treatment information

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Danish Diabetes Registers - short history

- ▶ **NDR** — established 2006, last year of update 2012
no T1D/T2D distinction

DADD: Danish Adult Diabetes Database - quality register updated annually

NPR: Nation Patient Register

NHSR: National Health Services Register

RMPS: Register of Medicinal Products Statistics - Prescription register

DiaBase: Quality database for eye-screening of diabetes patients

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- ▶ **DMreg** — established 2018 by SDCC Clinical Epidemiology
using Statistics Denmark, has T1D/T2D distinction, based on
DADD, NPR, NHSR, DiaBase & RMPS.
Covers **1996–2016** incl.

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- ▶ Inclusion start at 1.1.1990.

Inclusion criteria for the register

- ▶ Diagnosis of DM in NPR.

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- ▶ 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	7/54
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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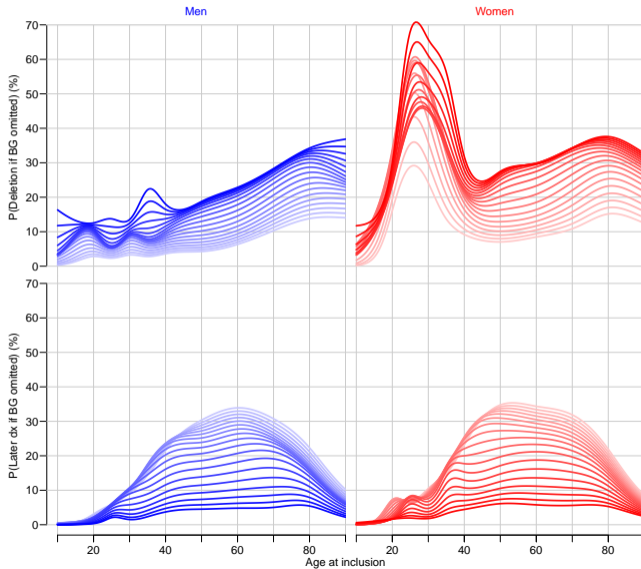
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- ▶ The new diagnostic criteria based on HbA1c makes the blood glucose criteria even more uncertain.
- ▶ No consensus on how to proceed.

Excluded if BG criteria omitted



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 - ▶ Diabetes, type 2

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RUKS definition of T1 DM

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- ▶ Not specified whether the person is excluded from registrations earlier than the 10 year limit.

Reconstructed Diabetes Register — sources

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- ▶ Inclusion data is the first occurrence in any of these as a diabetes patient

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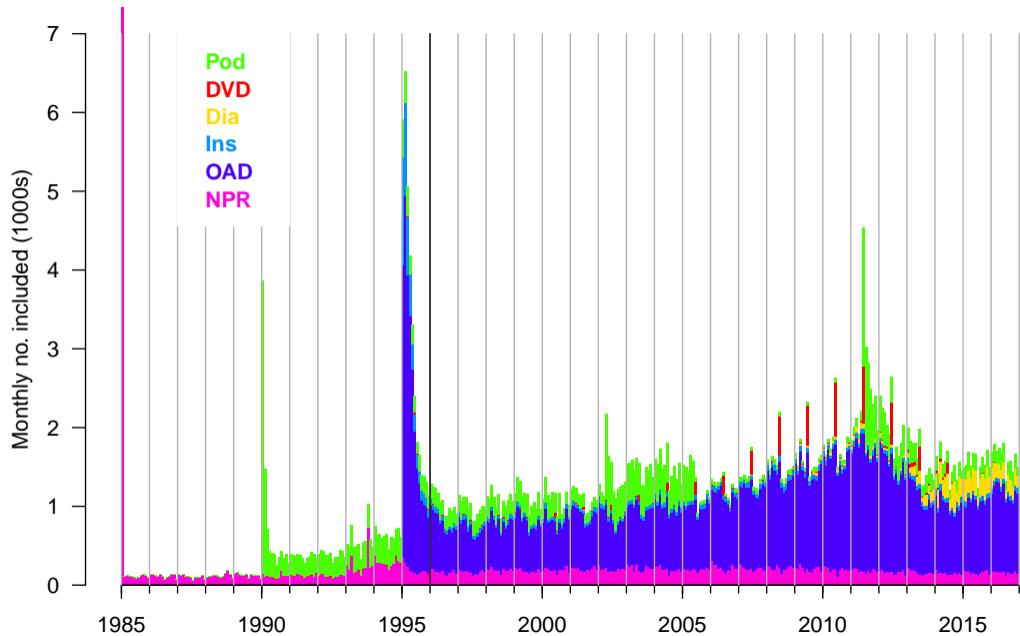
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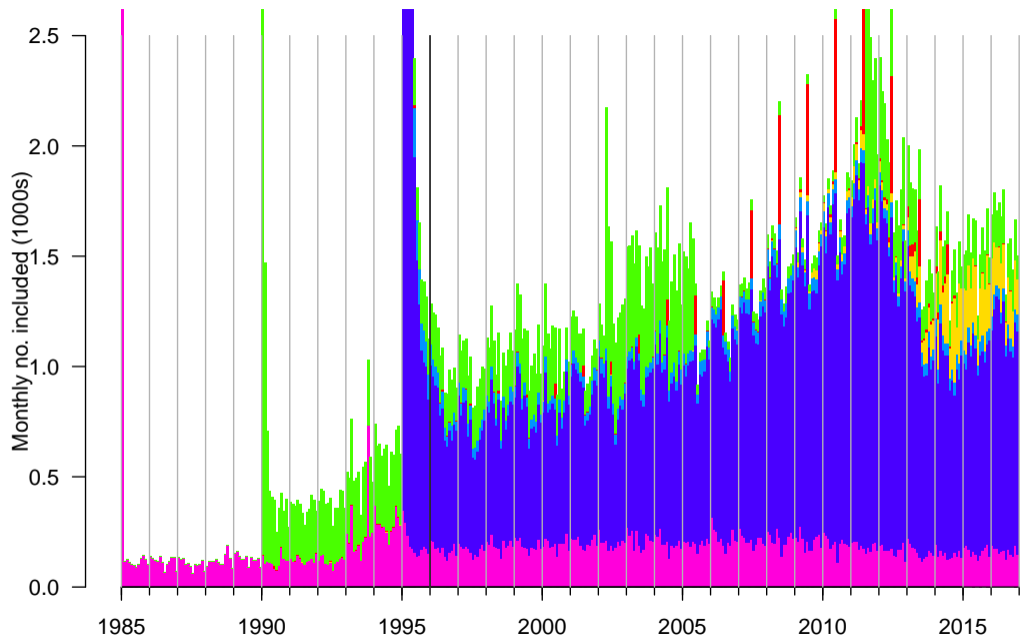
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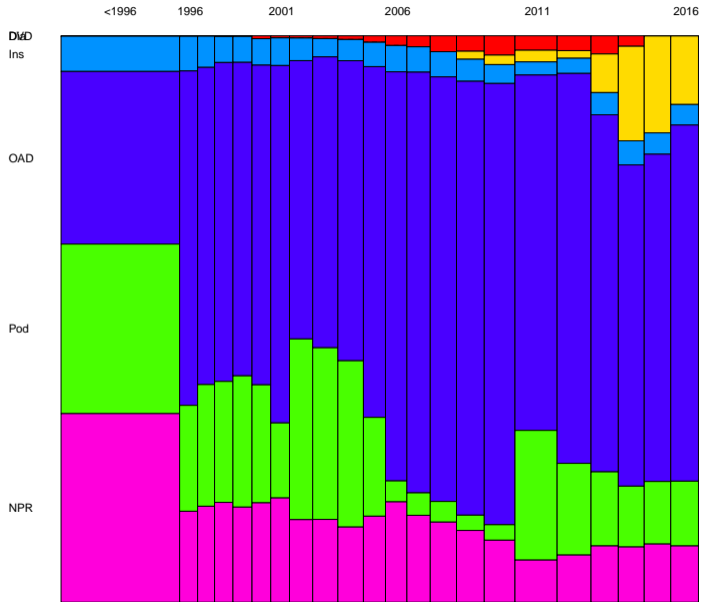
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 - ▶ Any insulin before age 30 → T1D

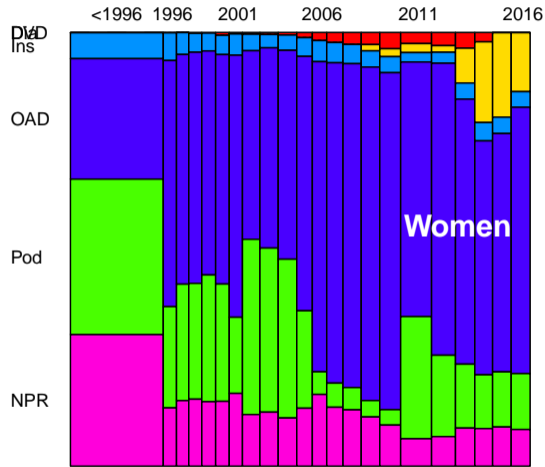
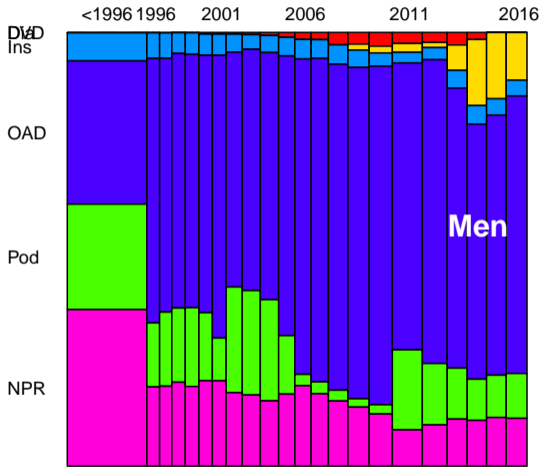
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- ▶ T1/T2 classification:
 - ▶ Based on DVDD (Danish Adult Diabetes Database)
 - ▶ Subsequently on NPR
 - ▶ Any OAD before age 15 → T1D
 - ▶ Any insulin before age 30 → T1D
 - ▶ Non-classifiable coded as T2D



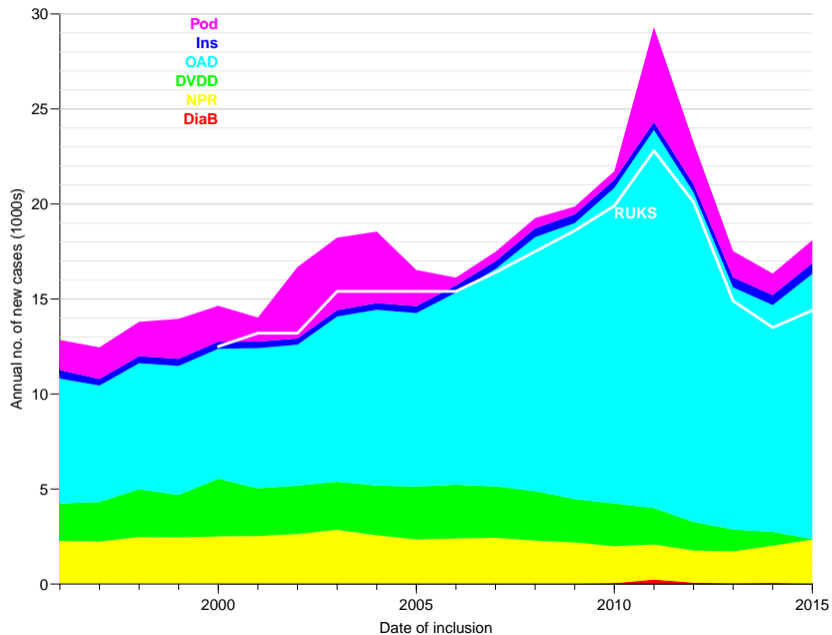




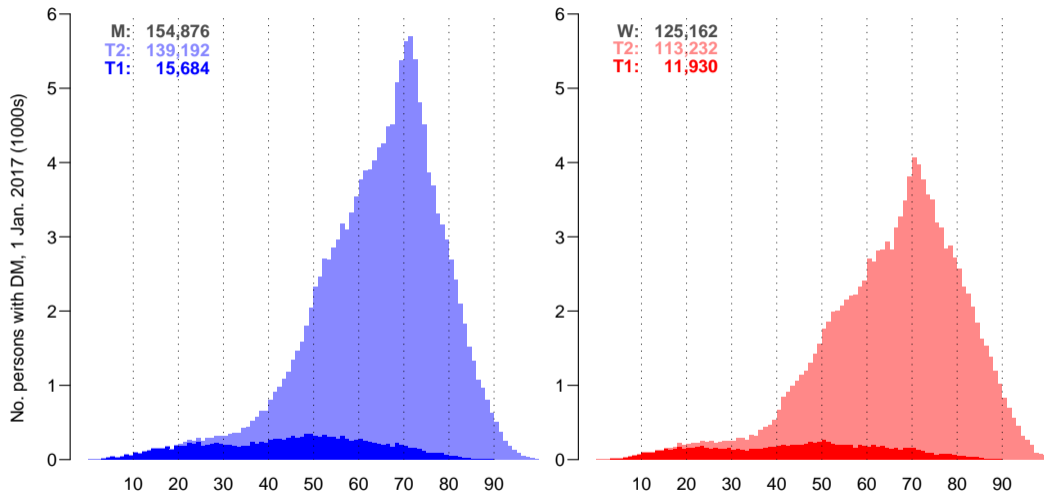


Annual number of cases by the reconstructed algorithm, according to first criterion met.

White line is the RUKS annual number included



Number of diabetes patients 2017-01-01



Prevalence: Methods

- ▶ Prevalent cases by 1 Jan 1995, . . . , 2017 tabulated by sex and 1-year age.

Prevalence: Methods

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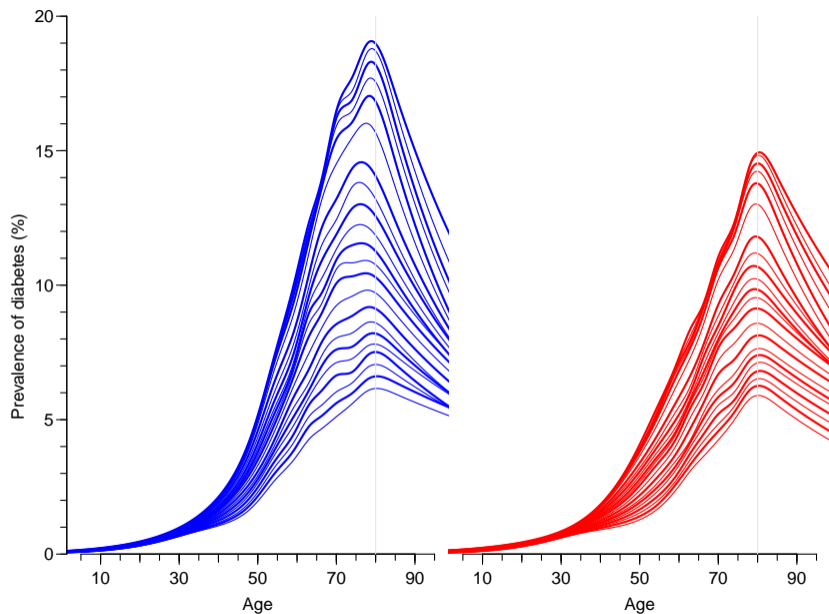
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- ▶ Prevalence analysed by a binomial model with log-link and the population size as denominator.
- ▶ Separate parametric terms used for each sex and date.
- ▶ One age-specific prevalence curve for each sex and year.

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

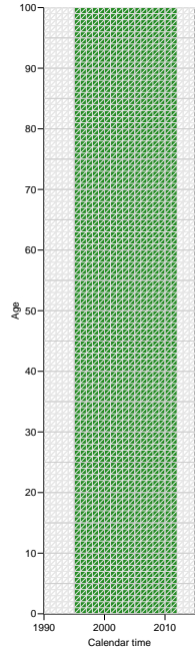


Incidence: New cases included

Period	T1D		T2D		All DM		
	M	W	M	W	M	W	M+W
1996	725	527	6,269	5,345	6,994	5,872	12,866
1997	649	528	6,192	5,264	6,841	5,792	12,633
1998	714	503	7,019	5,844	7,733	6,347	14,080
1999	654	451	7,415	6,203	8,069	6,654	14,723
2000	692	479	8,450	7,005	9,142	7,484	16,626
2001	655	455	7,391	6,090	8,046	6,545	14,591
2002	621	423	8,410	7,474	9,031	7,897	16,928
2003	588	412	9,468	8,140	10,056	8,552	18,608
2004	583	453	9,782	8,288	10,365	8,741	19,106
2005	585	427	9,163	7,621	9,748	8,048	17,796
2006	584	440	9,050	7,193	9,634	7,633	17,267
2007	585	450	9,636	7,966	10,221	8,416	18,637
2008	603	438	10,831	8,792	11,434	9,230	20,664
2009	596	392	10,962	8,509	11,558	8,901	20,459
2010	587	405	11,876	9,333	12,463	9,738	22,201
2011	537	401	13,363	11,084	13,900	11,485	25,385
2012	517	347	10,981	9,013	11,498	9,360	20,858
2013	495	398	8,650	6,829	9,145	7,227	16,372
2014	495	398	8,637	6,443	9,132	6,841	15,973
2015	520	406	9,569	7,354	10,089	7,760	17,849
2016	518	363	10,404	7,819	10,922	8,182	19,104
Sum	12,503	9,096	193,518	157,609	206,021	166,705	372,726

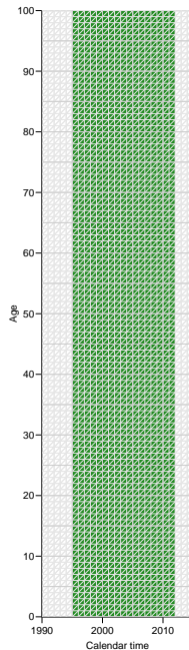
Incidence: Methods

- ▶ New cases tabulated by age and date of diagnosis (1996-2016) and date of birth, in 1-year classes.



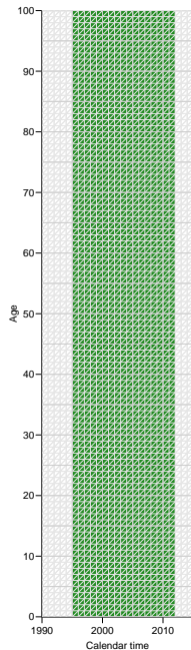
Incidence: Methods

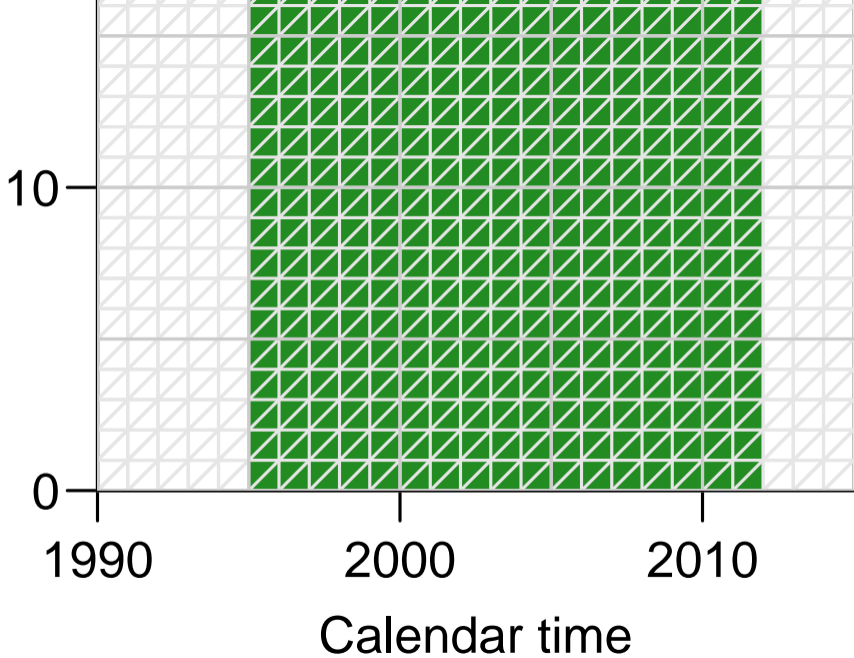
- ▶ New cases tabulated by age and date of diagnosis (1996-2016) and date of birth, in 1-year classes.
- ▶ Corresponding person-years figures from Statistics Denmark — person-years in the diabetes register subtracted.



Incidence: Methods

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- ▶ 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 and date of birth, using log-person-years as offset.





Digression: Lexis diagram



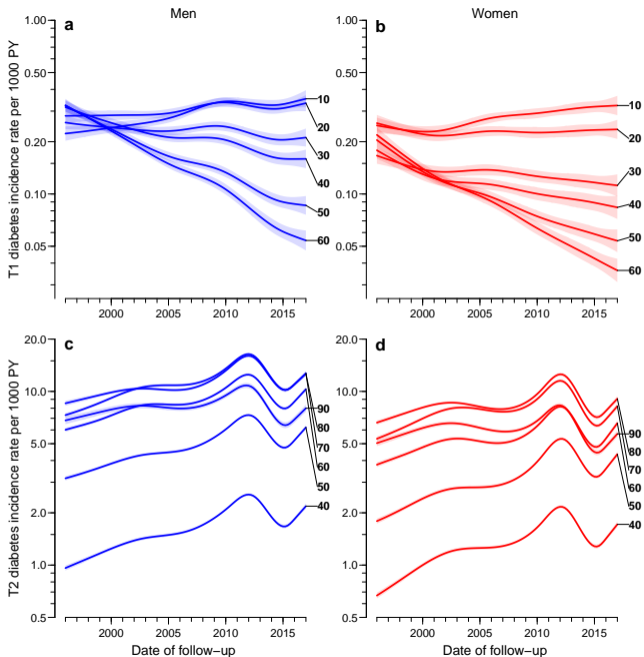
Wilhelm Lexis (1837–1914)
German demographer, statistician and
economist.



Incidence rates in different ages.

Note the different *y*-axes for T1D and T2D.

T2D is 10 times more common than T1D.



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.

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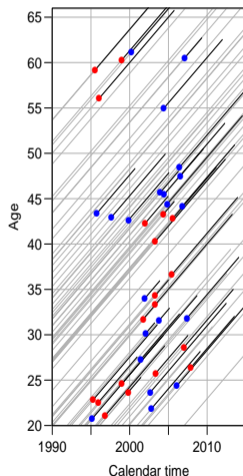
Methods: Mortality and SMR

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- ▶ SMR analysed using dataset amended by mortality among non-DM persons, using interaction between DM / non-DM and age / duration.

Number of deaths — imbalance

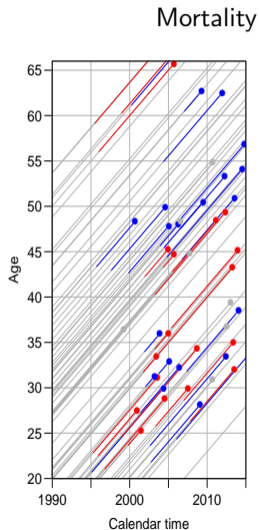
Year	New cases	Deaths	Surplus
1996	12,866	6,116	6,750
1997	12,633	6,306	6,327
1998	14,080	6,397	7,683
1999	14,723	6,841	7,882
2000	16,626	6,947	9,679
2001	14,591	7,054	7,537
2002	16,928	7,406	9,522
2003	18,608	7,747	10,861
2004	19,106	7,609	11,497
2005	17,796	7,902	9,894
2006	17,267	8,000	9,267
2007	18,637	8,158	10,479
2008	20,664	8,034	12,630
2009	20,459	8,716	11,743
2010	22,201	8,808	13,393
2011	25,385	8,839	16,546
2012	20,858	9,158	11,700
2013	16,372	9,431	6,941
2014	15,973	9,746	6,227
2015	17,849	10,079	7,770
2016	19,104	10,259	8,845

Incident cases

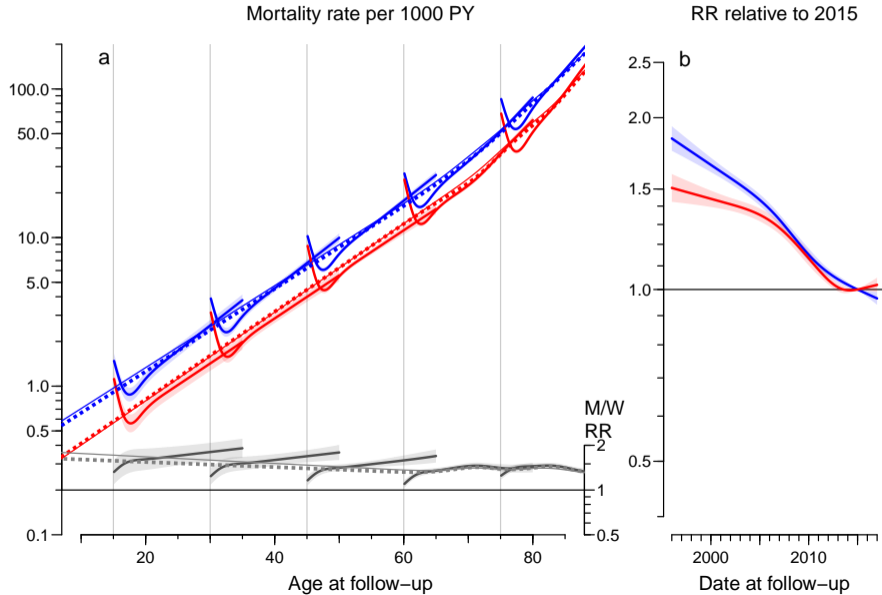


Number of deaths — imbalance

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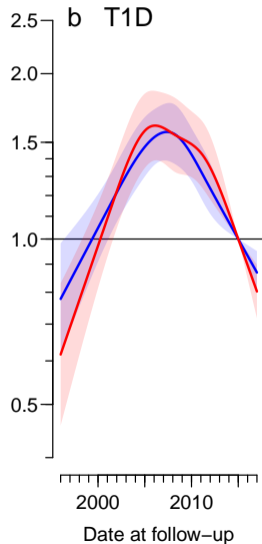
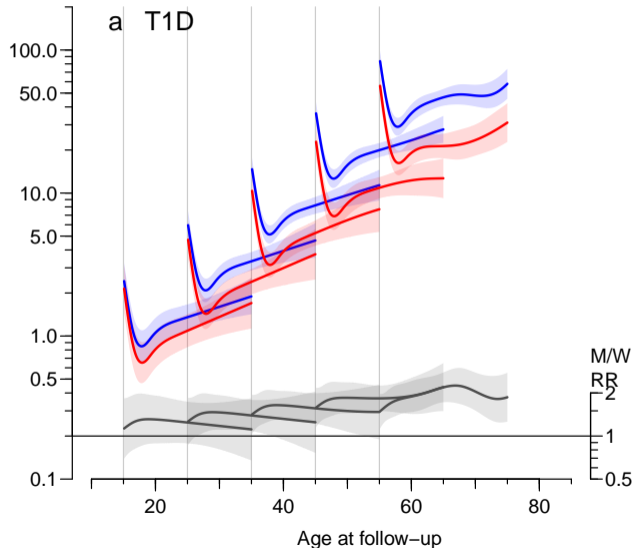
Mortality among DM patients



Mortality among T1D patients

Mortality rate per 1000 PY

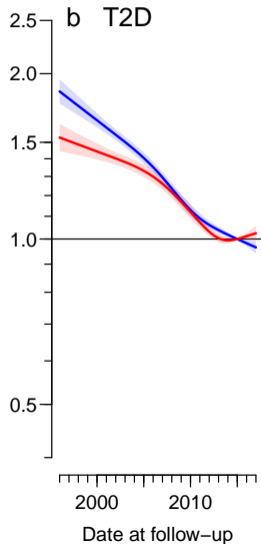
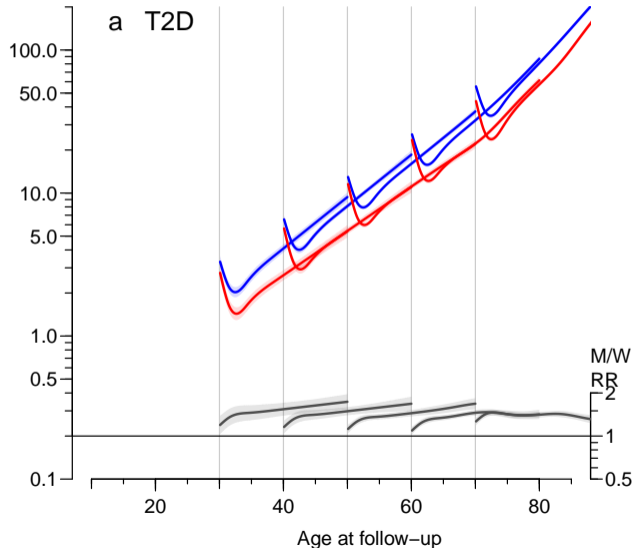
Rate ratio relative to 2015



Mortality among T2D patients

Mortality rate per 1000 PY

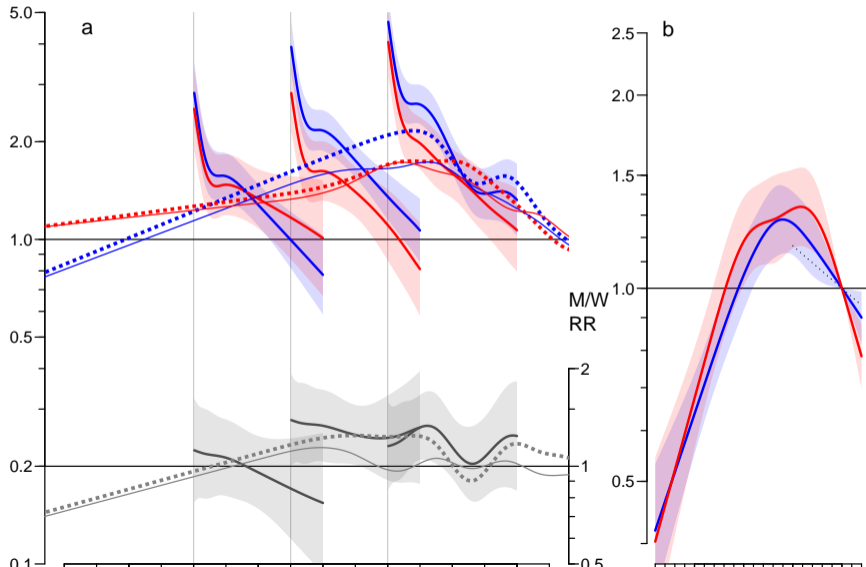
Rate ratio relative to 2015



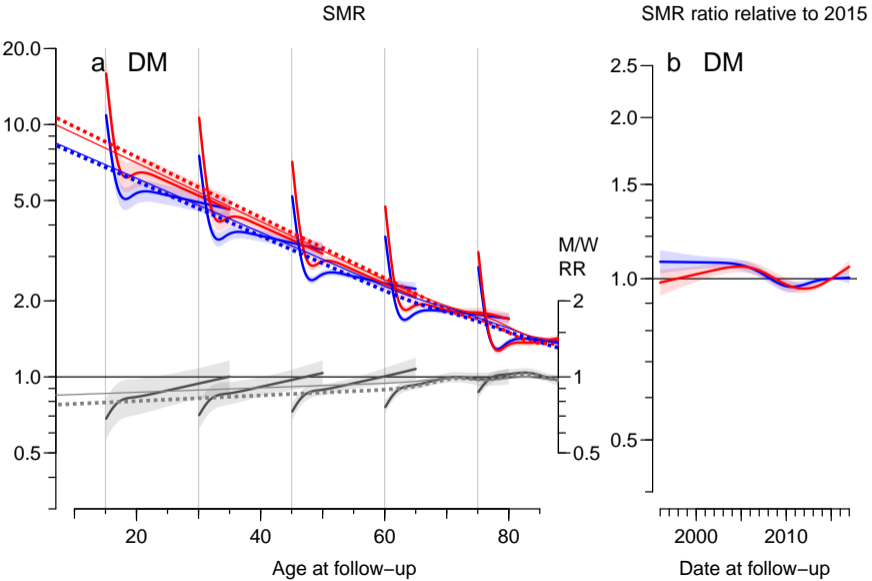
Mortality RR between T1D/T2D

T1D vs. T2D mortality rate-ratio at 2015

RR ratio relative to 2015



SMR relative to persons without DM



Mortality summary

- ▶ Mortality in DM patients increases exponentially by age.

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- ▶ Duration effects differs between T1D and T2D:
 - ▶ T1D: smaller mortality for longer duration
 - ▶ T2D: larger mortality for longer duration
- ▶ SMR is (almost) the same for men and women.
- ▶ SMR is 3 at age 45, 1.5 at 80

Cancer among diabetes patients

Cancer among diabetes patients

- ▶ Merge the Diabetes Register with the Danish Cancer Register.

Cancer among diabetes patients

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- ▶ Compute the RR of cancer between persons with and without diabetes.

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.

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Aims

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 - ▶ 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

Received: 5 April 2011 / Accepted: 31 October 2011 / Published online: 27 November 2011
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Abstract

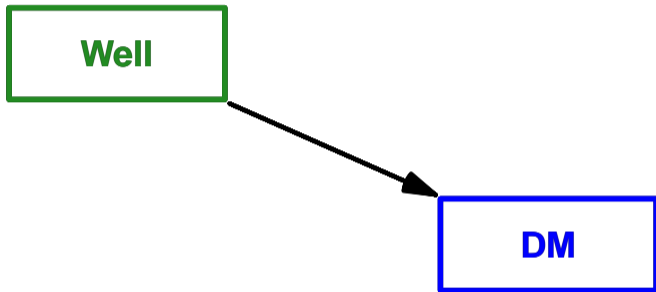
Aims/hypothesis Cancer is more frequent among diabetes patients, but it is unknown how this cancer excess with

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

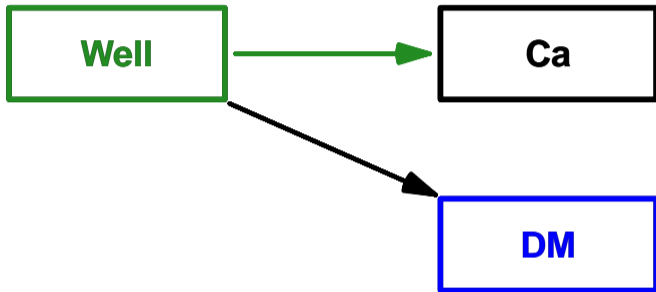
Follow-up of the Danish population

Well

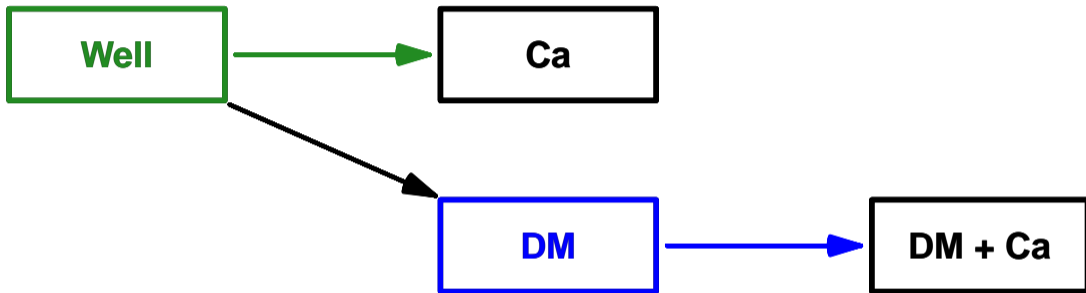
Follow-up of the Danish population



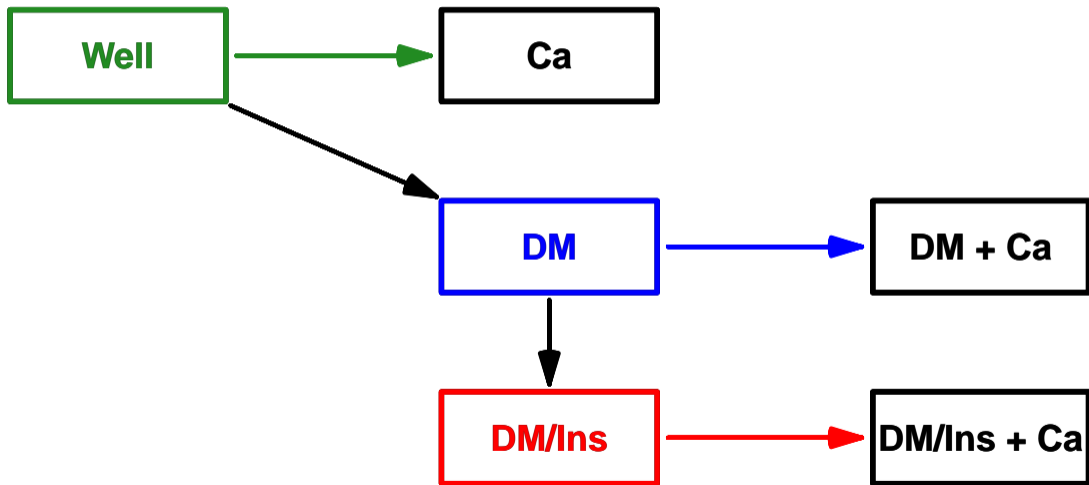
Follow-up of the Danish population



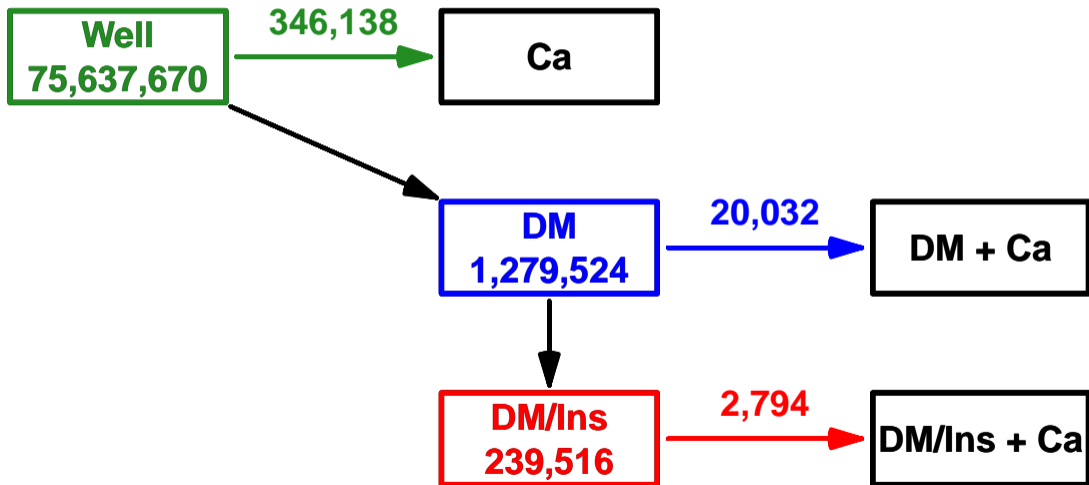
Follow-up of the Danish population



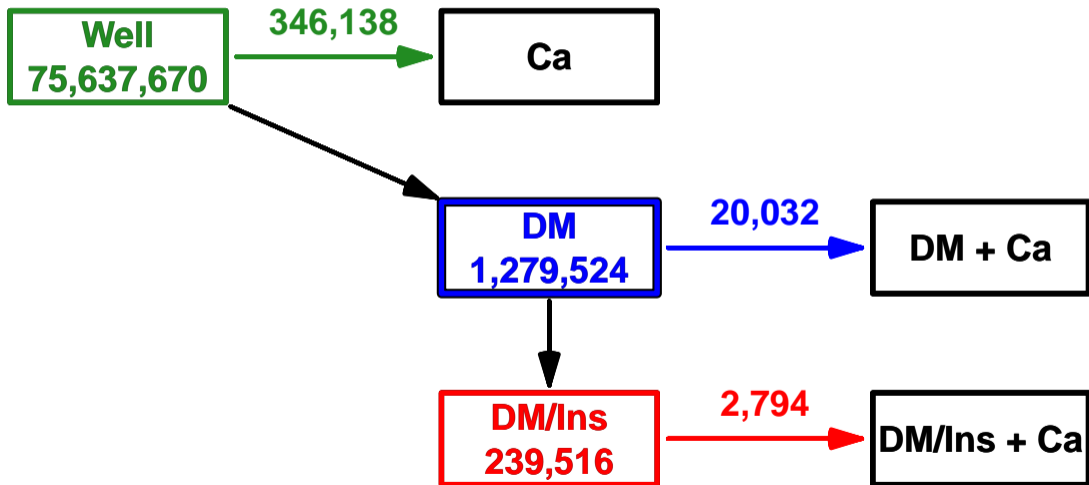
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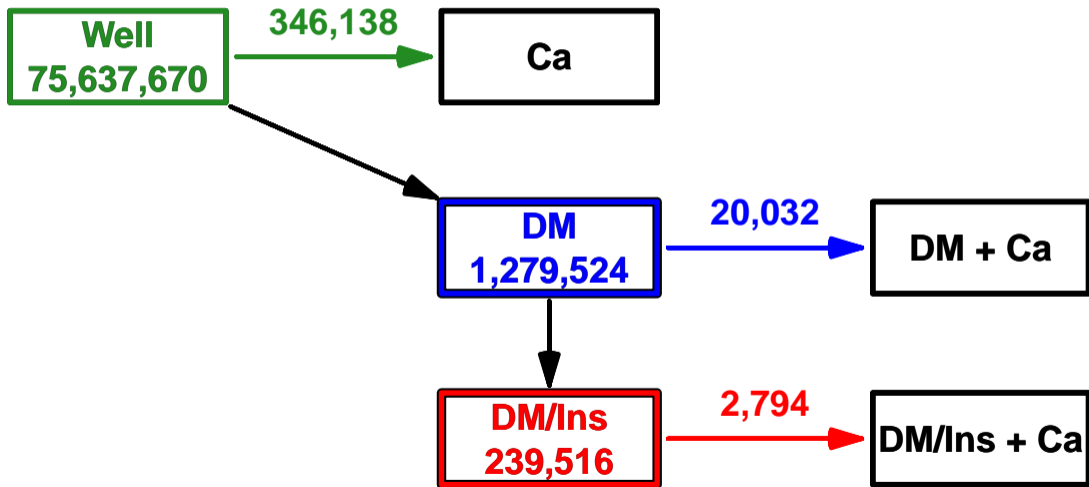
Follow-up of the Danish population



Follow-up of the Danish population



Follow-up of the Danish population



Follow-up in the population

Persons are followed 1 Jan 1995 to:

Follow-up in the population

Persons are followed 1 Jan 1995 to:

event: first primary cancer of a given type

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Persons are followed 1 Jan 1995 to:

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censoring: ▶ diagnosis of any other primary cancer

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censoring:

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- ▶ death

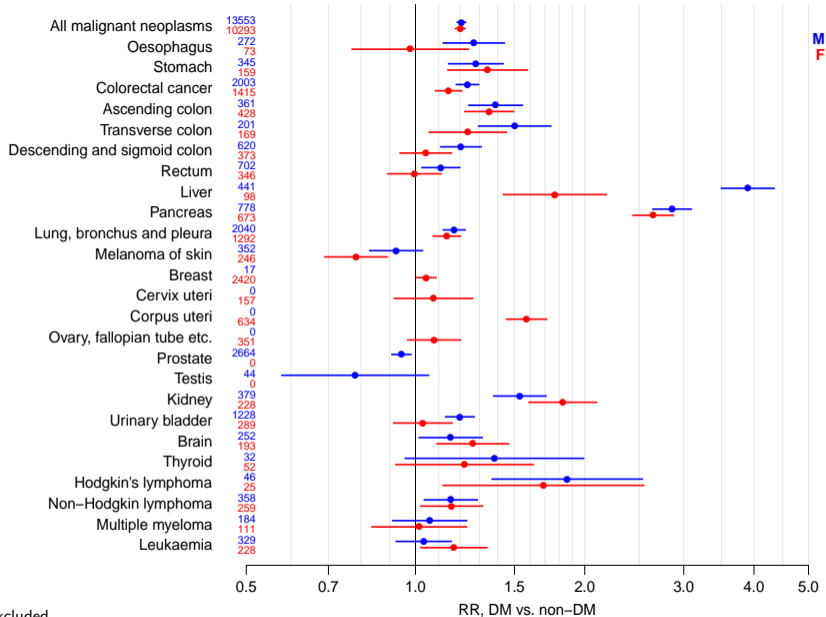
Follow-up in the population

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



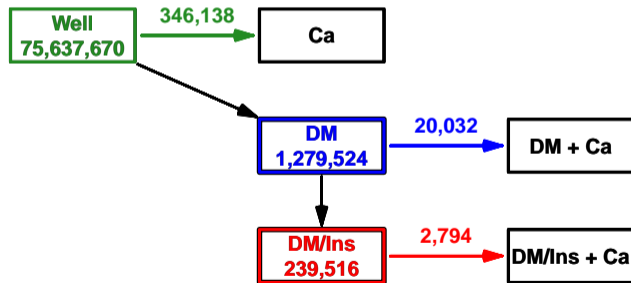
DM prevalent at 1.1.1995 excluded

Duration model

$$\text{rate} = f(\text{age}) \times g(\text{date of FU}) \times h(\text{date of birth})$$

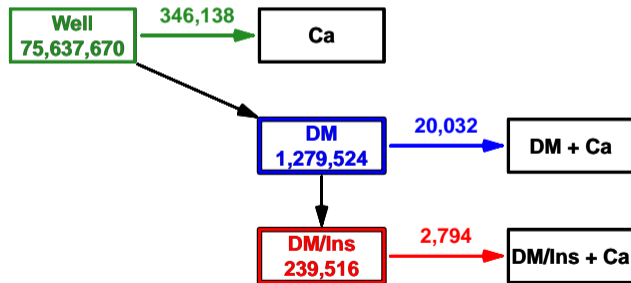
Duration model

$$\text{rate} = f(\text{age}) \times g(\text{date of FU}) \times h(\text{date of birth})$$



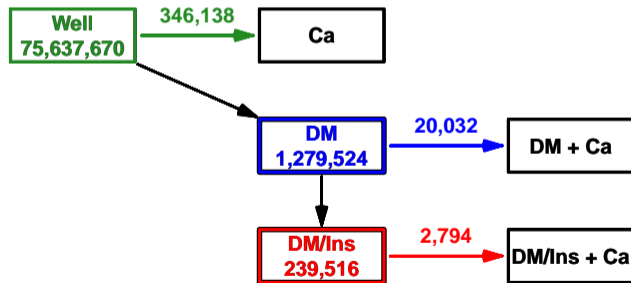
Duration model

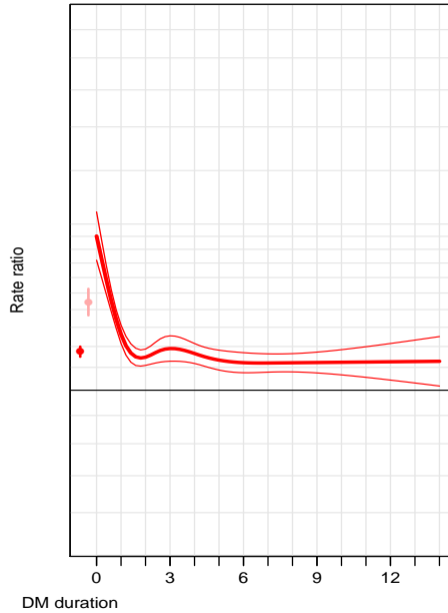
$$\text{rate} = f(\text{age}) \times g(\text{date of FU}) \times h(\text{date of birth}) \\ \times t(\text{DM-duration})$$

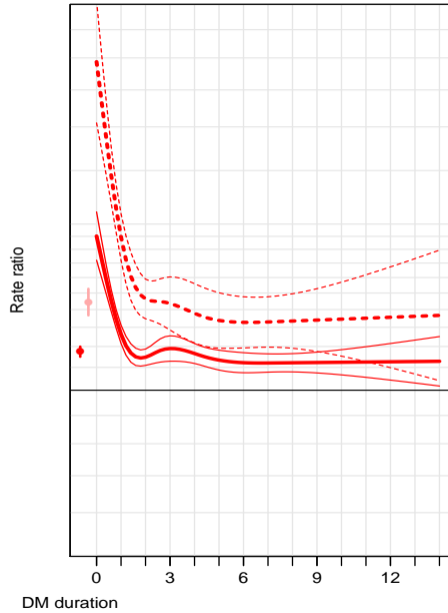


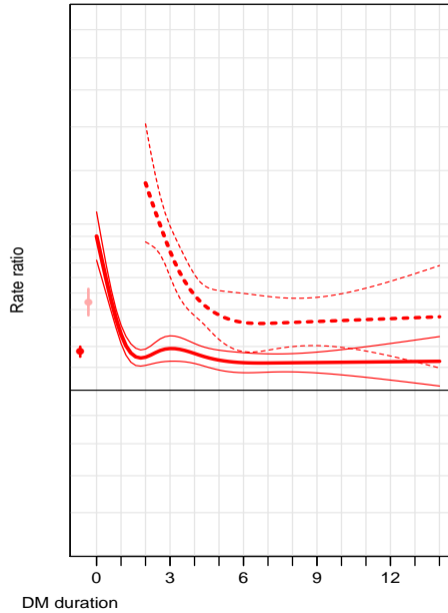
Duration model

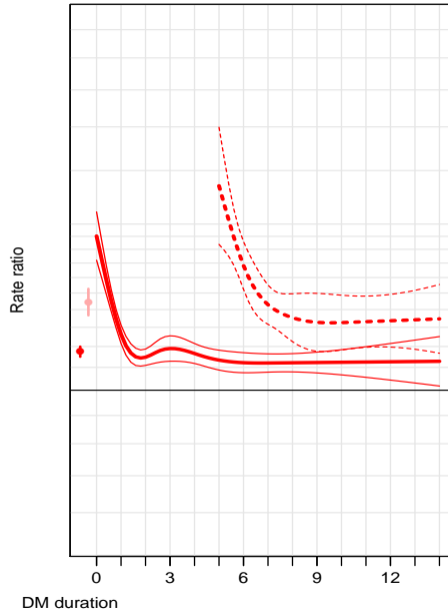
$$\begin{aligned} \text{rate} = & f(\text{age}) \times g(\text{date of FU}) \times h(\text{date of birth}) \\ & \times t(\text{DM-duration}) \\ & \times s(\text{Ins-duration}) \end{aligned}$$

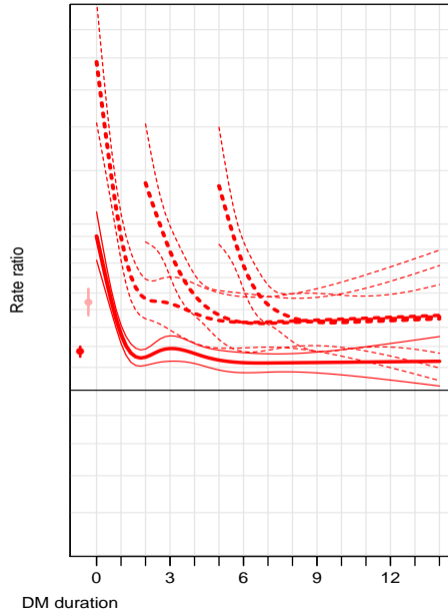




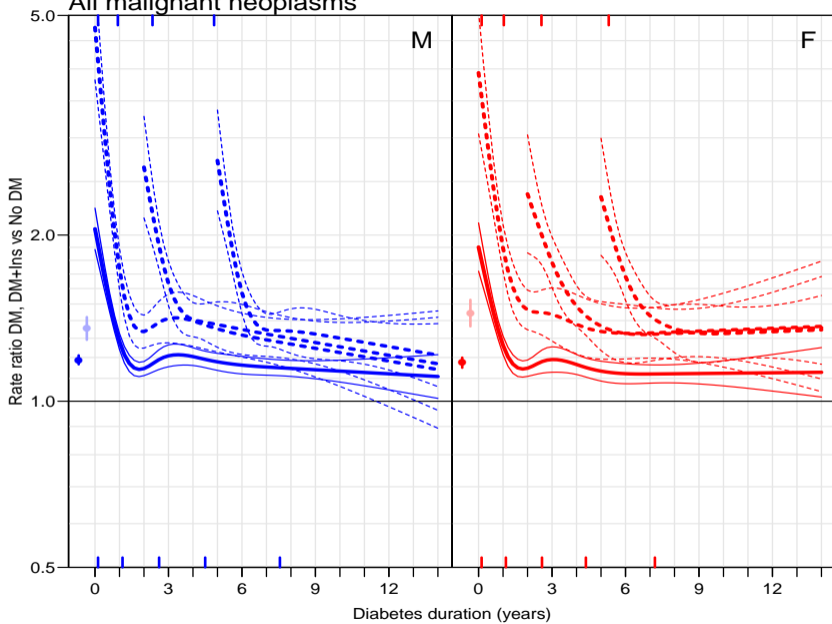




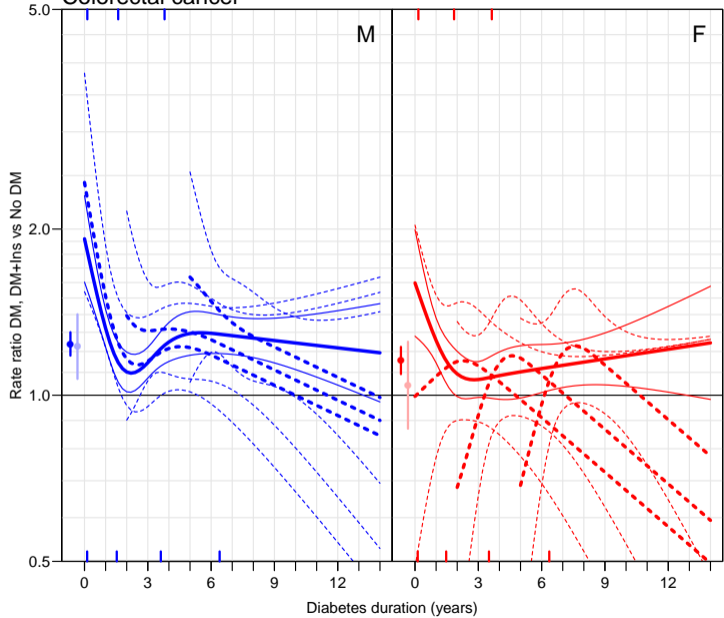




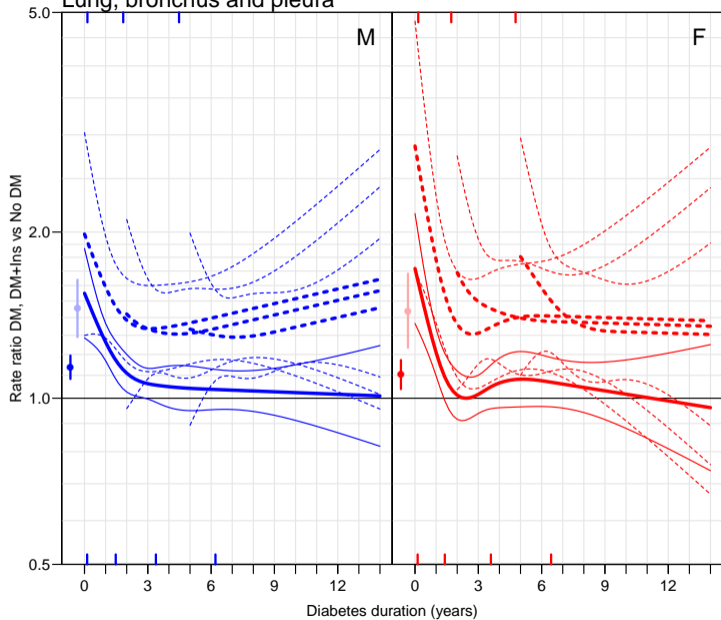
All malignant neoplasms

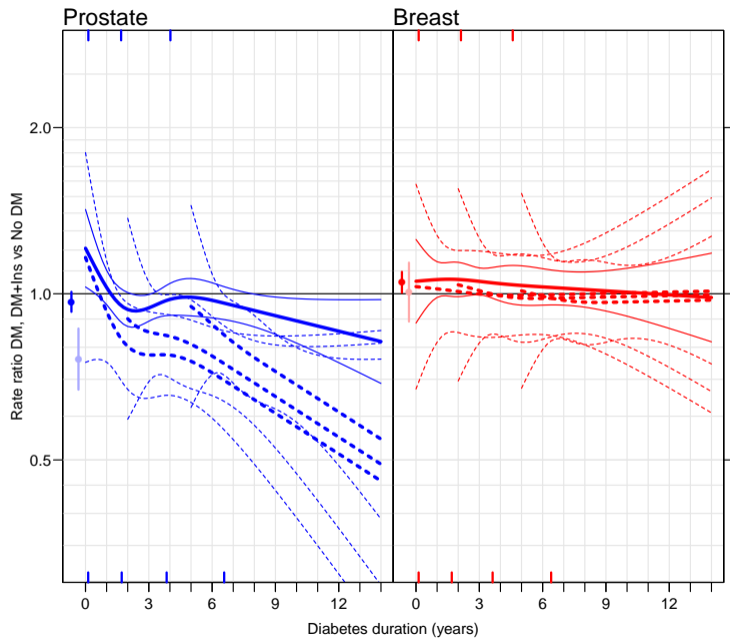


Colorectal cancer



Lung, bronchus and pleura





The Epidemiology of Diabetes and Cancer

Bendix Carstensen · Marit Eika Jørgensen · Søren Friis

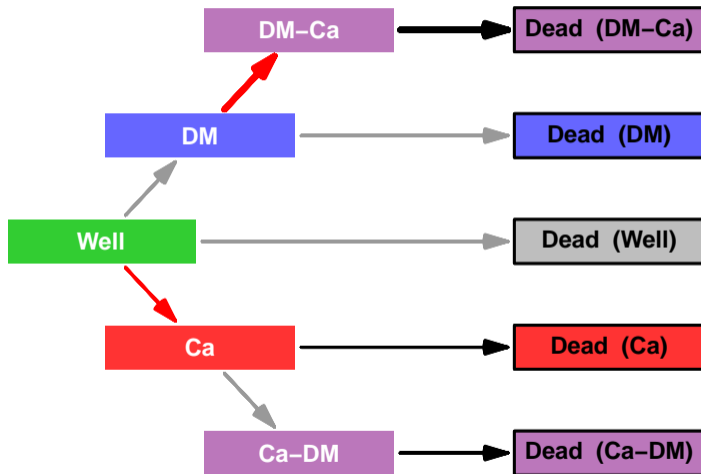
© Springer Science+Business Media New York 2014

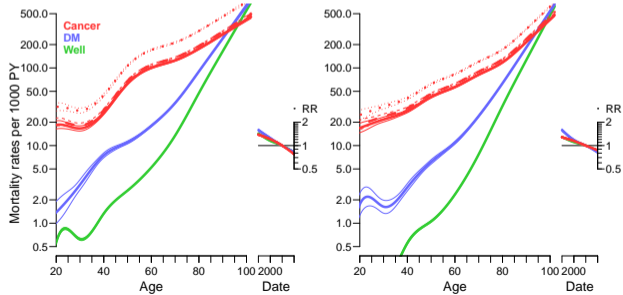
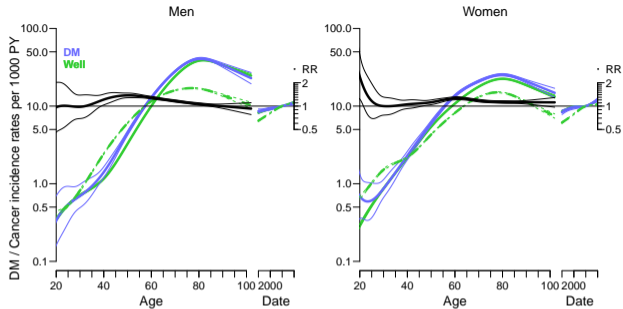
Abstract The literature on cancer occurrence in persons with diabetes has almost invariably been concerned with relative measures. In this paper, we briefly review this, but the aim is to quantify the absolute occurrence of diabetes and cancer in the population in order to give a fuller picture, which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

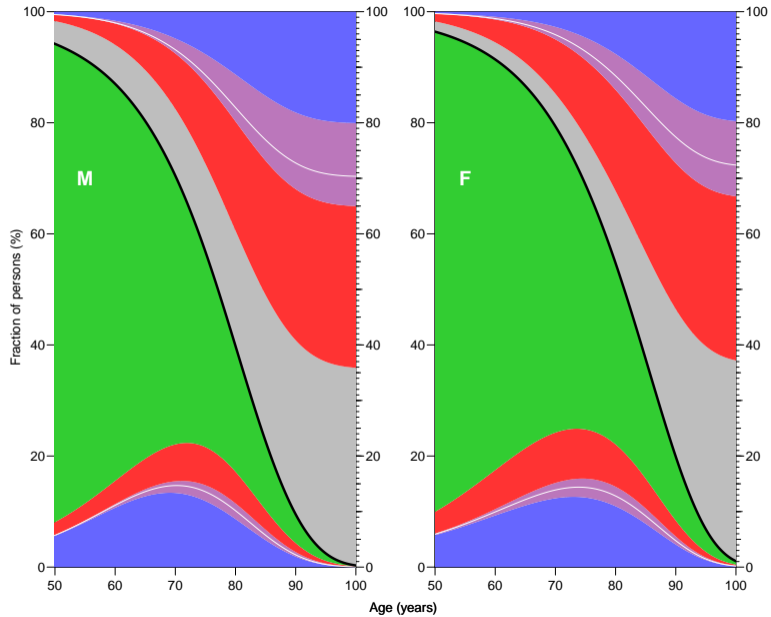
Introduction

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]. Based on the epidemiological

Demography: Life time risk







Demography: Cumulative risk

