

Register, Prevalence, Incidence and Mortality of T1 and T2 Diabetes in Denmark 1996–2016 and beyond

Bendix Carstensen Senior Statistician <http://BendixCarstensen.com>
Steno Diabetes Center Copenhagen
Clinical Epidemiology

Pernille F Rønn Post Doc, SDCC Clinical Epidemiology

Marit E Jørgensen Professor, Senior Consultant, Head, SDCC Clinical Epidemiology

NNFoundation, 21 January 2019

Background

- ▶ Indications that T2D is plateauing or decreasing lately

Background

- ▶ Indications that T2D is plateauing or decreasing lately
- ▶ Little is established on the relative occurrence of T1D and T2D

Background

- ▶ Indications that T2D is plateauing or decreasing lately
- ▶ Little is established on the relative occurrence of T1D and T2D

Background

- ▶ Indications that T2D is plateauing or decreasing lately
- ▶ Little is established on the relative occurrence of T1D and T2D

Key questions:

- ▶ How are trends in T1D resp. T2D prevalence and incidence

Background

- ▶ Indications that T2D is plateauing or decreasing lately
- ▶ Little is established on the relative occurrence of T1D and T2D

Key questions:

- ▶ How are trends in T1D resp. T2D prevalence and incidence
- ▶ Mortality by age, duration and diagnosis age

Background

- ▶ Indications that T2D is plateauing or decreasing lately
- ▶ Little is established on the relative occurrence of T1D and T2D

Key questions:

- ▶ How are trends in T1D resp. T2D prevalence and incidence
- ▶ Mortality by age, duration and diagnosis age
- ▶ Difference in mortality between T1D and T2D

Background

- ▶ Indications that T2D is plateauing or decreasing lately
- ▶ Little is established on the relative occurrence of T1D and T2D

Key questions:

- ▶ How are trends in T1D resp. T2D prevalence and incidence
- ▶ Mortality by age, duration and diagnosis age
- ▶ Difference in mortality between T1D and T2D

Background

- ▶ Indications that T2D is plateauing or decreasing lately
- ▶ Little is established on the relative occurrence of T1D and T2D

Key questions:

- ▶ How are trends in T1D resp. T2D prevalence and incidence
- ▶ Mortality by age, duration and diagnosis age
- ▶ Difference in mortality between T1D and T2D

Remedy: Population based registers in Denmark

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

Danish Diabetes Registers - short history

- ▶ **NDR** — established 2006, last year of update 2012
no T1D/T2D distinction
- ▶ **RUKS** — Started 2015, initially not available for linkage
has T1D/T2D distinction, based **only** on NPR & RMPS

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

Danish Diabetes Registers - short history

- ▶ **NDR** — established 2006, last year of update 2012
no T1D/T2D distinction
- ▶ **RUKS** — Started 2015, initially not available for linkage
has T1D/T2D distinction, based **only** on NPR & RMPS
- ▶ **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.

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

Sources for the DMreg

- ▶ NPR, National Patient Register

Sources for the DMreg

- ▶ NPR, National Patient Register
- ▶ RMPS, Register of Medicinal Product Statistics

Sources for the DMreg

- ▶ NPR, National Patient Register
- ▶ RMPS, Register of Medicinal Product Statistics
- ▶ NHSR, National Health Services Register

Sources for the DMreg

- ▶ NPR, National Patient Register
- ▶ RMPS, Register of Medicinal Product Statistics
- ▶ NHSR, National Health Services Register
- ▶ DADD, Danish Adult Diabetes Database
 - annual clinical status since 2005
 - complete for T1D, not for T2D
 - date only used if no other criteria met

Sources for the DMreg

- ▶ NPR, National Patient Register
- ▶ RMPS, Register of Medicinal Product Statistics
- ▶ NHSR, National Health Services Register
- ▶ DADD, Danish Adult Diabetes Database
 - annual clinical status since 2005
 - complete for T1D, not for T2D
 - date only used if no other criteria met
- ▶ DiaBase, Eyescreening database

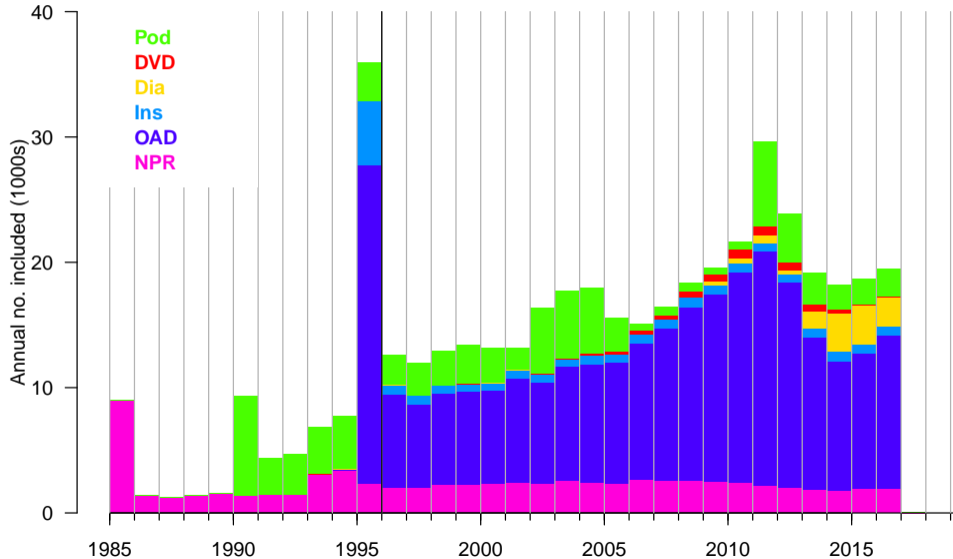
Sources for the DMreg

- ▶ NPR, National Patient Register
- ▶ RMPS, Register of Medicinal Product Statistics
- ▶ NHSR, National Health Services Register
- ▶ DADD, Danish Adult Diabetes Database
 - annual clinical status since 2005
 - complete for T1D, not for T2D
 - date only used if no other criteria met
- ▶ DiaBase, Eyescreening database
- ▶ **except** at least two recordings from NPR/RMPS are required
 - date/type of the second used as inclusion date/crit
 - similar to the RUKS requirements

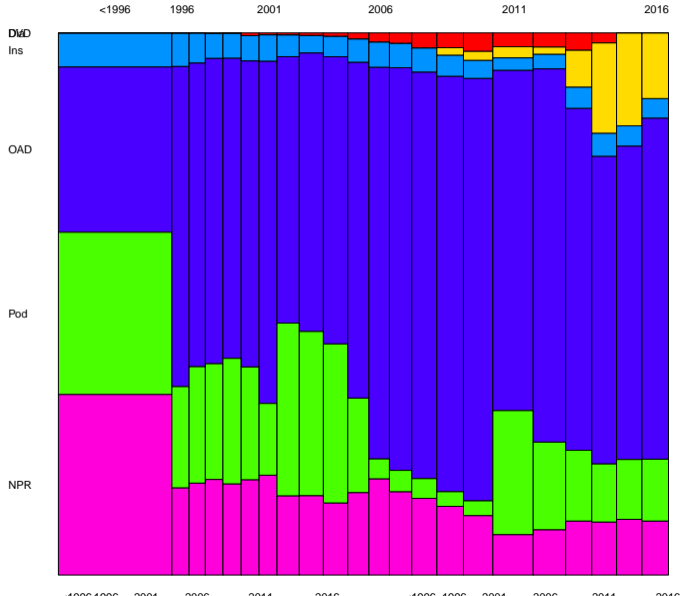
Sources for the DMreg

- ▶ NPR, National Patient Register
- ▶ RMPS, Register of Medicinal Product Statistics
- ▶ NHSR, National Health Services Register
- ▶ DADD, Danish Adult Diabetes Database
 - annual clinical status since 2005
 - complete for T1D, not for T2D
 - date only used if no other criteria met
- ▶ DiaBase, Eyescreening database
- ▶ **except** at least two recordings from NPR/RMPS are required
 - date/type of the second used as inclusion date/crit
 - similar to the RUKS requirements
- ▶ **Inclusion date:** first of any of these

Inclusion criteria in DMreg



Inclusion criteria in DMreg



Sources for type classification in DMreg

- ▶ **Clinical register, DADD:**
T1D diagnosis (only persons alive > 2004)

Sources for type classification in DMreg

- ▶ **Clinical register, DADD:**
T1D diagnosis (only persons alive > 2004)
- ▶ **National patient register:**
T1D diagnosis if not known from the clinical register

Sources for type classification in DMreg

- ▶ **Clinical register, DADD:**
T1D diagnosis (only persons alive > 2004)
- ▶ **National patient register:**
T1D diagnosis if not known from the clinical register
- ▶ used if more than half records are T1D resp. T2D — otherwise unspec.

Sources for type classification in DMreg

- ▶ **Clinical register, DADD:**
T1D diagnosis (only persons alive > 2004)
- ▶ **National patient register:**
T1D diagnosis if not known from the clinical register
- ▶ used if more than half records are T1D resp. T2D — otherwise unspec.
- ▶ **Prescription register:**
any GLD < 15 years, any insulin < 30 years

Sources for type classification in DMreg

- ▶ **Clinical register, DADD:**
T1D diagnosis (only persons alive > 2004)
- ▶ **National patient register:**
T1D diagnosis if not known from the clinical register
- ▶ used if more than half records are T1D resp. T2D — otherwise unspec.
- ▶ **Prescription register:**
any GLD < 15 years, any insulin < 30 years
- ▶ A person cannot be classified as T1D without insulin purchase

Sources for type classification in DMreg

- ▶ **Clinical register, DADD:**
T1D diagnosis (only persons alive > 2004)
- ▶ **National patient register:**
T1D diagnosis if not known from the clinical register
- ▶ used if more than half records are T1D resp. T2D — otherwise unspec.
- ▶ **Prescription register:**
any GLD < 15 years, any insulin < 30 years
- ▶ A person cannot be classified as T1D without insulin purchase

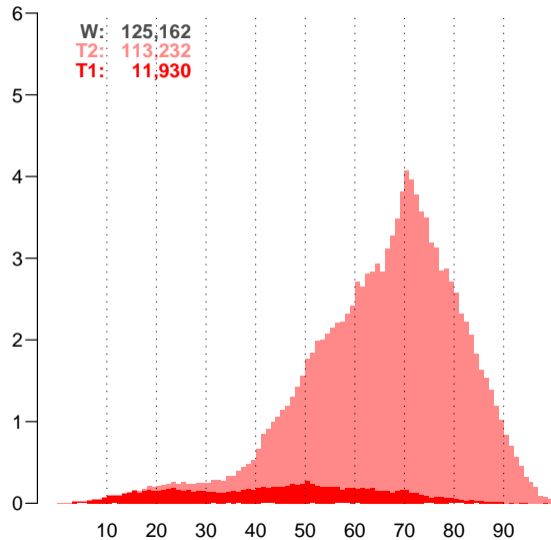
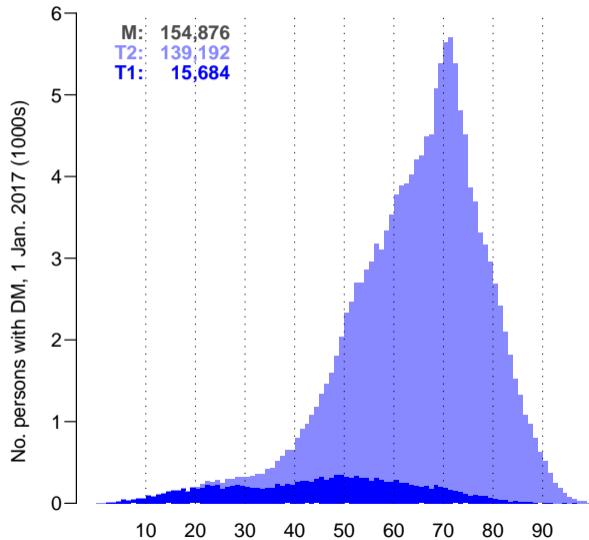
Sources for type classification in DMreg

- ▶ **Clinical register, DADD:**
T1D diagnosis (only persons alive > 2004)
- ▶ **National patient register:**
T1D diagnosis if not known from the clinical register
- ▶ used if more than half records are T1D resp. T2D — otherwise unspec.
- ▶ **Prescription register:**
any GLD < 15 years, any insulin < 30 years
- ▶ A person cannot be classified as T1D without insulin purchase

Persons not classified as T1D, are labeled T2D.

Note that we are formally conditioning on the future...

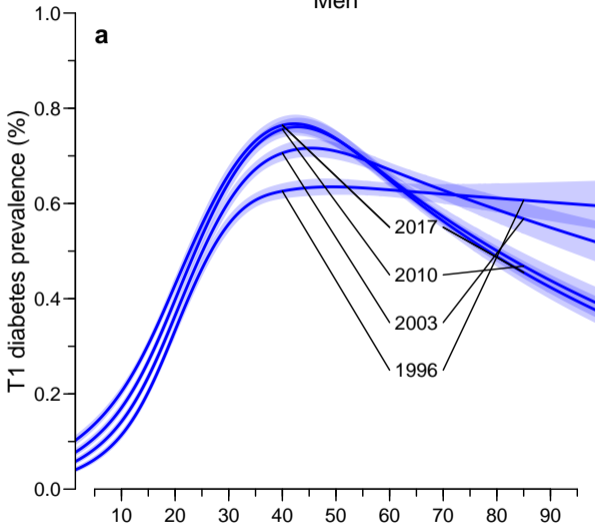
Prevalence of diabetes 2017-01-01



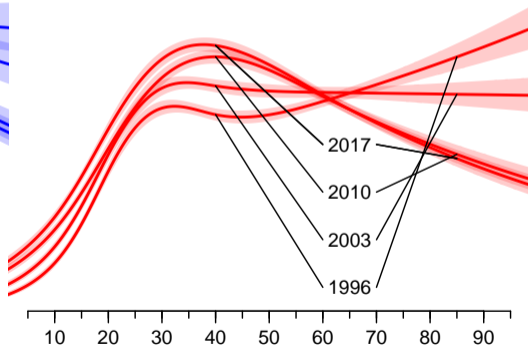
T1D prevalence

Men

Women



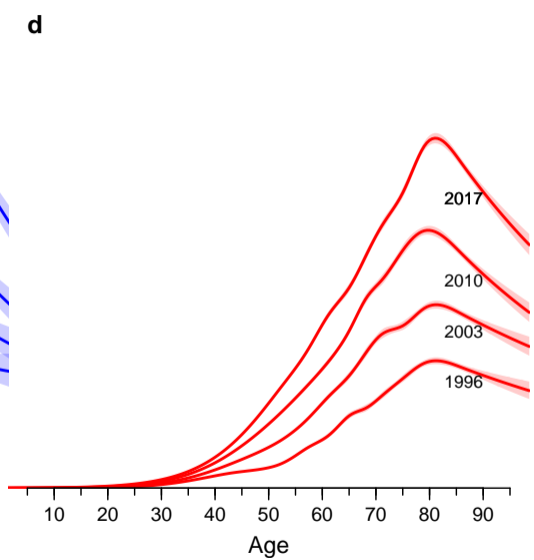
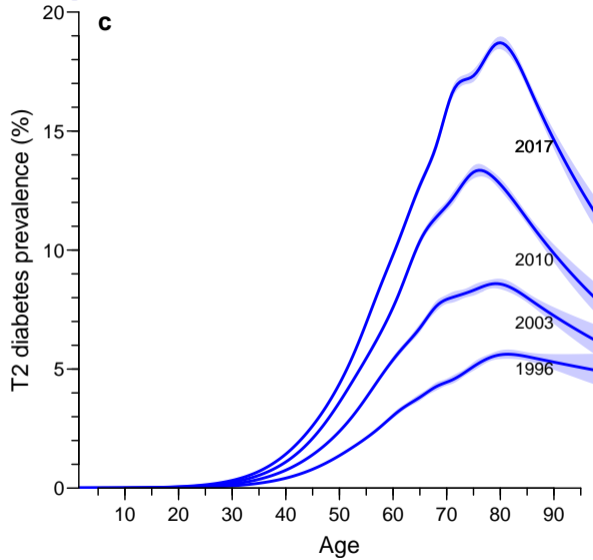
b



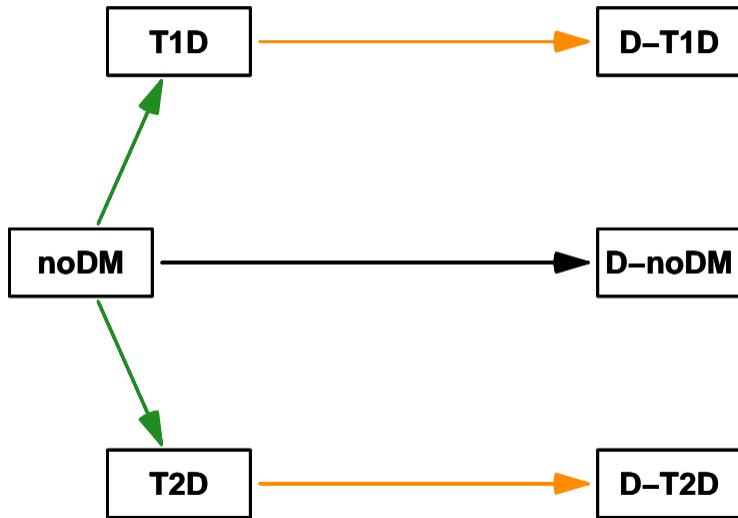
c

d

T2D prevalence



Incidence and mortality rates



Methods for incidence and mortality rates

- ▶ Entire Danish population followed 1996-01-01→2016-12-31

Methods for incidence and mortality rates

- ▶ Entire Danish population followed 1996-01-01→2016-12-31
- ▶ Follow-up classified as noDM, T1D, T2D

Methods for incidence and mortality rates

- ▶ Entire Danish population followed 1996-01-01→2016-12-31
- ▶ Follow-up classified as noDM, T1D, T2D
- ▶ Tabulation by age, calendar time, date of birth, and duration of T1D/T2D, 1-year classes (PY, deaths, T1D, T2D diagnoses)

Methods for incidence and mortality rates

- ▶ Entire Danish population followed 1996-01-01→2016-12-31
- ▶ Follow-up classified as noDM, T1D, T2D
- ▶ Tabulation by age, calendar time, date of birth, and duration of T1D/T2D, 1-year classes (PY, deaths, T1D, T2D diagnoses)
- ▶ Poisson models with smooth effect of age, date of follow-up, date of birth, age at diagnosis and duration of diabetes

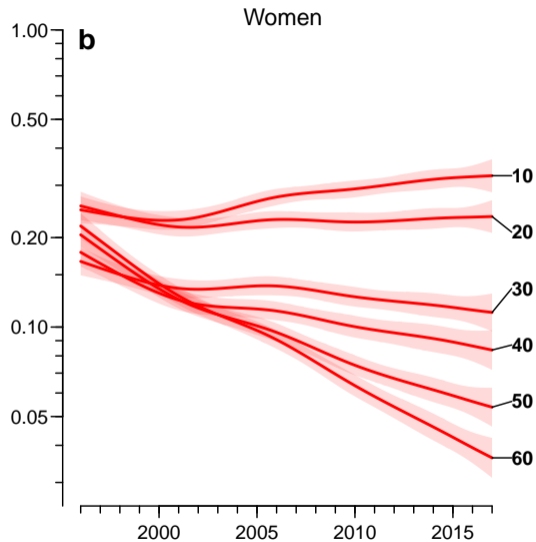
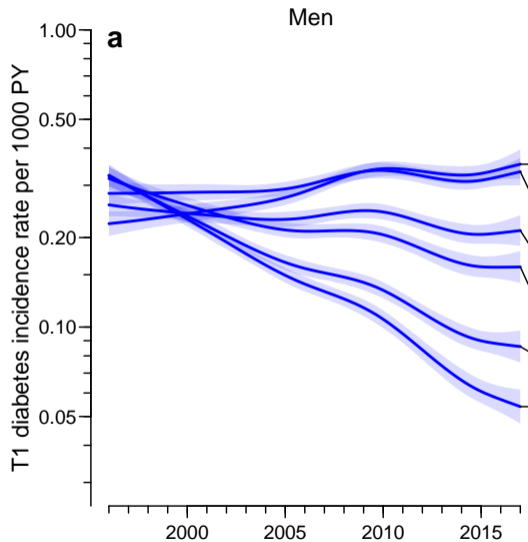
Methods for incidence and mortality rates

- ▶ Entire Danish population followed 1996-01-01→2016-12-31
- ▶ Follow-up classified as noDM, T1D, T2D
- ▶ Tabulation by age, calendar time, date of birth, and duration of T1D/T2D, 1-year classes (PY, deaths, T1D, T2D diagnoses)
- ▶ Poisson models with smooth effect of age, date of follow-up, date of birth, age at diagnosis and duration of diabetes
- ▶ **Incidence** rates at different ages by calendar time

Methods for incidence and mortality rates

- ▶ Entire Danish population followed 1996-01-01→2016-12-31
- ▶ Follow-up classified as noDM, T1D, T2D
- ▶ Tabulation by age, calendar time, date of birth, and duration of T1D/T2D, 1-year classes (PY, deaths, T1D, T2D diagnoses)
- ▶ Poisson models with smooth effect of age, date of follow-up, date of birth, age at diagnosis and duration of diabetes
- ▶ **Incidence** rates at different ages by calendar time
- ▶ **Mortality** rates by age for different ages at diagnosis
— RR by calendar time

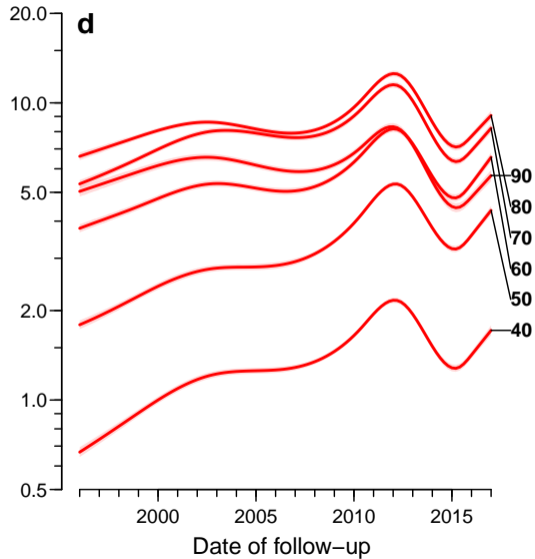
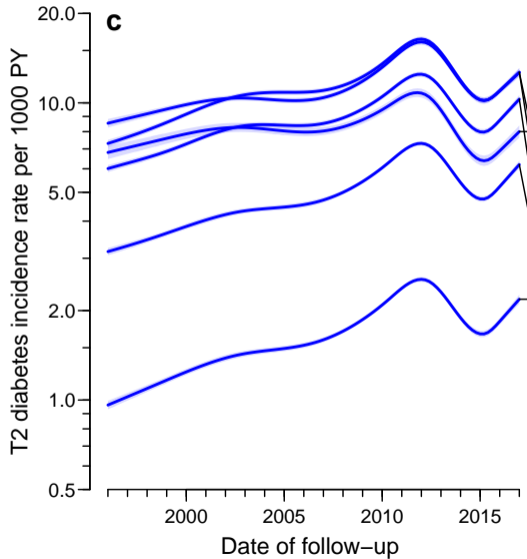
Time trends in T1D incidence



c

d

Time trends in T2D incidence



Incidence conclusion

T1:

Incidence conclusion

T1:

- ▶ slight increase in younger ages

Incidence conclusion

T1:

- ▶ slight increase in younger ages
- ▶ decrease in older ages

Incidence conclusion

T1:

- ▶ slight increase in younger ages
- ▶ decrease in older ages
- ▶ registration artefact?

Incidence conclusion

T1:

- ▶ slight increase in younger ages
- ▶ decrease in older ages
- ▶ registration artefact?

T2:

Incidence conclusion

T1:

- ▶ slight increase in younger ages
- ▶ decrease in older ages
- ▶ registration artefact?

T2:

- ▶ increase till 2011, dip till 2014, increase again

Incidence conclusion

T1:

- ▶ slight increase in younger ages
- ▶ decrease in older ages
- ▶ registration artefact?

T2:

- ▶ increase till 2011, dip till 2014, increase again
- ▶ same pattern in all ages

Incidence conclusion

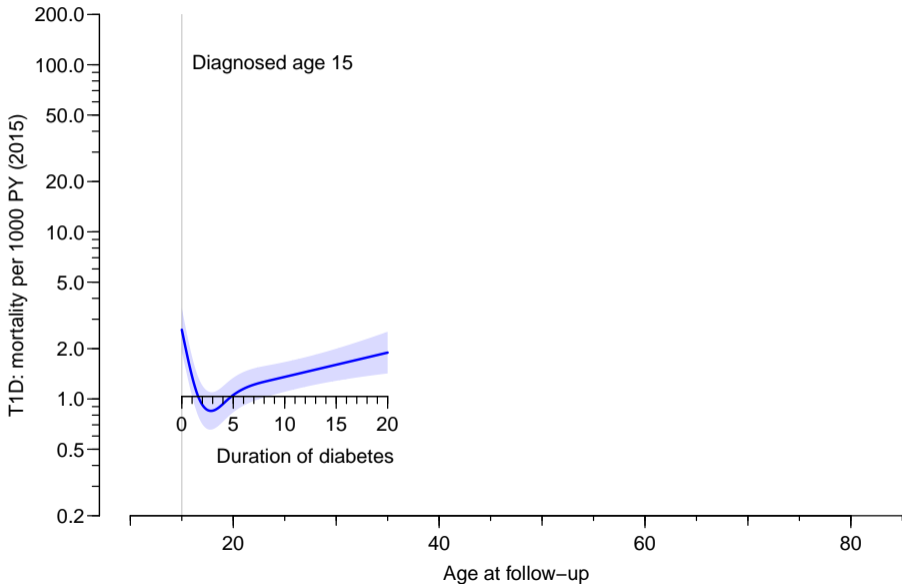
T1:

- ▶ slight increase in younger ages
- ▶ decrease in older ages
- ▶ registration artefact?

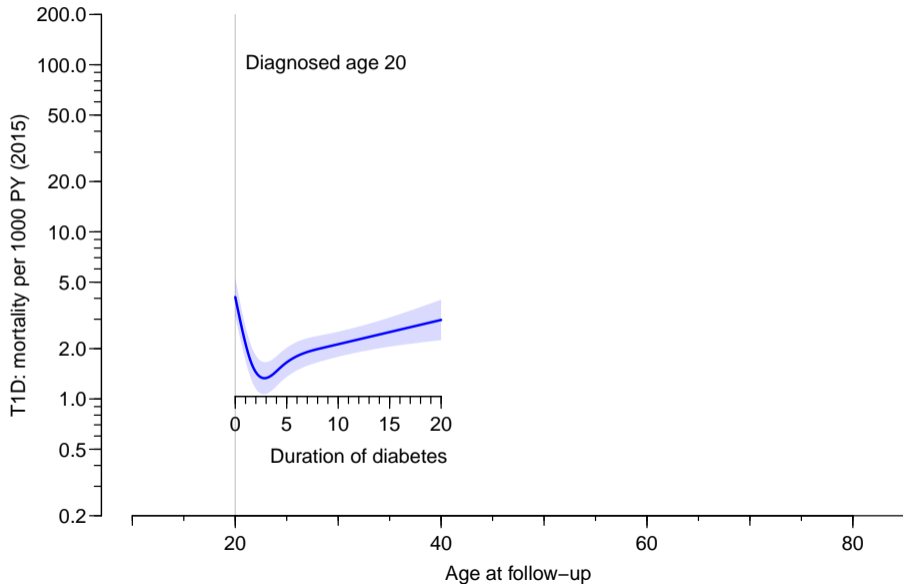
T2:

- ▶ increase till 2011, dip till 2014, increase again
- ▶ same pattern in all ages
- ▶ influence of HbA_{1c} criteria — no data (yet)

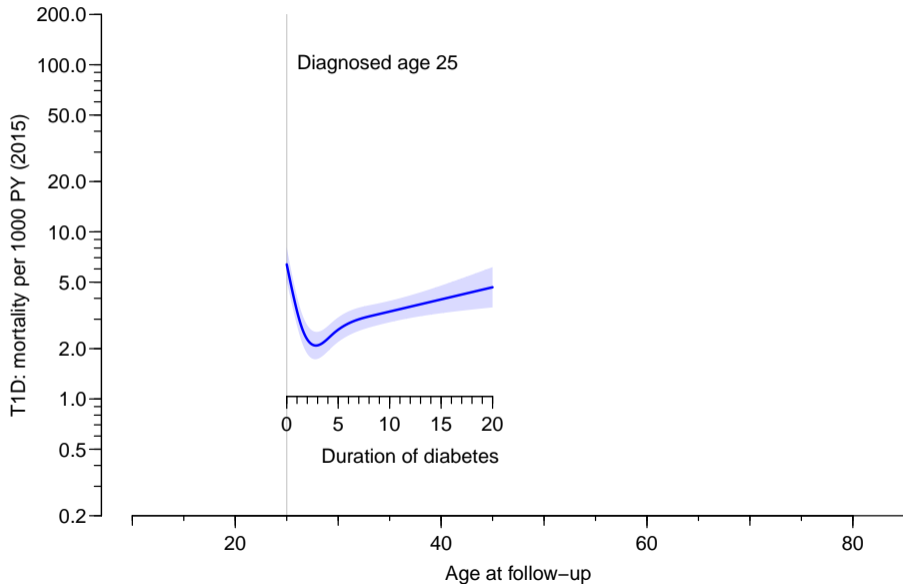
T1D mortality



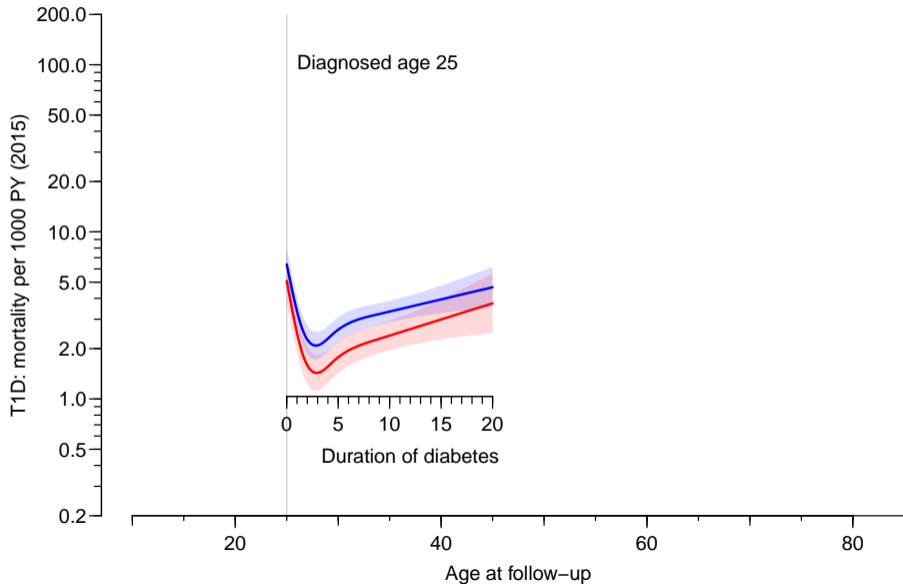
T1D mortality



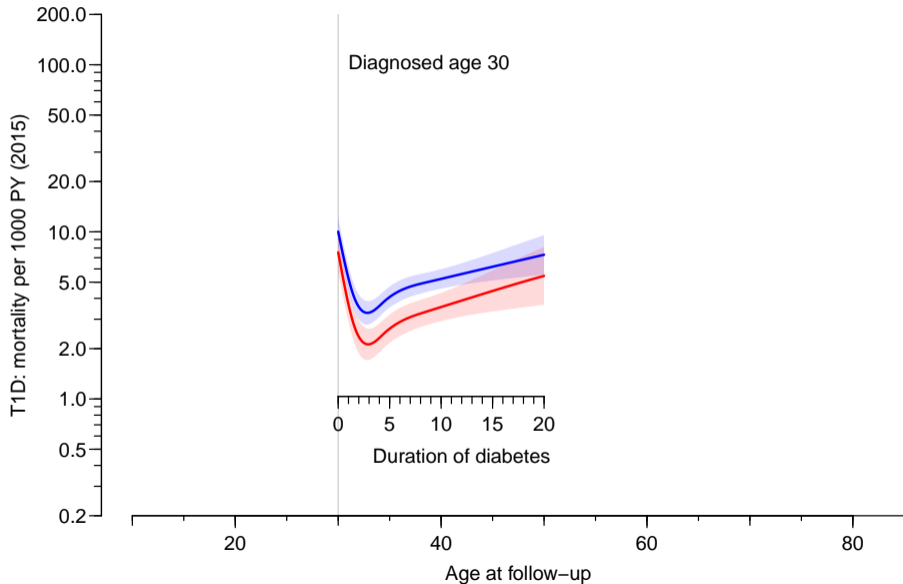
T1D mortality



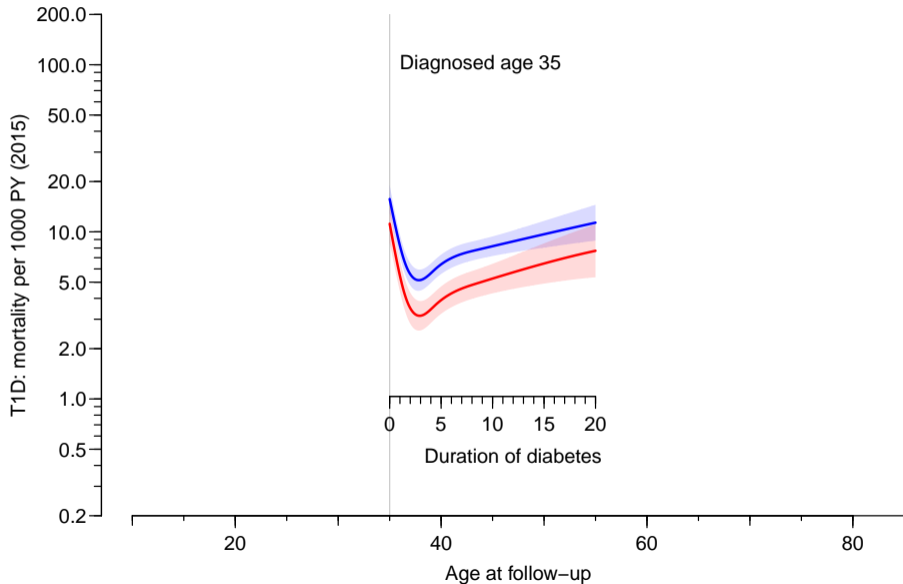
T1D mortality



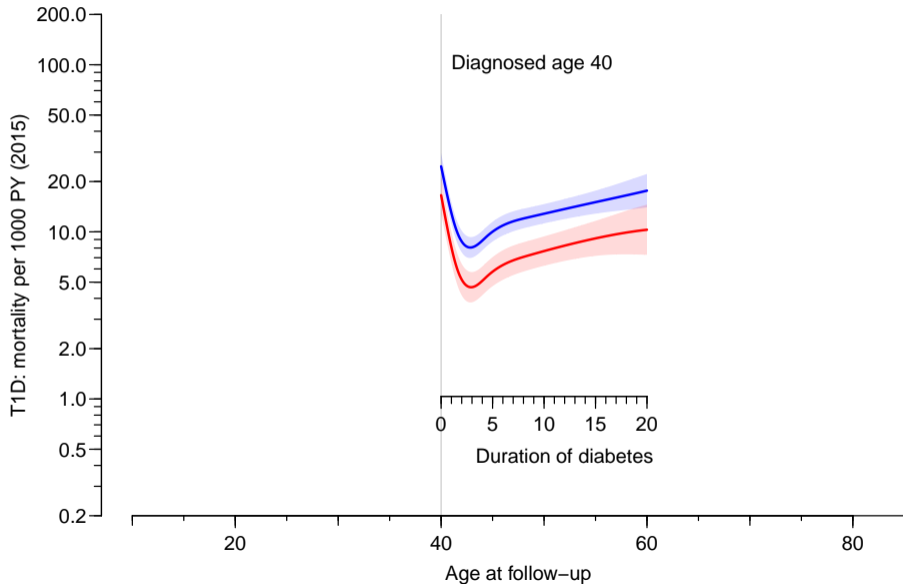
T1D mortality



T1D mortality



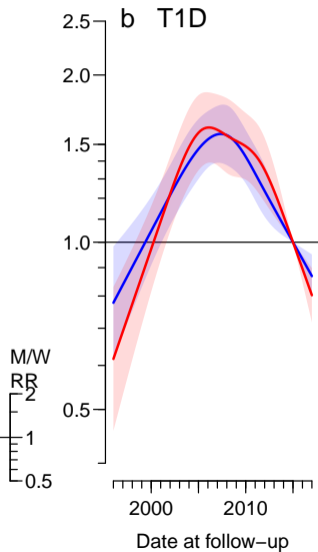
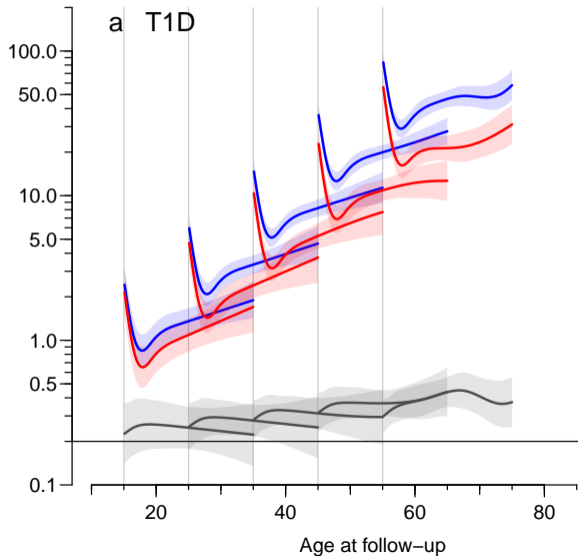
T1D mortality



T1D mortality, age at diagnosis 15, 25, 35, 45 and 55

Mortality rate per 1000 PY

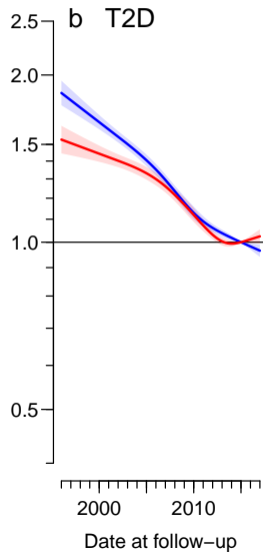
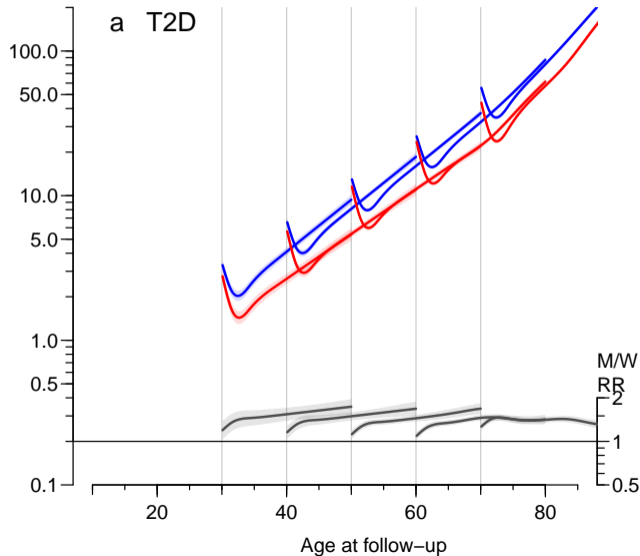
Rate ratio relative to 2015

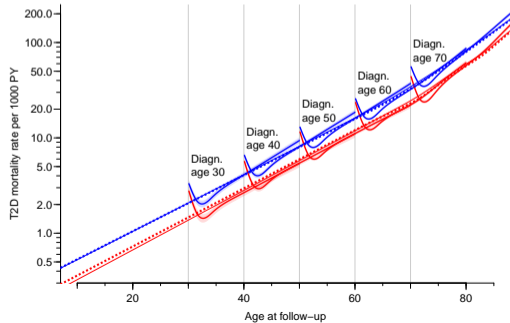
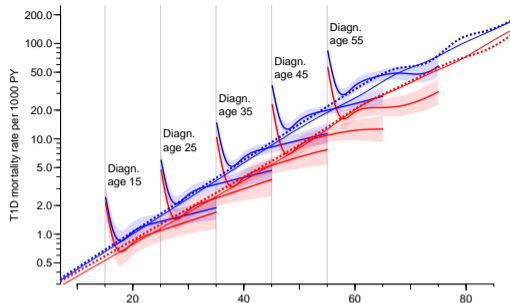


T2D mortality, age at diagnosis 30, 40, 50, 60 and 70

Mortality rate per 1000 PY

Rate ratio relative to 2015





Mortality conclusion

- ▶ T1D mortality decreasing after 2009
 - early T1D deaths may be misclassified as T2

Mortality conclusion

- ▶ T1D mortality decreasing after 2009
 - early T1D deaths may be misclassified as T2
- ▶ T2D mortality decrease by calendar time

Mortality conclusion

- ▶ T1D mortality decreasing after 2009
 - early T1D deaths may be misclassified as T2
- ▶ T2D mortality decrease by calendar time
- ▶ Mortality increased the first 2 years after diagnosis
 - likely a clinical artifact:
severely ill persons over-represented in newly diagnosed

Mortality conclusion

- ▶ T1D mortality decreasing after 2009
 - early T1D deaths may be misclassified as T2
- ▶ T2D mortality decrease by calendar time
- ▶ Mortality increased the first 2 years after diagnosis
 - likely a clinical artifact:
severely ill persons over-represented in newly diagnosed
- ▶ T1D: early diagnosis associated with lower mortality

Mortality conclusion

- ▶ T1D mortality decreasing after 2009
 - early T1D deaths may be misclassified as T2
- ▶ T2D mortality decrease by calendar time
- ▶ Mortality increased the first 2 years after diagnosis
 - likely a clinical artifact:
severely ill persons over-represented in newly diagnosed
- ▶ T1D: early diagnosis associated with lower mortality
- ▶ T2D: early diagnosis associated with higher mortality for men,
no effect for women

Mortality conclusion

- ▶ T1D mortality decreasing after 2009
 - early T1D deaths may be misclassified as T2
- ▶ T2D mortality decrease by calendar time
- ▶ Mortality increased the first 2 years after diagnosis
 - likely a clinical artifact:
severely ill persons over-represented in newly diagnosed
- ▶ T1D: early diagnosis associated with lower mortality
- ▶ T2D: early diagnosis associated with higher mortality for men, no effect for women
- ▶ M/W mortality RR is about 1.5 regardless of sex and type

Summary of time trends in DK — % per year

% change per year	T1D	T2D	no DM
Prevalence	0.5	5.5	
Incidence rate	-3.5	3.8	
Mortality rate	-0.3	-2.9	-2.6

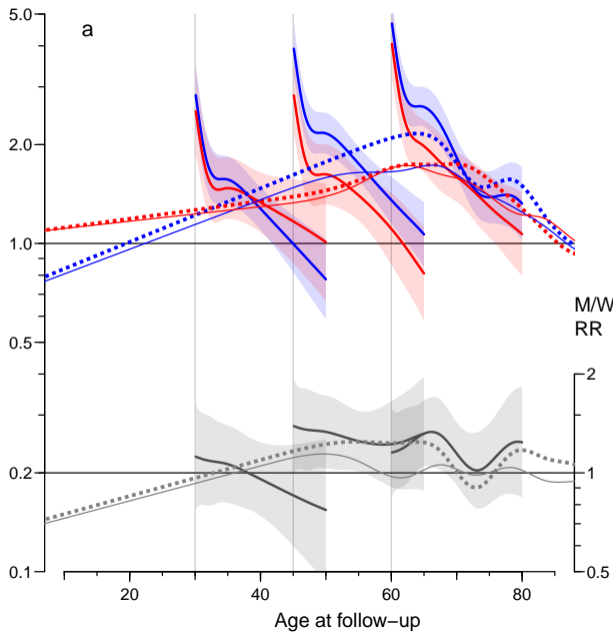
Relative mortality T2D vs. T1D: **0.58**

— T2D patients have a 42% **lower** mortality than T1D

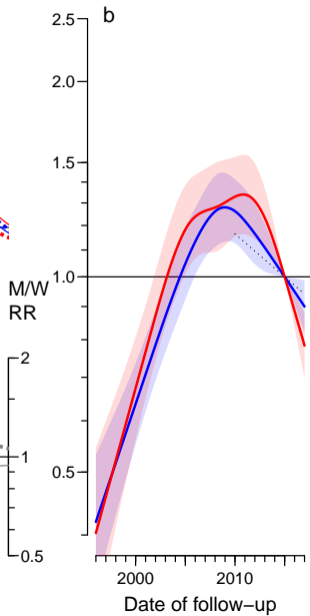
Relative mortality Men vs. Women: **1.6**

— averaged over type and age

T1D vs. T2D mortality rate-ratio at 2015

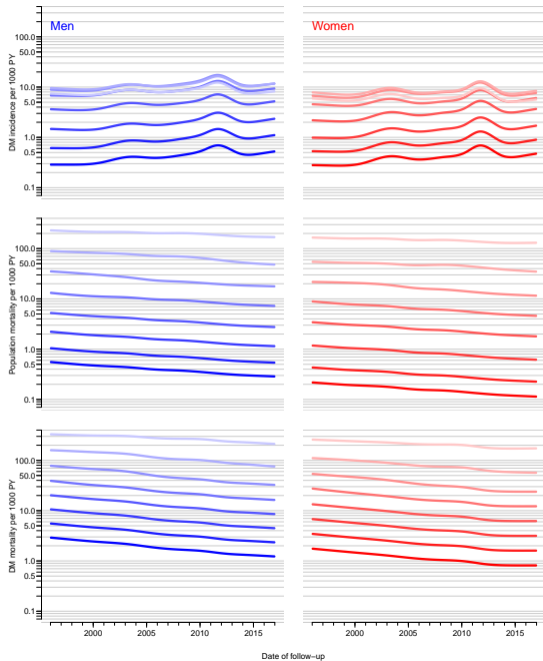


RR ratio relative to 2015

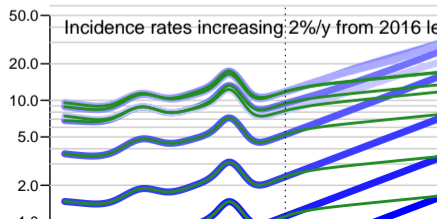
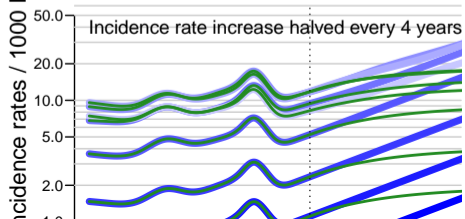
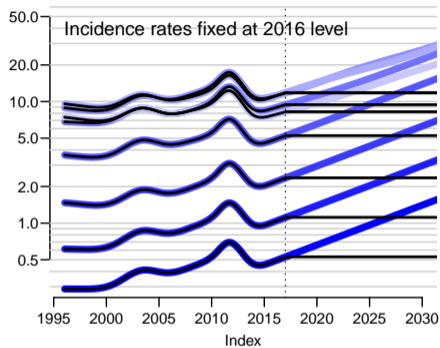
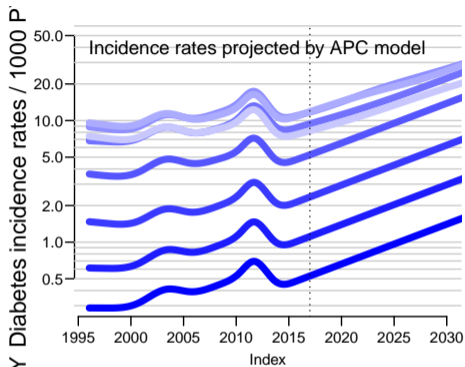


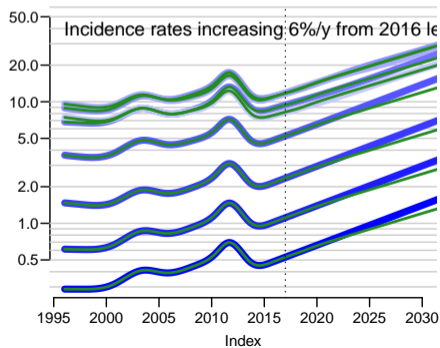
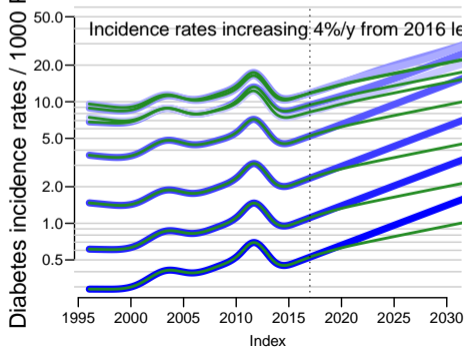
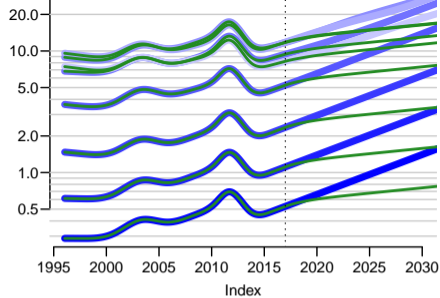
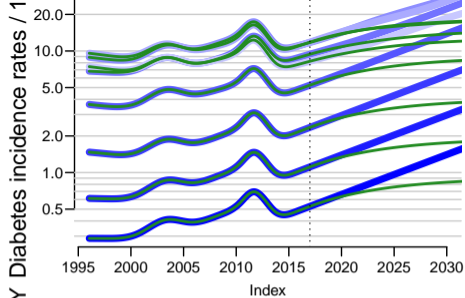
Incidence and mortality rates

ages 20, 30, ..., 90

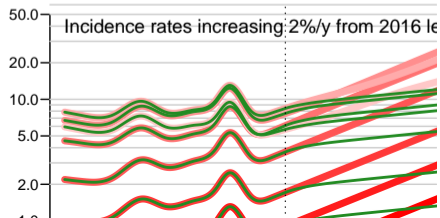
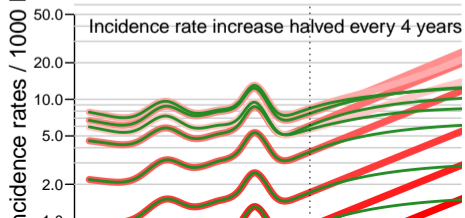
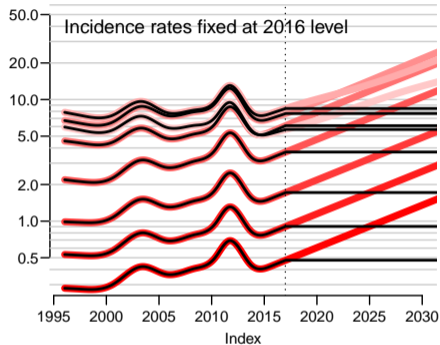
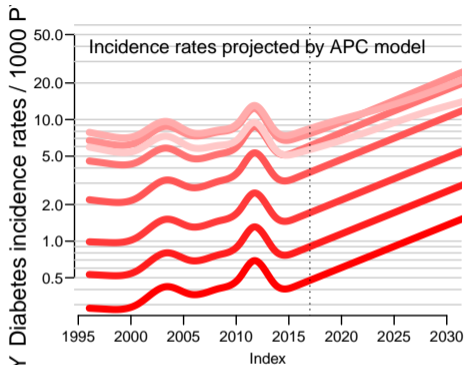


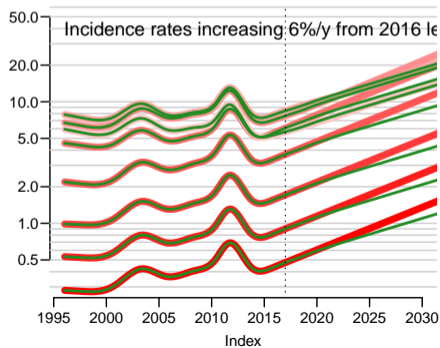
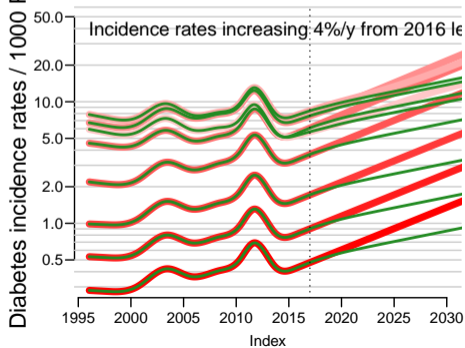
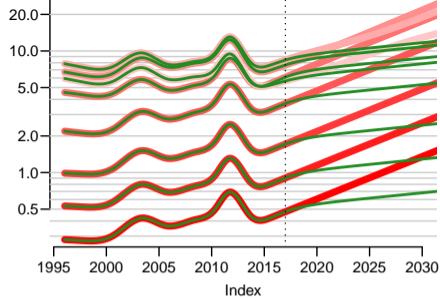
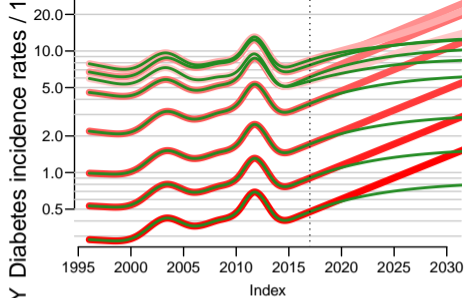
Incidence rates in the future





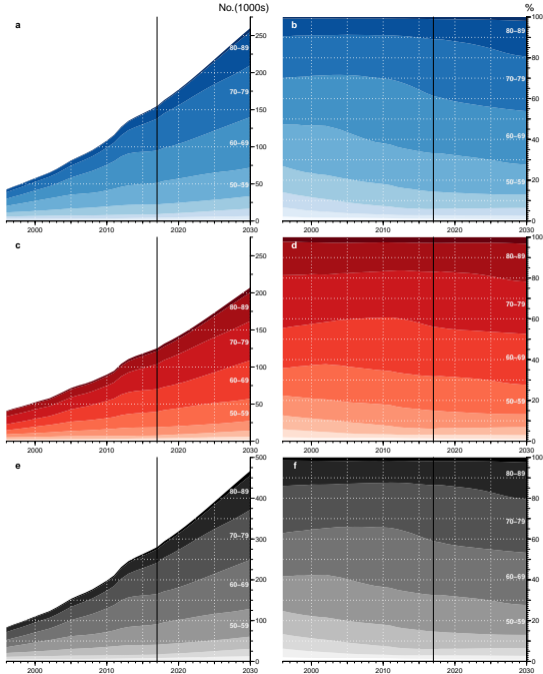
Incidence rates in the future

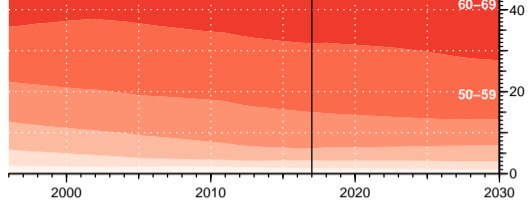
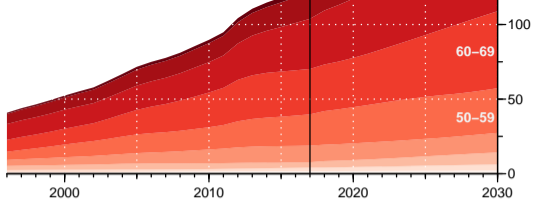




Number of future prevalent cases of DM

... using attenuation:
halving of slope every 5 years





e

