Registers in Denmark

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Use of routine care data in research

- Registers in Denmark
- Clinical register at SDC
  (Electronic Medical Records, EMR)
- Register-based projects at
  Steno Diabetes Center

Reasons to do register-based studies

- Long-term follow up
- Mortality
- Natural history of disease
- Side effects of medication
- Selection bias
- Exclusion criteria in clinical trials
- Low participation rate in observational studies

Clinical records (SDC electronic patient records)

- Complete history of patients:
  - HbA_{1c}
  - blood pressure
  - lipids
  - ...
- Information on:
  - dates of measurement (visit)
  - date of diagnosis
  - date of birth
  - date of (adverse) event(s)
- Note: Intervals between visits depend on patients' status

Clinical registers (e.g. Danish Adult Diabetes Database)

- Data collection (recording) at fixed intervals (once a year, e.g.)
- Clinical data on individuals
- Data collection independent of patients' clinical status
- Missing data:
  - a patient was not seen for an entire year
  - a patient has moved
  - a patient died (but was not recorded as such)
- Used for quality monitoring:
- What percentage of pateints have had eyexamination within the last 2 years etc.

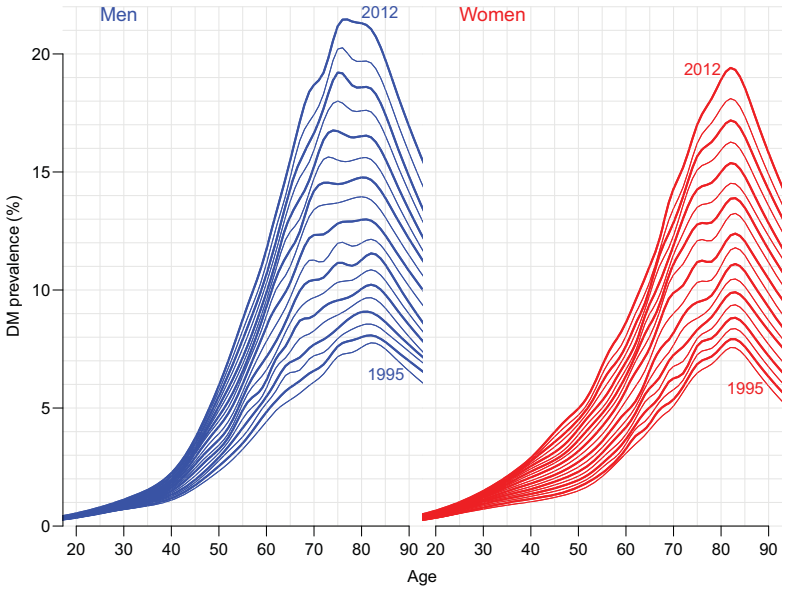
Population level registers (Danish National Diabetes Register)

- Aims to cover the entire population:
- Limited information on each patient:
  - date of birth
  - date of diagnosis
  - date of death
  - sex
- Monitoring of demographics:
  - prevalence of DM
  - DM occurrence (incidence rates)
  - mortality of DM patients
- Important because we have:
  - long term follow-up
  - no patient drop-out

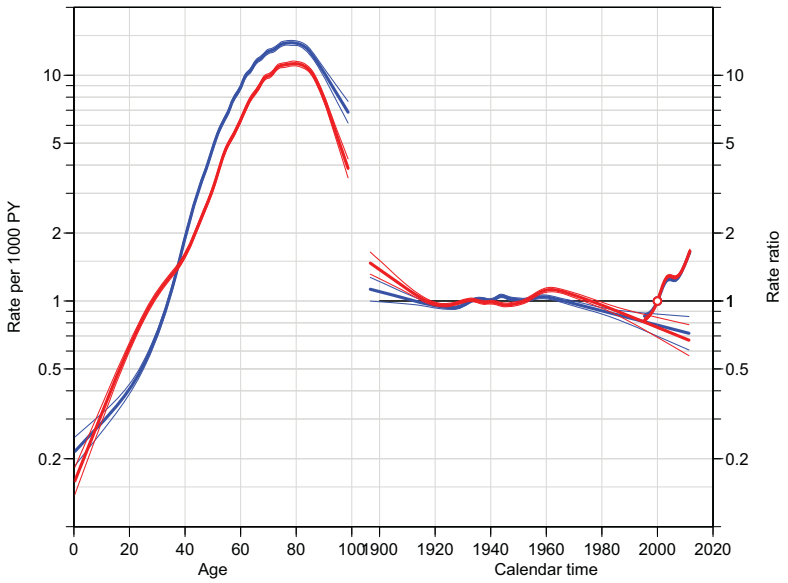
NDR 1995-2012: Adding population data

- Combine with populations data:
  - population size
  - population risk time (person-years)
- . . . in order to compute:
  - Prevalence of DM at different dates
  - Incidence rates of DM in the non-DM population
  - Mortality of DM patients
  - Relative mortality of DM patients (SMR)

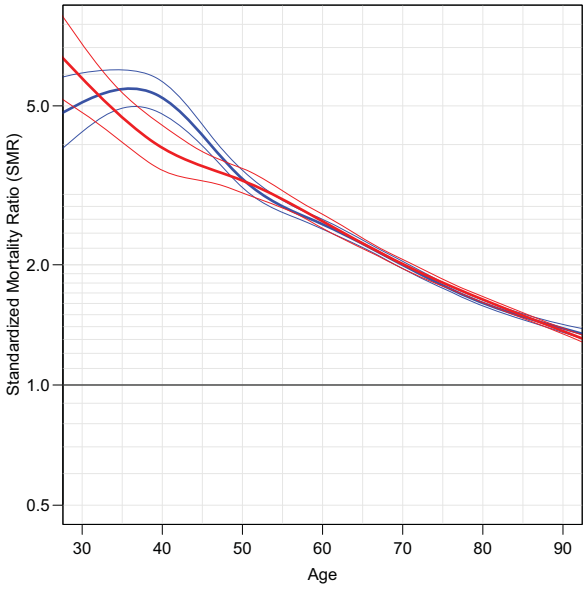
NDR 1995-2012: Prevalence[1]



NDR 1995-2012: Incidence rates[1]



NDR 1995-2012: SMR[1]



Mortality among SDC T1 & T2 patients

Patients followed 1 Jan 2002 to 31 Dec 2010 [2, 3]

	T1		T2	
	Men	Women	Men	Women
No. patients	2,614	2,207	3,423	2,421
Annual decrease (%):				
Mortality	6.6	4.8	5.5	3.3
SMR	4.3	2.6	3.0	1.4

So also in SDC patients mortality has been declining **more** than in the general population.

Renal disease, CVD and death

SDC T1 patients [4, 5] with DN

- Patients with DN (diabetic nephropathy)
- Occurrence of:
  - ESRD
    (end stage renal disease: dialysis or transplant)
  - Death
- How do rates depend on clinical parameters?
- How is long-term outcome dependent on clinical status?

SDC:
T1DM patients with kidney compliations

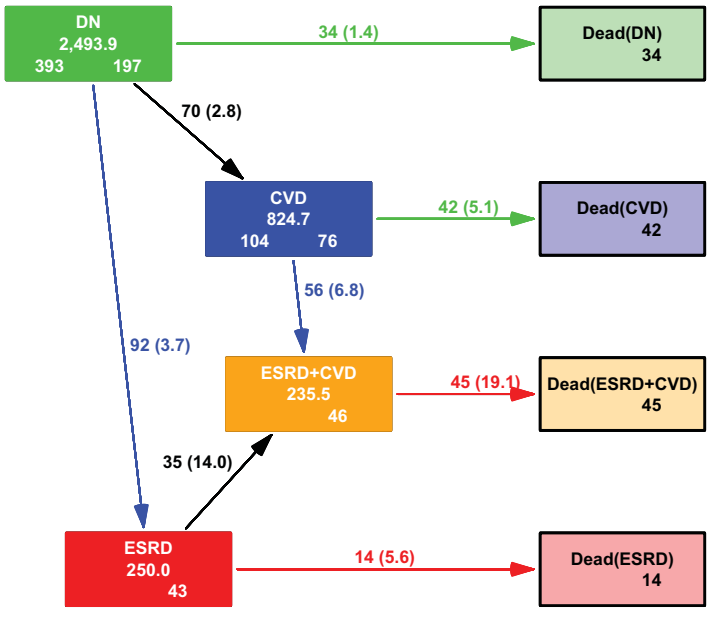
- G. Andresdottir, M. L. Jensen, B. Carstensen, H. H. Parving, K. Rossing, T. W. Hansen, and P. Rossing: **Improved Survival and Renal Prognosis of Patients With Type 2 Diabetes and Nephropathy With Improved Control of Risk Factors**
  Diabetes Care, Mar 2014.
- G. Andresdottir, M. L. Jensen, B. Carstensen, H. H. Parving, P. Hovind, T. W. Hansen, P. Rossing: **Improved prognosis of diabetic nephropathy in type 1 diabetes**
  Accepted in Kidney International on 17 April 2014.

SDC:
T1DM patients with kidney compliations

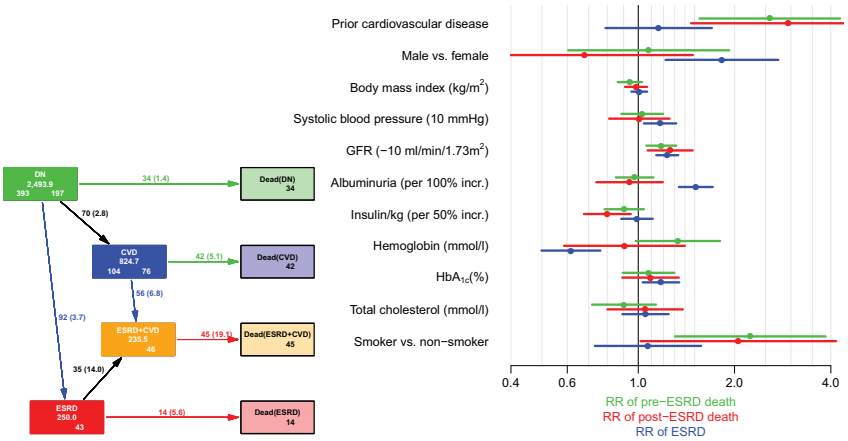
Extract patients with Diabetic Nephropathy (DN) from the SDC patient records and record:

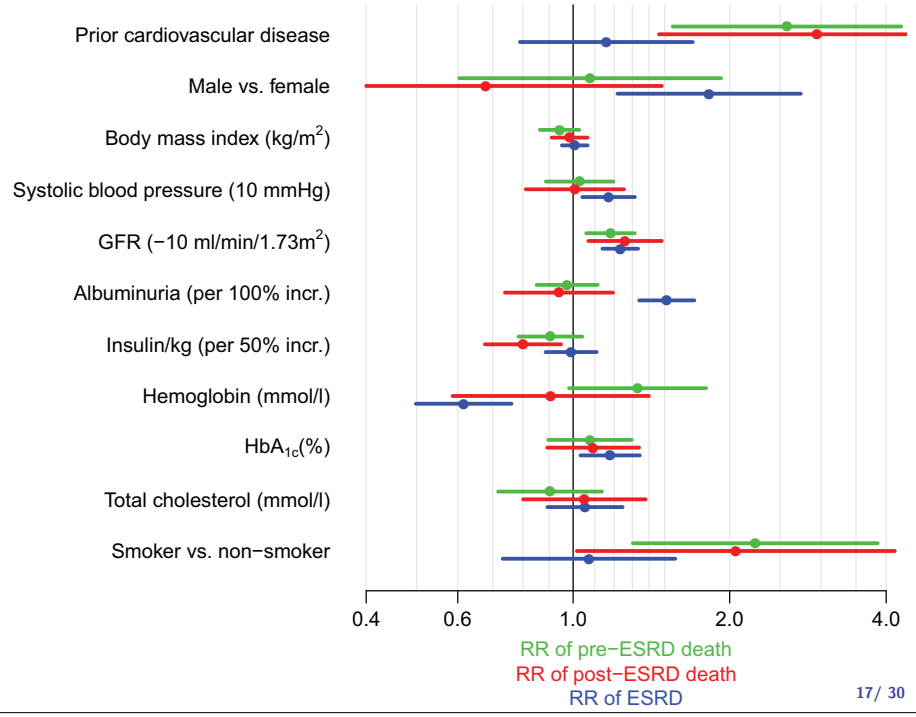
- Date of birth
- Date of diabetes
- Date of DN
- Date of CVD
- Date of ESRD
- Date of death
- Clinical parameters at date of DN (baseline)

T1DM patients with kidney compliations



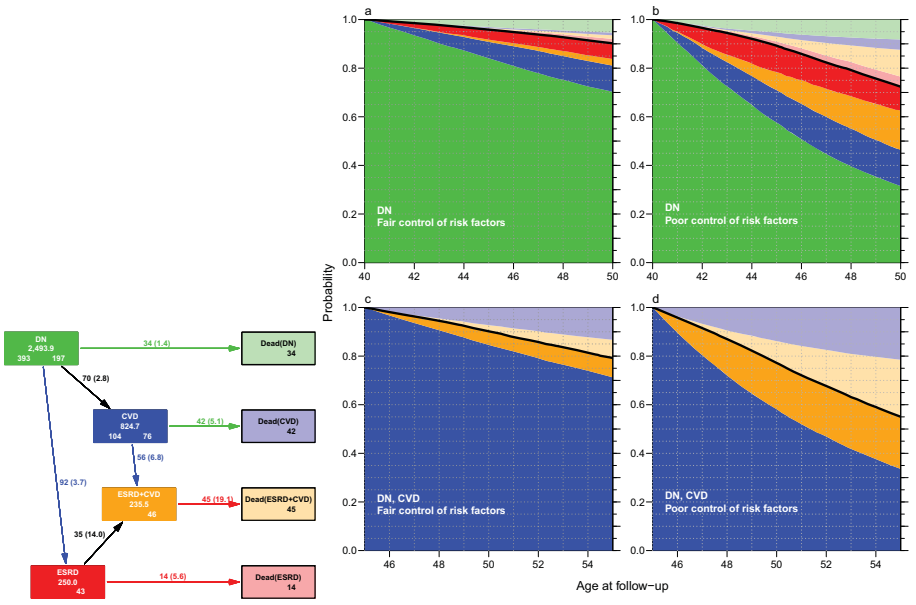
Covariate effects

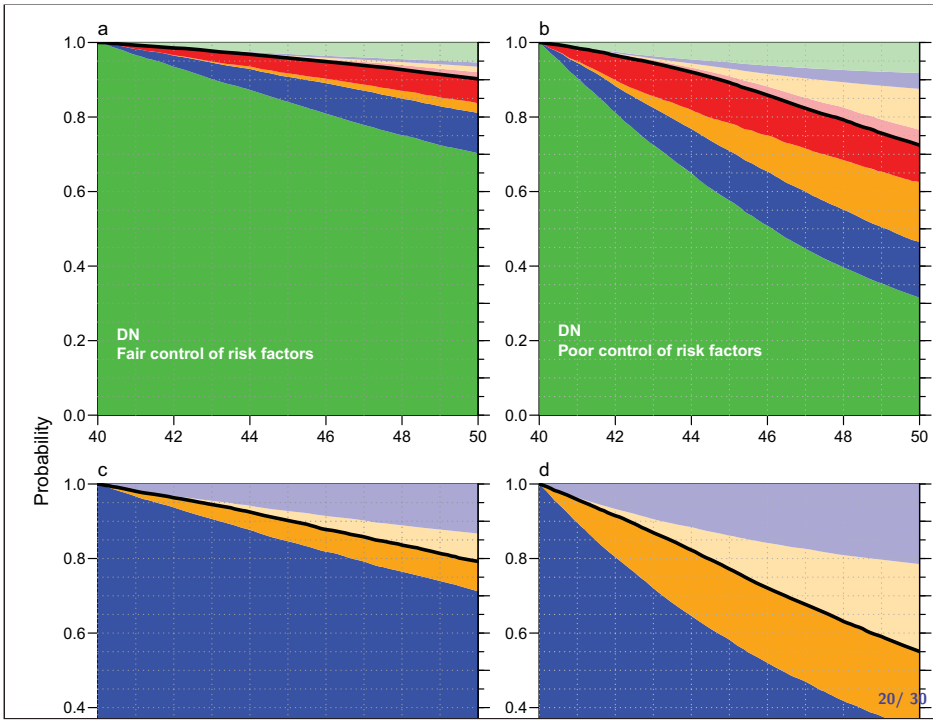


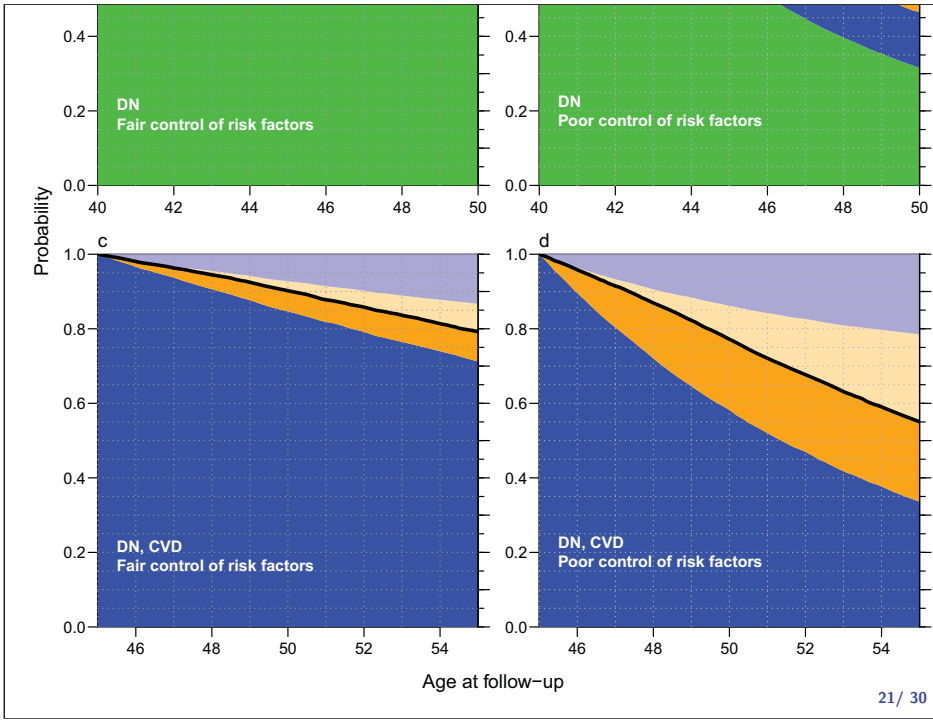


Example patients

Regulation	Fair	Poor
Sex	Man	Man
Age	40/45	40/45
Time since DN	5	5
Diabetes duration	25	25
HbA$_{1c}$	7.5	9.0
Systolic blood pr.	130	150
Total cholesterol	4.5	5.5
Albumin	300	1000
Smoking	never, <3	4–20, 20+
BMI	22	22
GFR	70	70
Hemoglobin	8	8
Insulin dose per kg	0.75	0.75


a
b
c
d
DN
Fair control of risk factors
DN
Poor control of risk factors
DN, CVD
Fair control of risk factors
DN, CVD
Poor control of risk factors
Probability
Age at follow−up
DN
2,493.9
393 197
CVD
824.7
104 76
ESRD+CVD
235.8
46
ESRD
250.0
43
34 (1.4)
70 (2.8)
42 (5.1)
56 (6.8)
92 (3.7)
45 (19.1)
35 (14.0)
14 (5.6)
Dead(DN)
34
Dead(CVD)
42
Dead(ESRD+CVD)
45
Dead(ESRD)
14


a
b
c
d
DN
Fair control of risk factors
DN
Poor control of risk factors
Probability


DN
Fair control of risk factors
DN
Poor control of risk factors
c
d
DN, CVD
Fair control of risk factors
DN, CVD
Poor control of risk factors
Probability
Age at follow−up

Prediction of lifecourse of patients

- Only possible if we **model** the entire lifecourse.
- Only events (ESRD, CVD, Death) are modelled
- Changes in clinical parameters are ignored — all is conditional on baseline **only**.
- Possible to model rates as a function of **current** clinical parameters (time-updated variables)
  - no model for the clinical parameters (HbA_{1c}, cholesterol, ...)
  - so we lose the ability to predict the lifecourse
- This was not done in the Danish kidney-complications study.
- ... but it is possible with the SDC EPR.

Modelling rates with current parameters

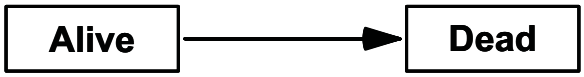
- But we gain the possibility to **compare** populations (e.g. HK & DK) with respect to
  - occurrence rates
  - **conditional** on clinical parameters:
  - are there differences that cannot be explained in terms of the clinical status of patients?
  - *i.e.* are there factors that influence rates that are not mediated through the measured clinical variables?

Modelling rates with current parameters

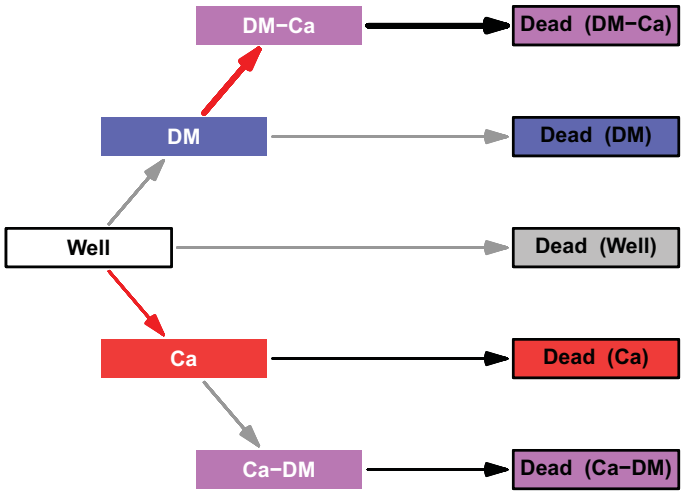
- Also gain the possibility to evaluate time-trends in mortality:
  - If trend in mortality by calendar time is negative, overall patient prognosis is improving
  - But trend may be less negative or even positive when controlling for updated clinical variables, **conditional** on current (updated) clinical parameters:
  - improvement in overall patient prognosis mediated through improvement in clinical variables?

Population level prediction

- Demographers compute the life expectancy in a population
- as the expected length of life
- **under the assumption** that rates are as seen in the population
- at a certain point in time:



Population level prediction

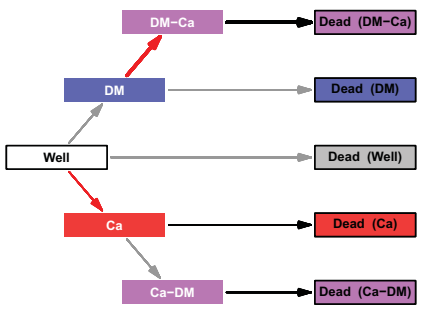


Population burden of DM & Cancer

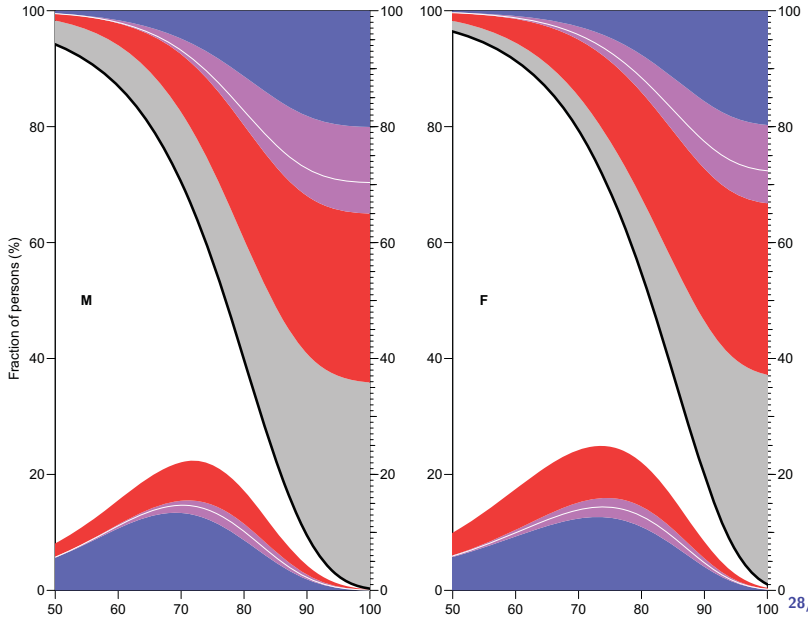
- How many people get cancer?
- How many people get diabetes?
- How many people get both DM and cancer?

How are the persons distributed between states at a given point in life?

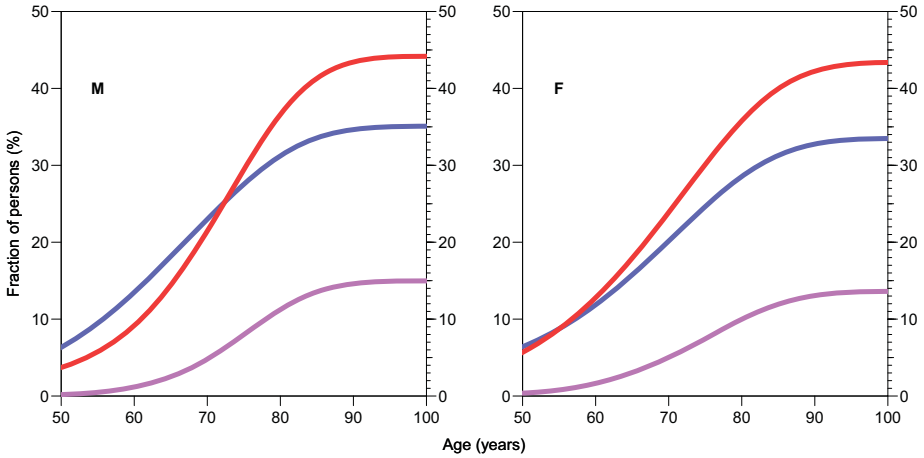
Depends on **all** the transition rates



Population burden of DM & Cancer



How many get DM/Cancer before age a



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