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.

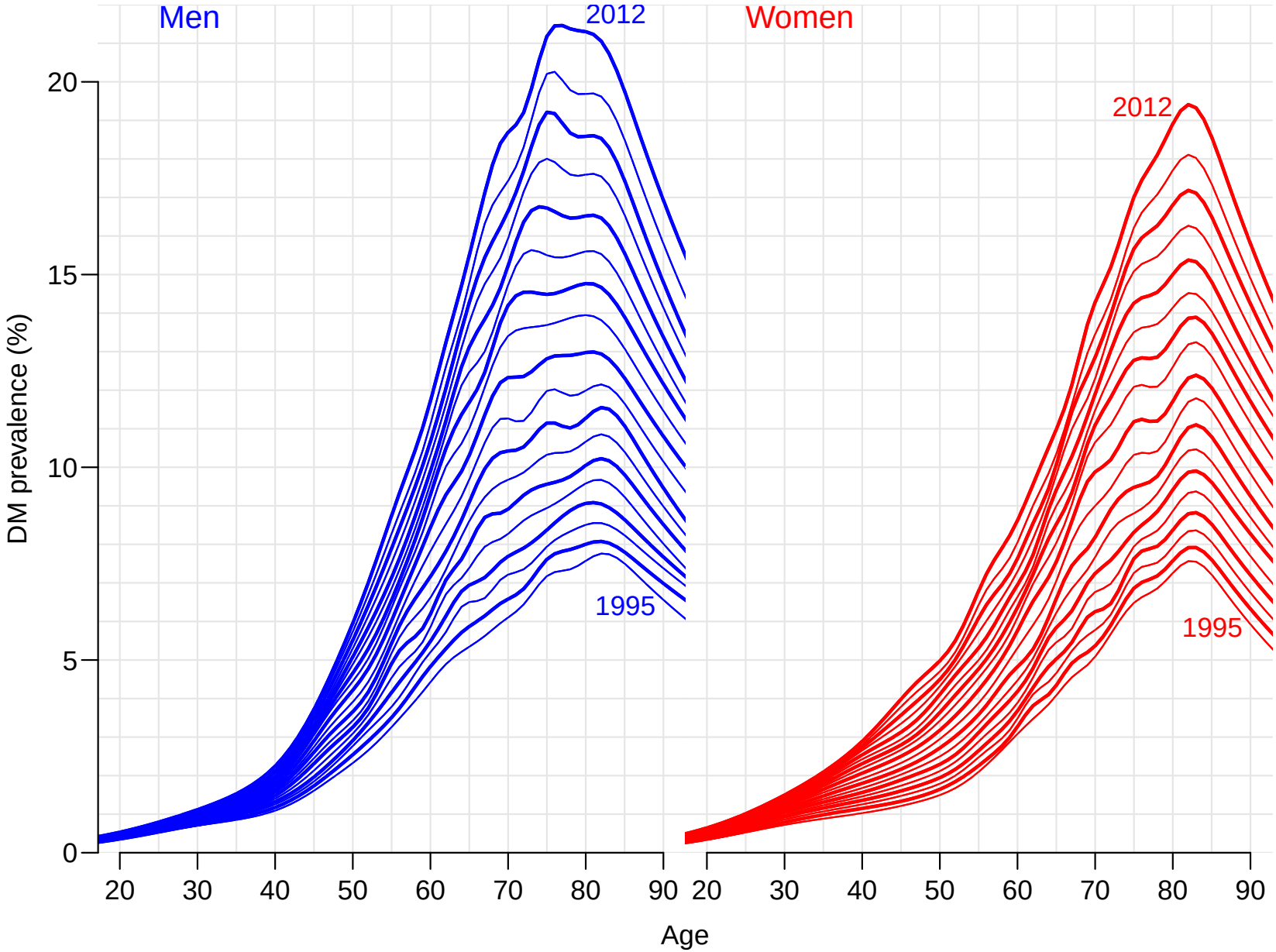
Population level registers (Danish National Diabetes Register)

- 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

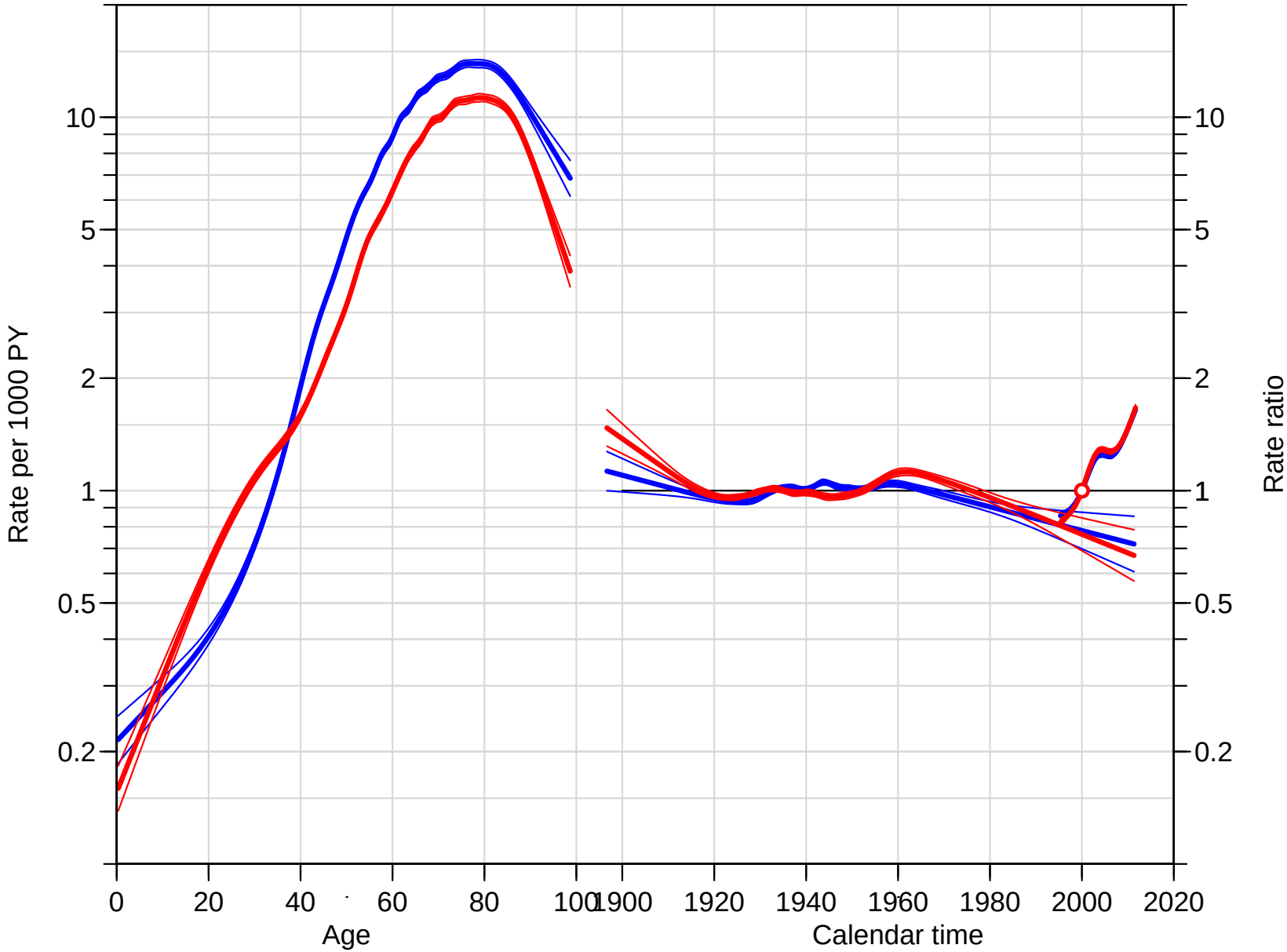
NDR 1995-2012: Adding population data

- 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)

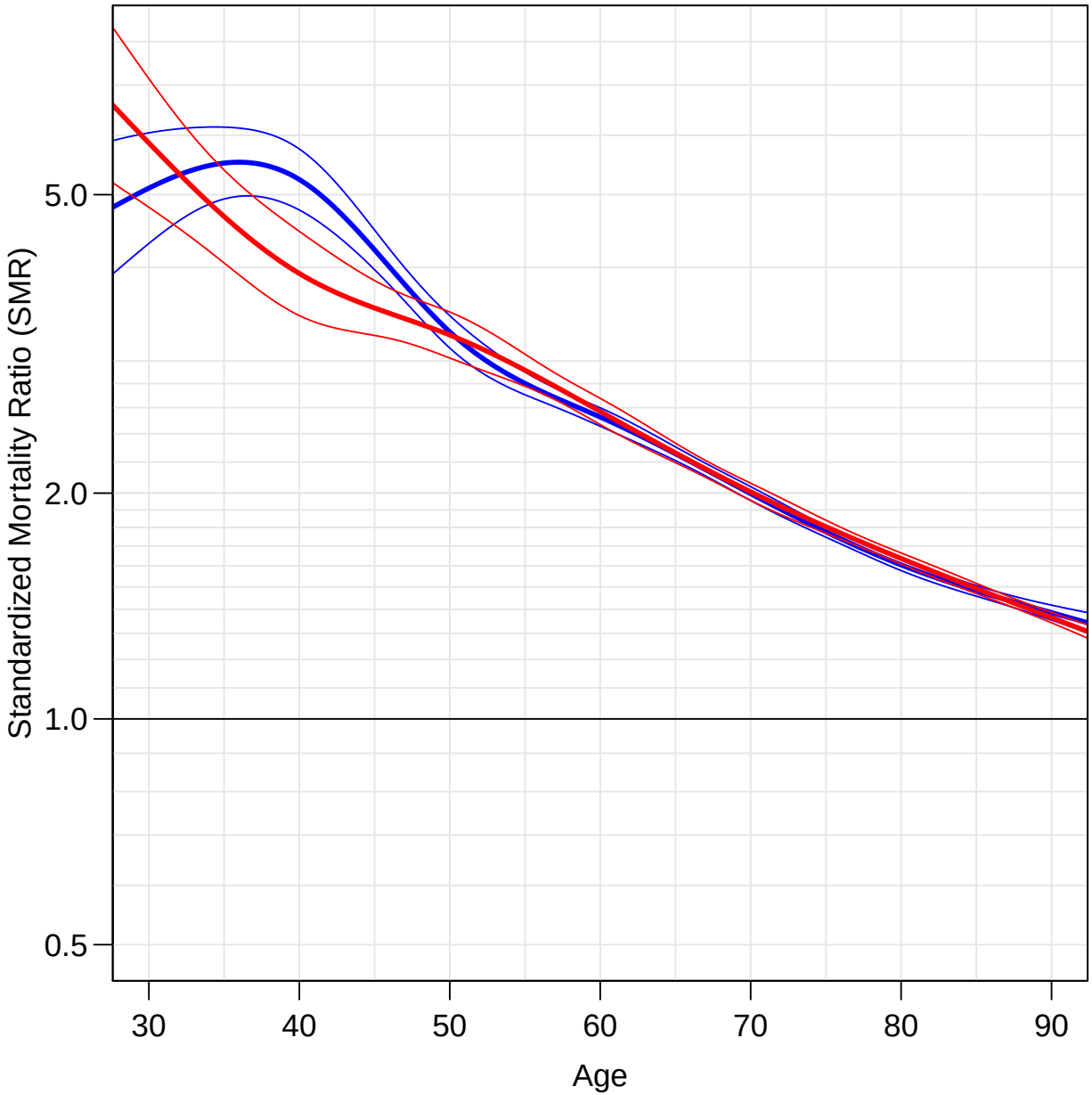
NDR 1995-2012: Prevalence[1]



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.

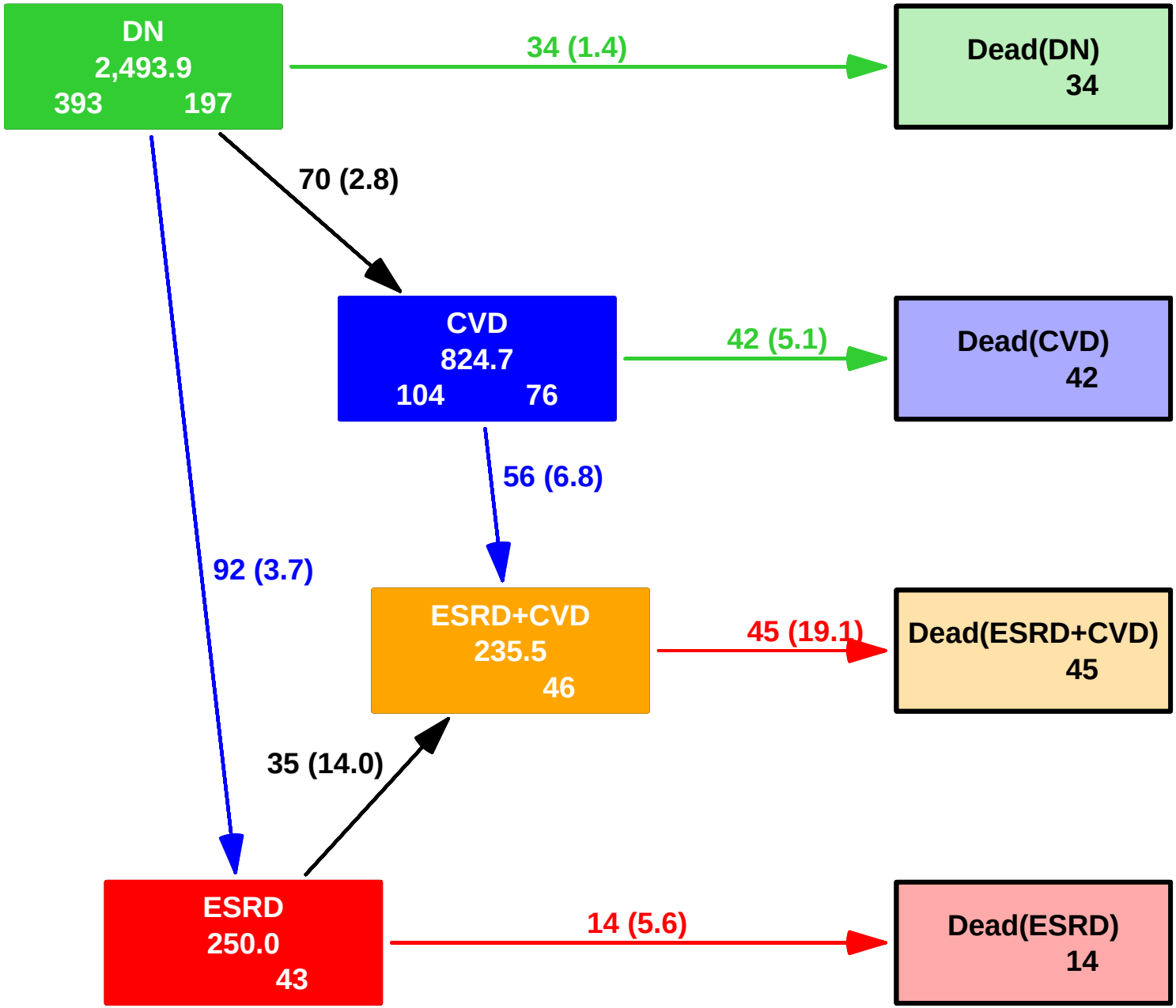
- G. Andresdottir, M. L. Jensen, B. Carstensen, H. H. Parving, P. Hovind, T. W. Hansen, P. Rossing: **Improved prognosis of diabetic nephropathy in type 1 diabetes**
  Accepted in Kidney International on 17 April 2014.

SDC:
T1DM patients with kidney compliations

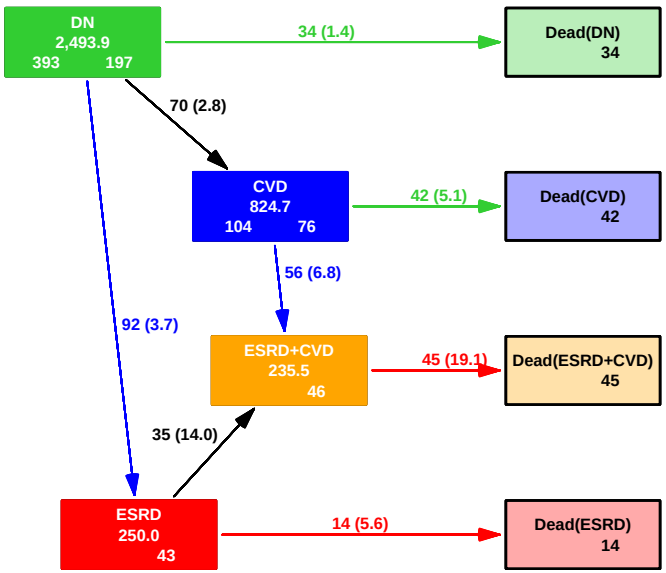
Extract patients with Diabetic Nephropathy (DN) from the SDC patient records and record:

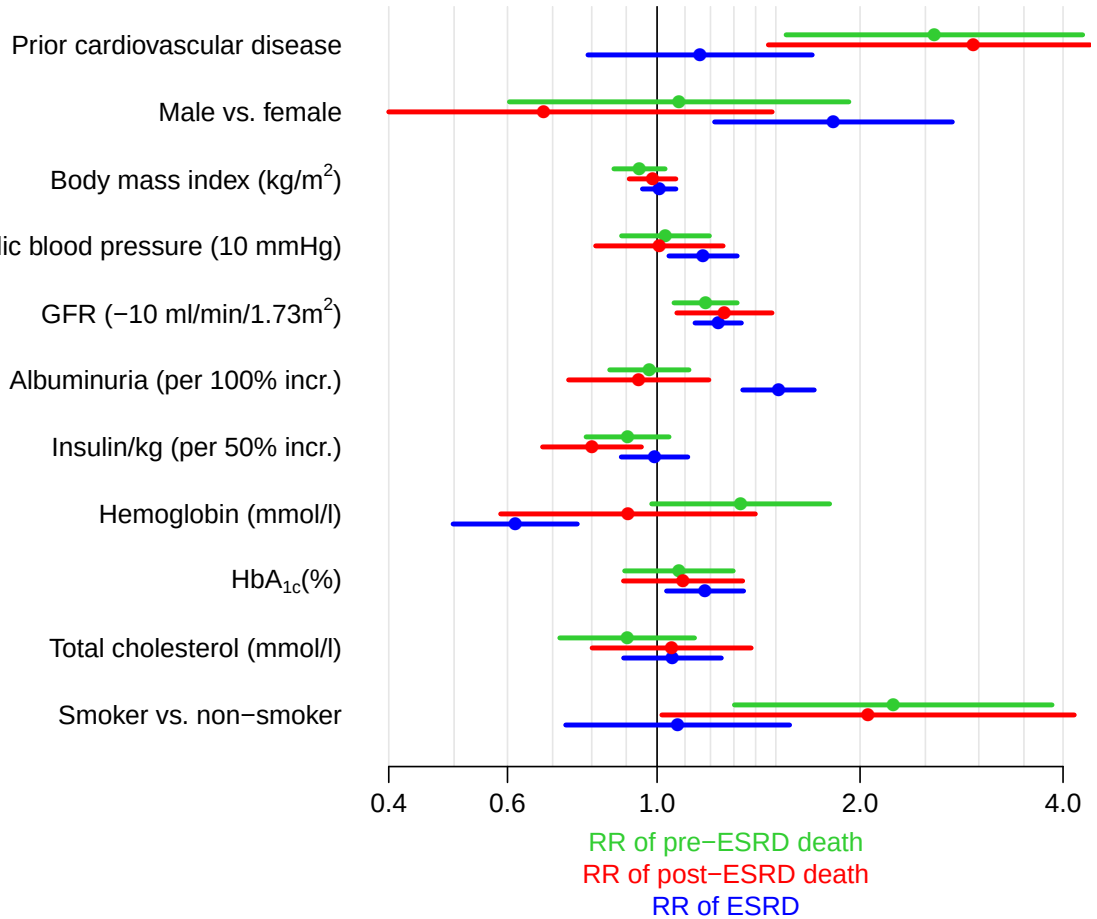
- Date of birth
- Date of diabetes
- Date of DN
- Date of CVD
- Date of ESRD
- Date of death
- Clinical parameters at date of DN (baseline)

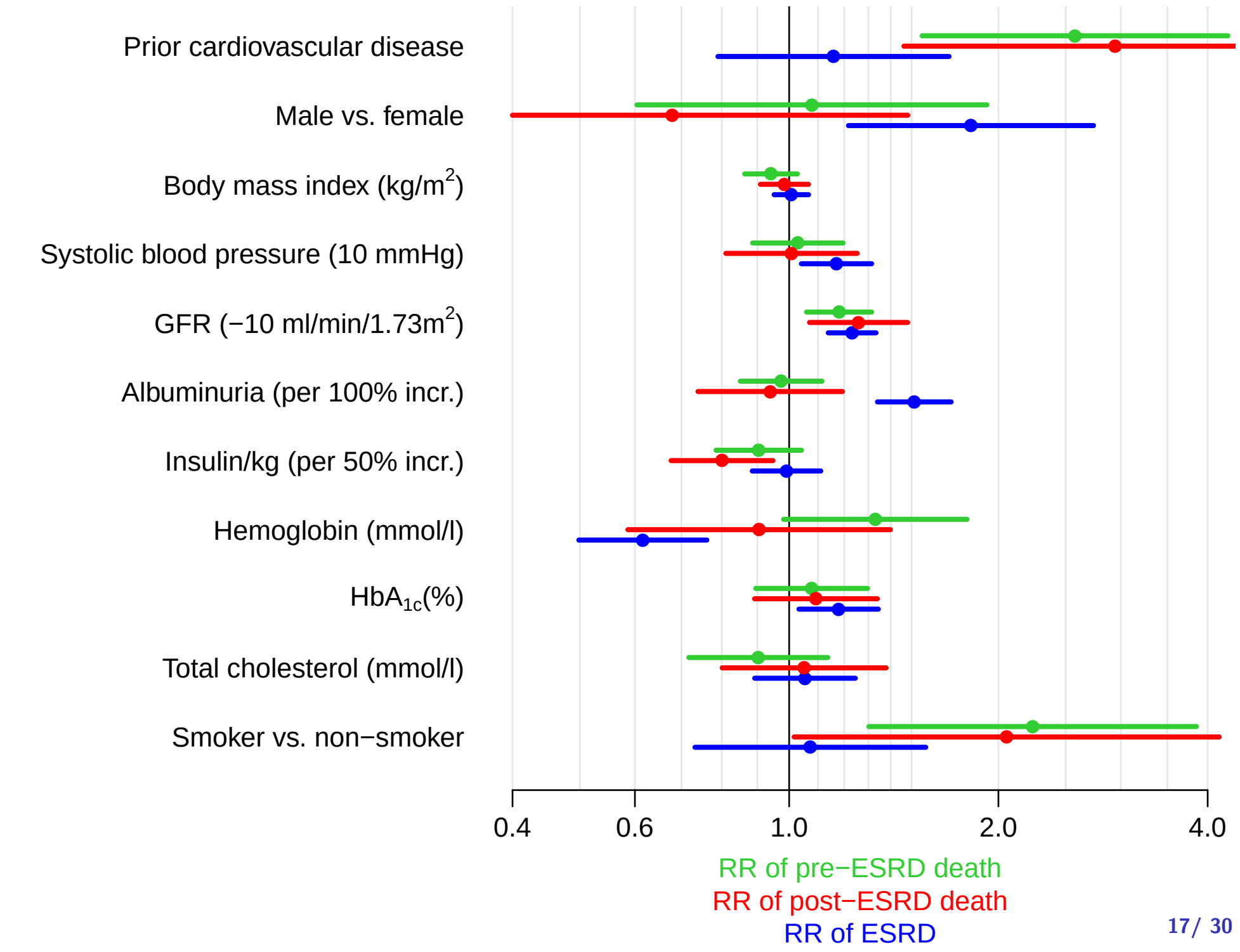
T1DM patients with kidney compliations



Covariate effects

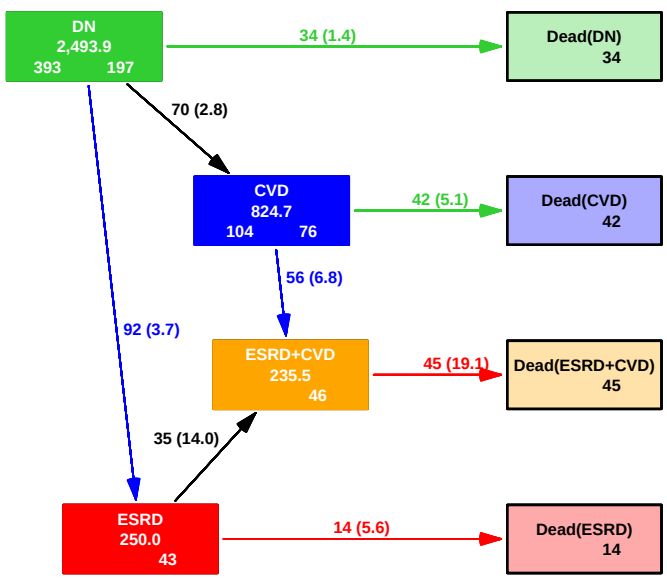


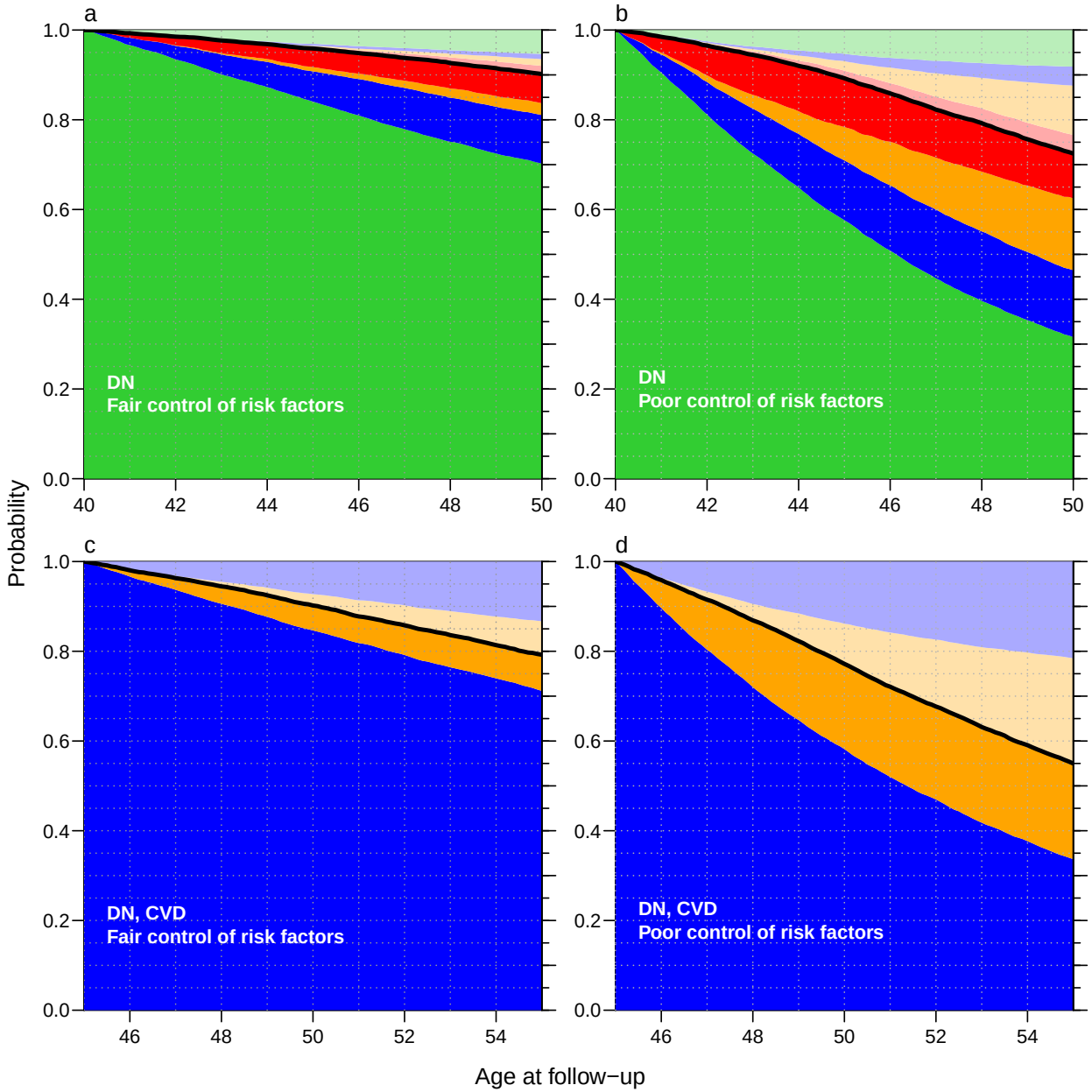


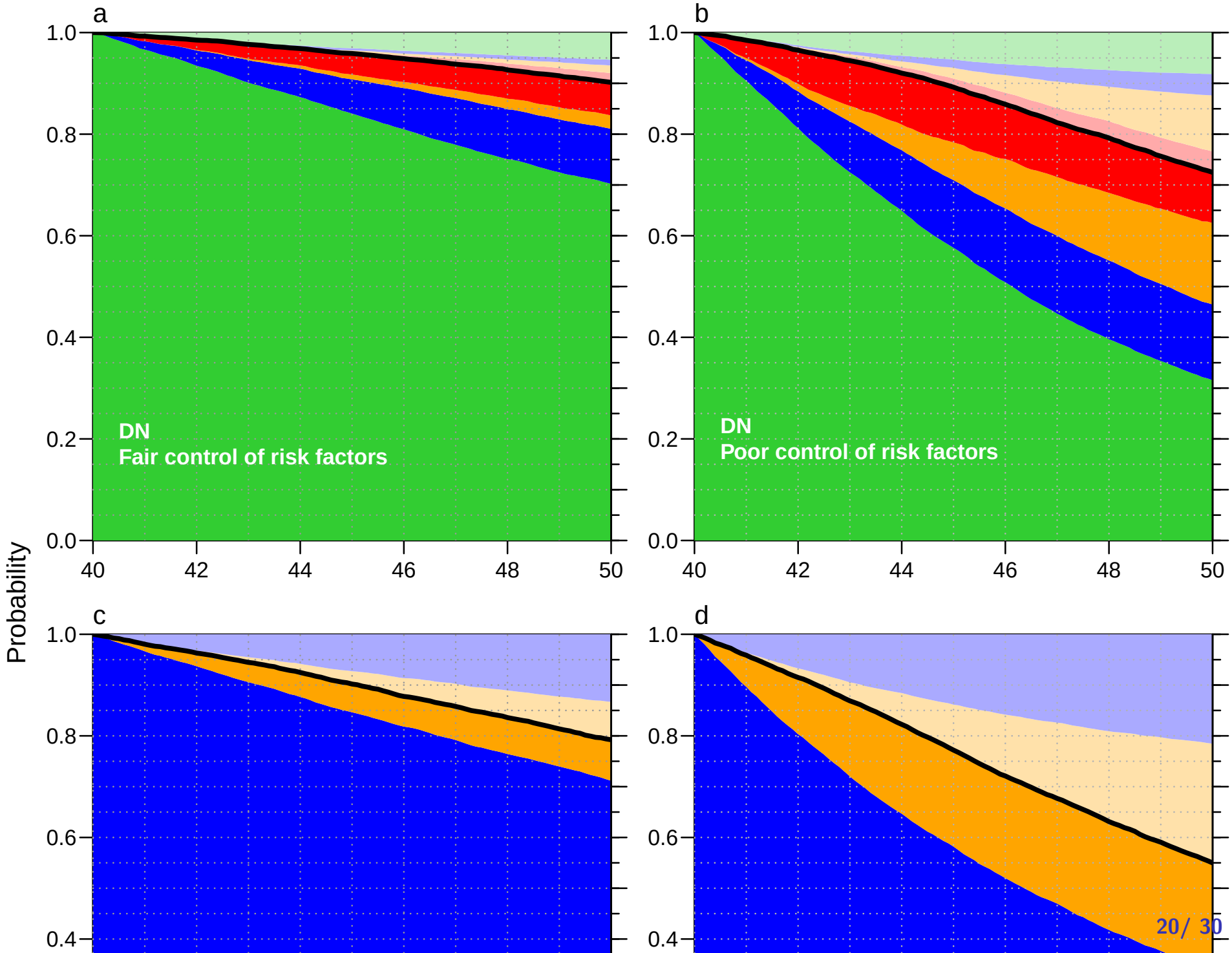

Prior cardiovascular disease
Male vs. female
Body mass index (kg/m^2)
Systolic blood pressure (10 mmHg)
GFR (−10 ml/min/1.73m^2)
Albuminuria (per 100% incr.)
Insulin/kg (per 50% incr.)
Hemoglobin (mmol/l)
HbA$_{1c}$(%)
Total cholesterol (mmol/l)
Smoker vs. non−smoker
0.4
0.6
1.0
2.0
4.0
RR of pre−ESRD death
RR of post−ESRD death
RR of ESRD

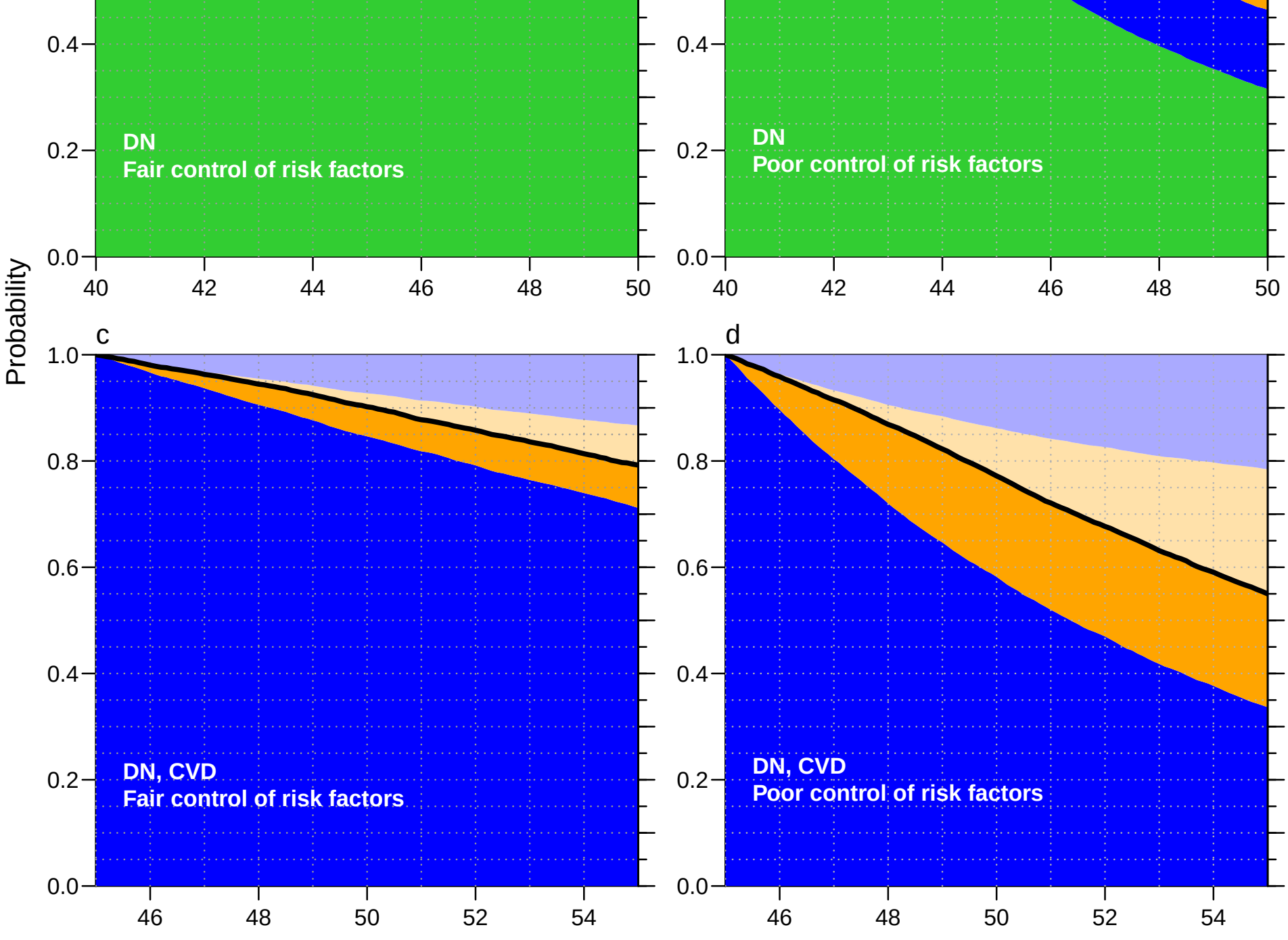
Example patients

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


DN
2,493.9
393 197
34 (1.4)
Dead(DN)
34
70 (2.8)
CVD
824.7
104 76
42 (5.1)
Dead(CVD)
42
56 (6.8)
92 (3.7)
ESRD+CVD
235.5
46
45 (19.1)
Dead(ESRD+CVD)
45
35 (14.0)
ESRD
250.0
43
14 (5.6)
Dead(ESRD)
14


a
b
c
d
Probability
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
Age at follow−up


a
b
c
d
Probability
1.0
0.8
0.6
0.4
0.2
0.0
40
42
44
46
48
50
DN
Fair control of risk factors
DN
Poor control of risk factors


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
0.0
0.2
0.4
0.6
0.8
1.0
40
42
44
46
48
50
52
54

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

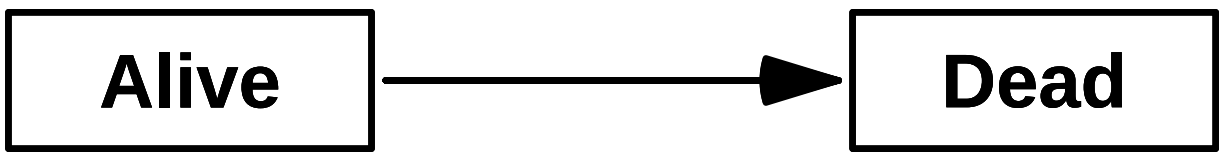
- But we gain the possibility to **compare** populations (e.g. HK & DK) with respect to
  - occurrence rates
  - **conditional** on clinical parameters:
  - are there differences that cannot be explained in terms of the clinical status of patients?
  - *i.e.* are there factors that influence rates that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

Modelling rates with current parameters

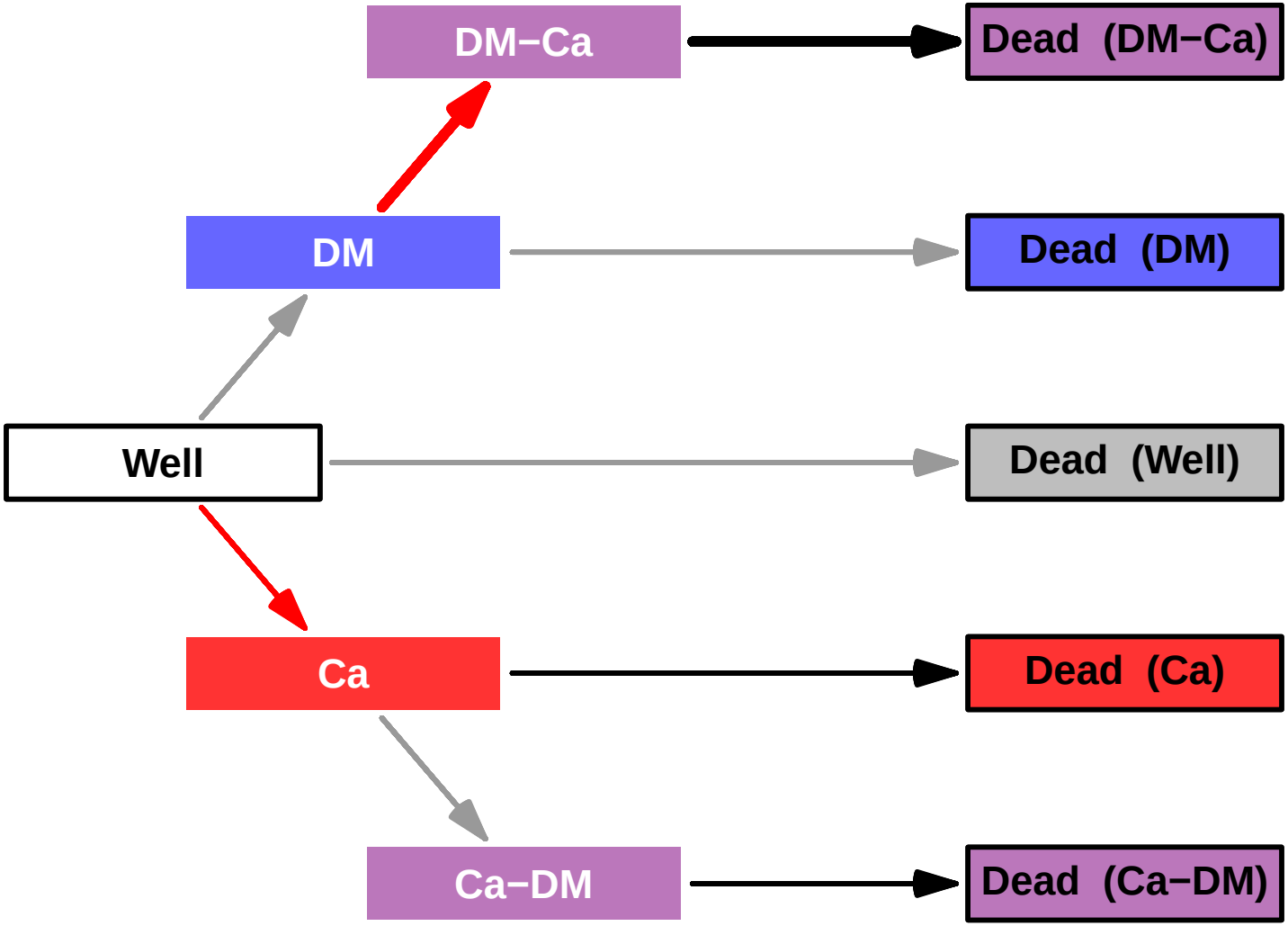
- Also gain the possibility to evaluate time-trends in mortality:
  - If trend in mortality by calendar time is negative, overall patient prognosis is improving
  - But trend may be less negative or even positive when controlling for updated clinical variables, **conditional** on current (updated) clinical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

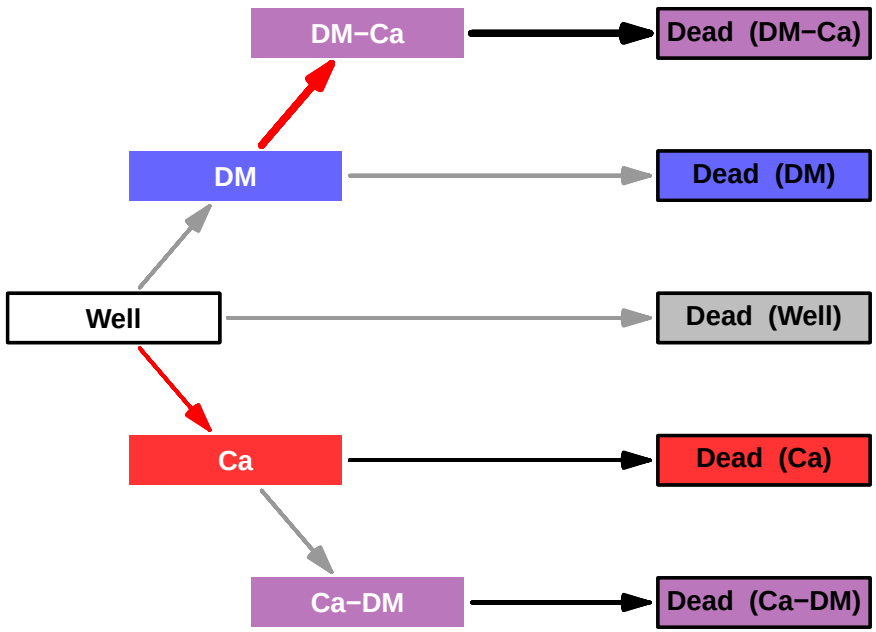


Population burden of DM & Cancer

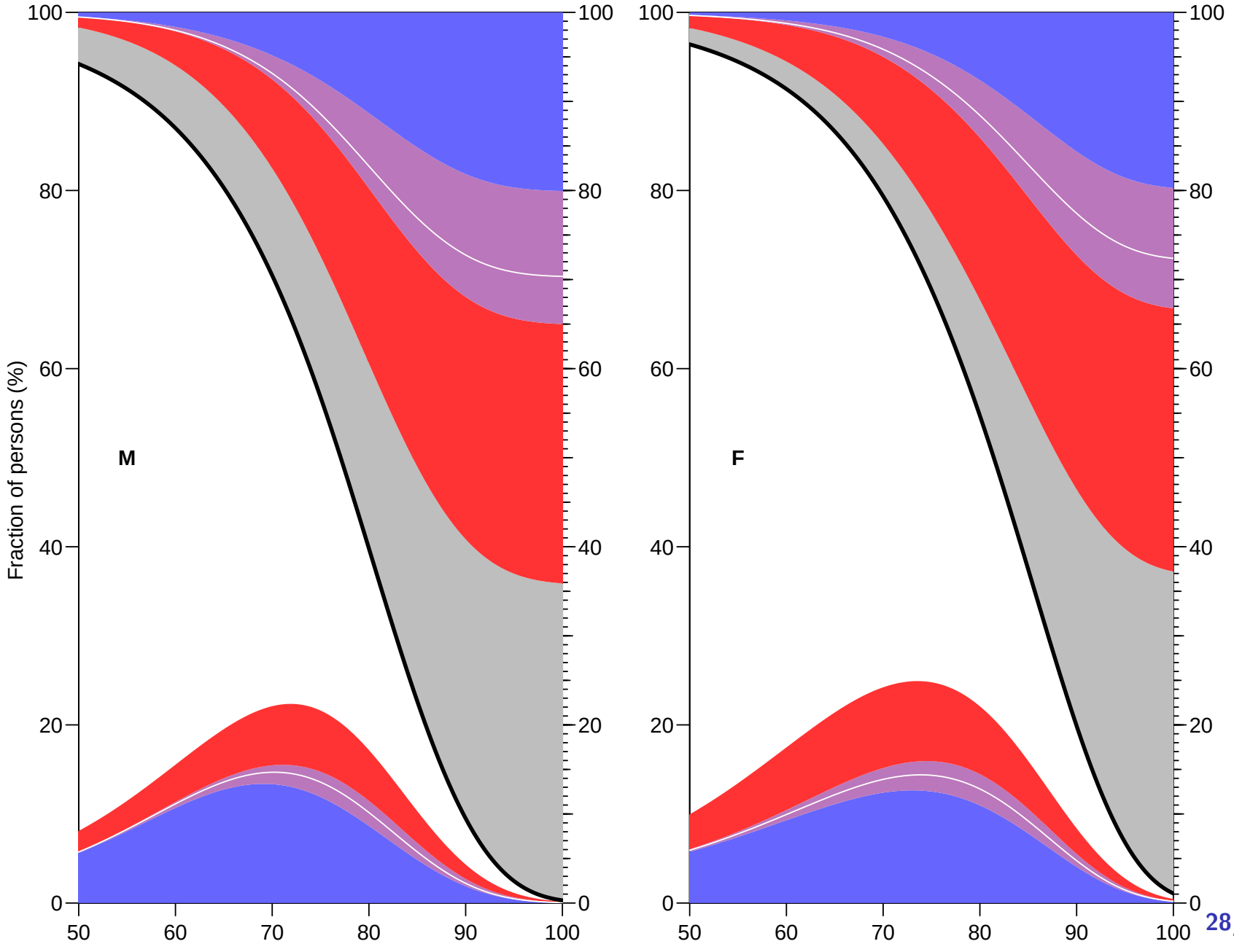
- How many people get cancer?
- How many people get diabetes?
- How many people get both DM and cancer?

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

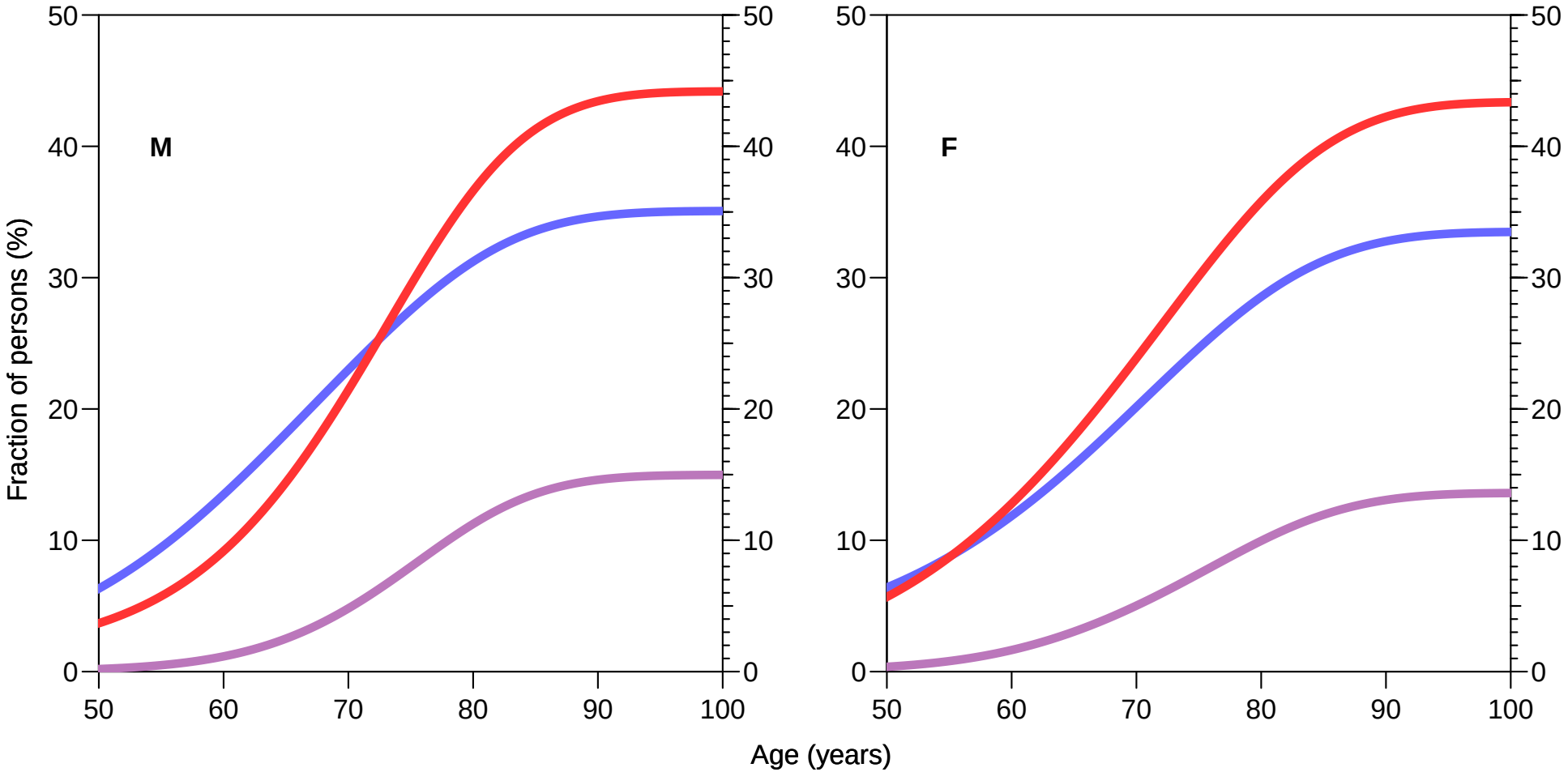
Depends on **all** the transition rates



Population burden of DM & Cancer



How many get DM/Cancer before age a



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