Methodological challenges in estimating YLD/DALY

Findings from the German Burden of Disease Study

Michael Porst + BURDEN 2020 study group
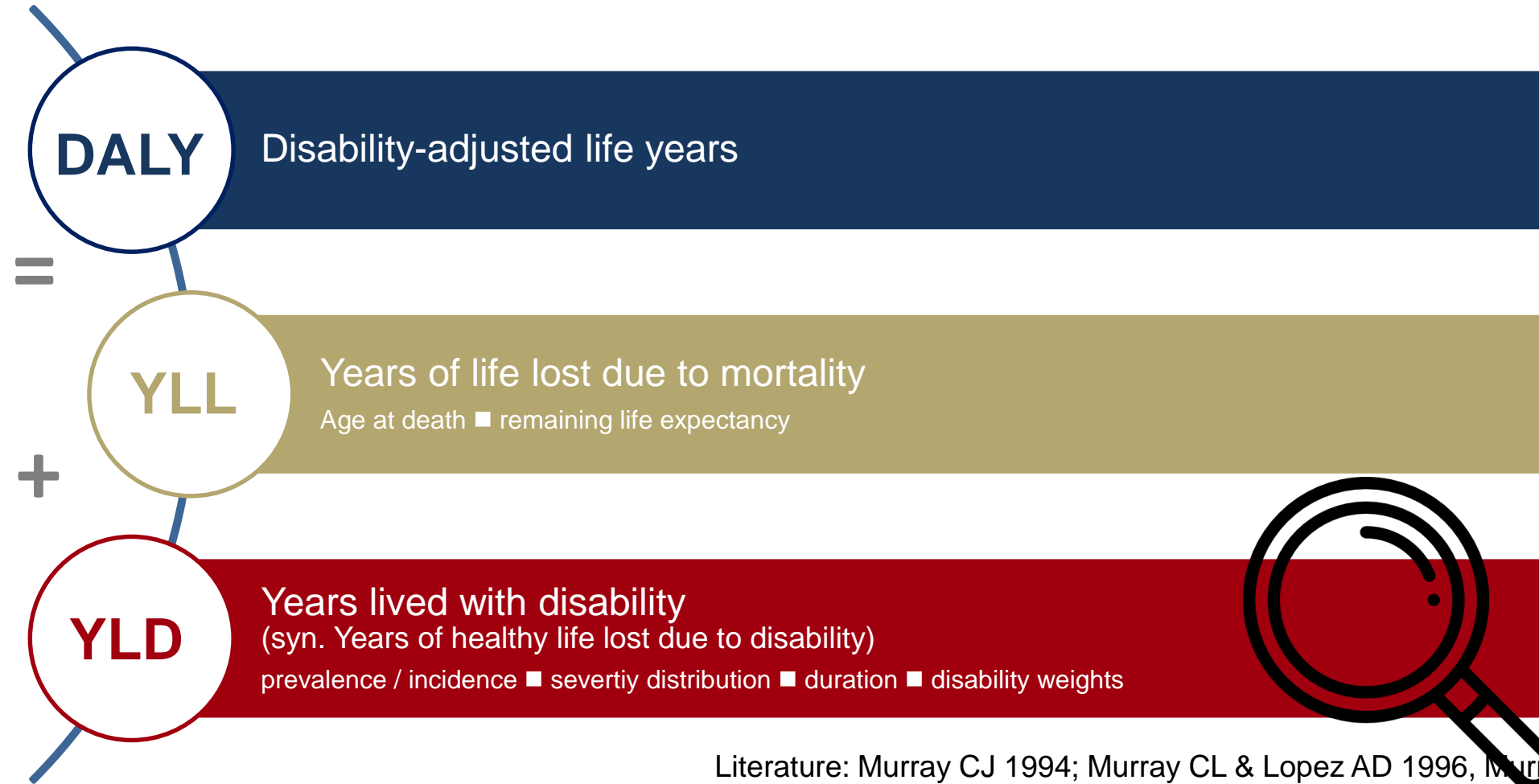
Agenda

1. Reminder: concept
2. Questions to be answered:
   I.   Where to start? - selection of diseases
   II. Which data are appropriate? - data sources
   III. Which methods do we have to apply? - methodology
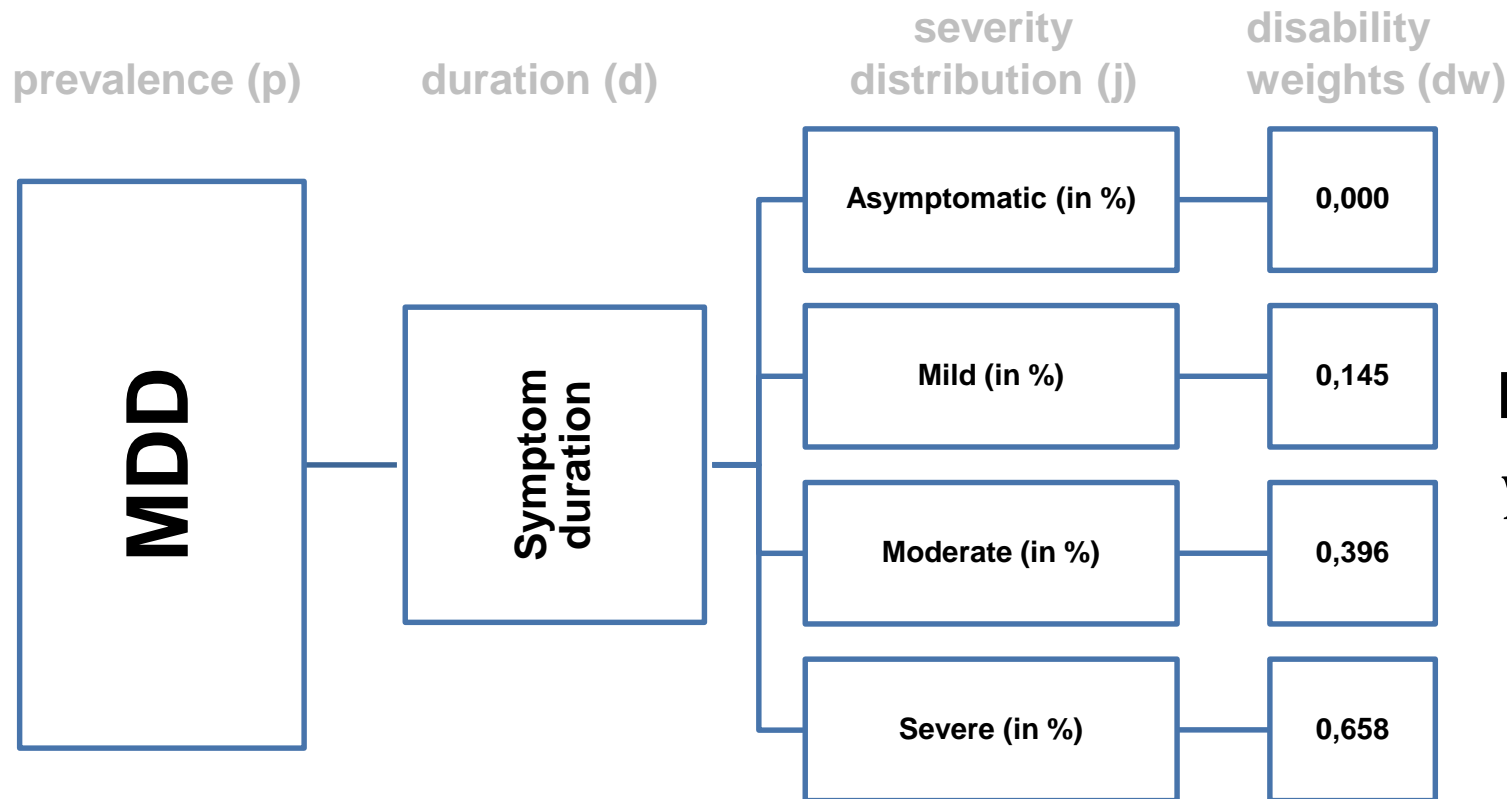3. Results

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Burden of disease indicators

DALY — Disability-adjusted life years

=

YLL — Years of life lost due to mortality
Age at death ■ remaining life expectancy

+

YLD — Years lived with disability
(syn. Years of healthy life lost due to disability)
prevalence / incidence ■ severtiy distribution ■ duration ■ disability weights

Literature: Murray CJ 1994; Murray CL & Lopez AD 1996, Murray CJ et al. 2012

Example: Major depressive disorder (MDD)

prevalence (p)   duration (d)   severity distribution (j)   disability weights (dw)

MDD — **Symptom duration**

Severity	dw
Asymptomatic (in %)	0,000
Mild (in %)	0,145
Moderate (in %)	0,396
Severe (in %)	0,658

Formula:

$$YLD_{a,s,r,c} = \Sigma_{j=1}^{k} \, p_{a,s,r,c,j} * dw_{c,j}$$

Literature: James et al. 2018

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Diseases with high Public Health relevance

Level 1	Level 2	Ranking	Level 3 (selection)	Share DALY on total for Germany (in %)
NCD	Cardiovascular diseases	1	Ischemic Heart Disease	9.3
NCD	Musculoskeletal disorders	2	Low back pain	6.6
NCD	Neoplasms	3	Tracheal, bronchial and lung cancer	4.0
NCD	Cardiovascular diseases	4	Stroke	4.0
NCD	Chronic respiratory diseases	5	Chronic obstructive pulmonary disease	3.9
NCD	Neurological disorders	6	Alzheimer- and other dementias	3.6
NCD	Diabetes and chronic kidney disease	7	Diabetes mellitus	2.9
NCD	Neurological disorders	8	Headache disorders	2.7
NCD	Musculoskeletal disorders	9	Neck pain	2.3
NCD	Mental disorders	10	Depressive disorders	2.2
NCD	Neoplasms	11	Colon and rectum cancer	2.1
NCD	Mental disorders	12	Anxiety disorders	1.9
NCD	Neoplasms	13	Breast cancer	1.7
NCD	Substance use disorders	14	Alcohol use disorders	1.3
Injury	Transport injuries	15	Road injuries	1.3
CD	Respiratory infections and tuberculosis	16	Lower respiratory infections	1.2
NCD	Neoplasms	17	Prostate cancer	1.0
NCD	Cardiovascular diseases	18	Hypertensive heart disease	1.0
		Ranking	**Total**	**53.0**

Data sources: cause list

Health insurance data

Routine data of AOK (WIdO)

Prevalence / incidence; severity distribution, duration

Official statistics

Road accident statistics

Prevalence

Survey data

e.g. Study on Back pain, Neck pain, and Headache Disorders (RKI); Epidemiological Survey of Substance Abuse (IFT)

Prevalence; severity distribution; duration

GBD-results

Severity distribution

Disability weights

Cardiovascular diseases
Neoplasms
Chronic respiratory diseases
Neurological disorders (Dementias)
Diabetes and chronic kidney disease
Mental disorders
Respiratory infections and tuberculosis

Transport injuries

Musculoskeletal disorders
Neurological disorders (Headache disorders)
Substance use disorders

Data sources: strength and limitations

Health insurance data

Routine data of AOK (WIdO)
Prevalence / incidence; severity distribution, duration

- ✓ High number of cases (by age, sex and region)
- ✓ Different information to define cases (ICD-10-codes, ATC, OPS, etc.)
- ✓ High plausibility for diseases which causes health care needs (e.g. myocardial infarction)
- ✗ Underestimation for diseases that do not require a doctor's visit (e.g. migraine)
- ✗ Not representative → Extrapolation method (Breitkreuz et al. 2019)

Official statistics

Road accident statistics
Prevalence

- ✓ High number of cases (by age, sex and region)
- ✗ Underestimation of frequency, since only cases that were recorded by the police are covered → Adjustment for cases that weren't recorded by the police based on survey estimates (Porst et al. 2022b)

Survey data

e.g. Study on Back pain, Neck pain, and Headache Disorders (RKI); Epidemiological Survey of Substance Abuse (IFT)
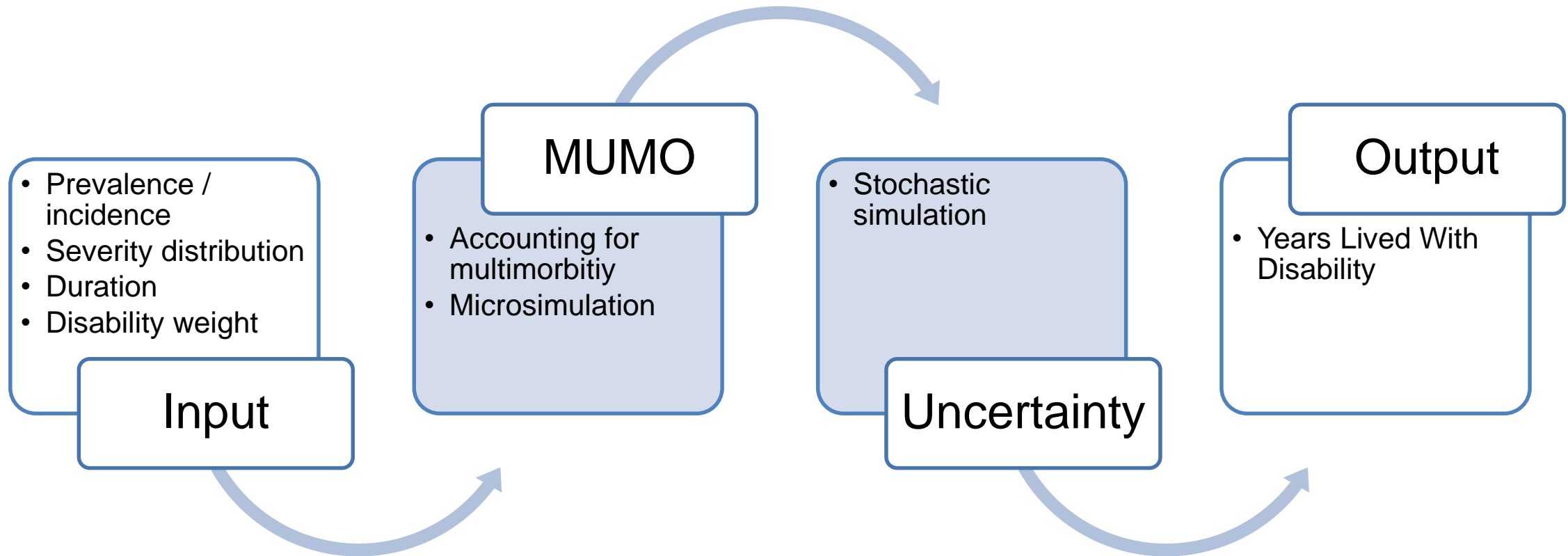Prevalence; severity distribution; duration

- ✓ Specific information to define cases (questionnaire)
- ✓ Representative for the population
- ✗ Small number of cases (need for survey weights) → Application of Small Area Estimation methods
- ✗ Selection into sample (e.g. higher educated, health)

GBD-results
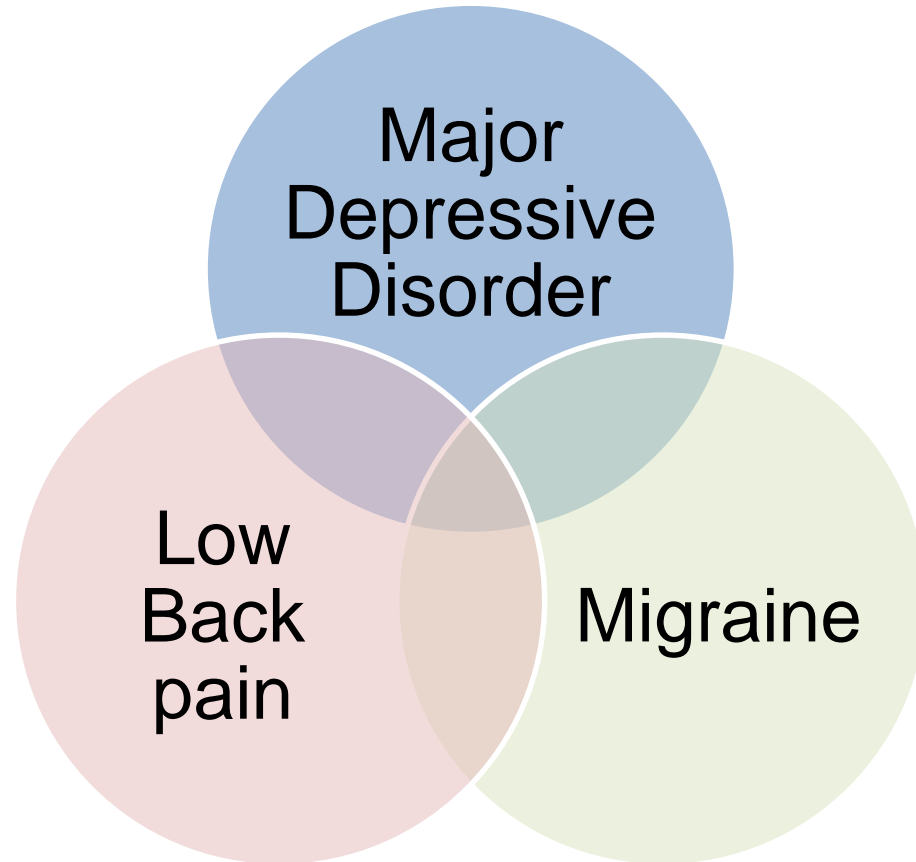
Severity distribution
Disability weights

- ✓ Data are available
- ✗ Methodological issues/critical aspects

Path from prevalence to YLD

Input
- Prevalence / incidence
- Severity distribution
- Duration
- Disability weight

MUMO
- Accounting for multimorbitiy
- Microsimulation

Uncertainty
- Stochastic simulation
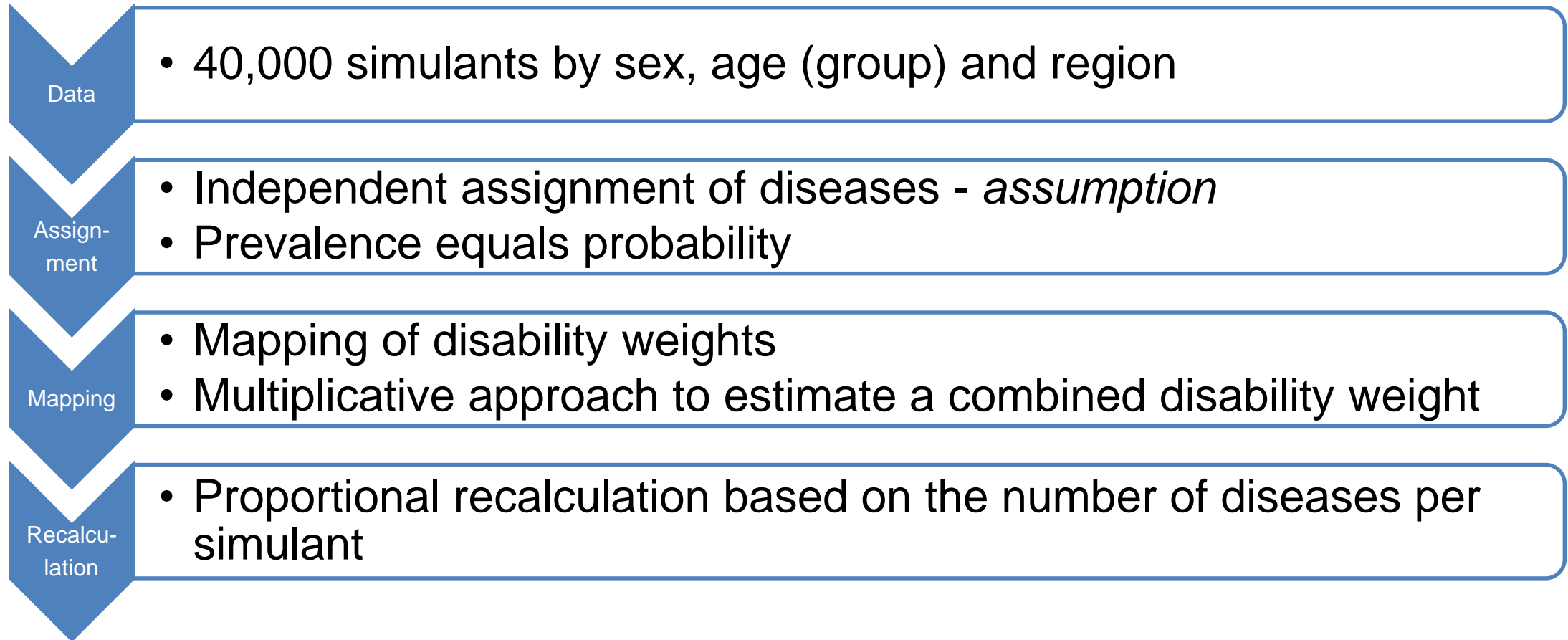
Output
- Years Lived With Disability

Multimorbidity adjustment (short MUMO)

- Correlation patterns between diseases
  - Leads to the fact of **multimorbidity**
- Without adjustment for multimorbidity we would **overestimate** YLD (Hilderink et al. 2016)
- Adjustment at overall YLD / DW → **combined DW (CDW)**
- Multiplicative approach (James et al. 2018):
  $$CDW_{ij} = 1 - ((1 - DW_i) * (1 - DW_j))$$
  → Individual burden converges to 1, but it doesn´t reach it

Microsimulation steps

Data
- 40,000 simulants by sex, age (group) and region

Assign-ment
- Independent assignment of diseases - *assumption*
- Prevalence equals probability

Mapping
- Mapping of disability weights
- Multiplicative approach to estimate a combined disability weight

Recalcu-lation
- Proportional recalculation based on the number of diseases per simulant

for details see James et al. 2018; for some more details regarding the BURDEN 2020 project see Porst et al. 2022b

Adjusted vs. unadjusted YLD

Significant reduction in YLD up to 5.6 %
- Calculated based on independent assignment
- YLD are still overestimated

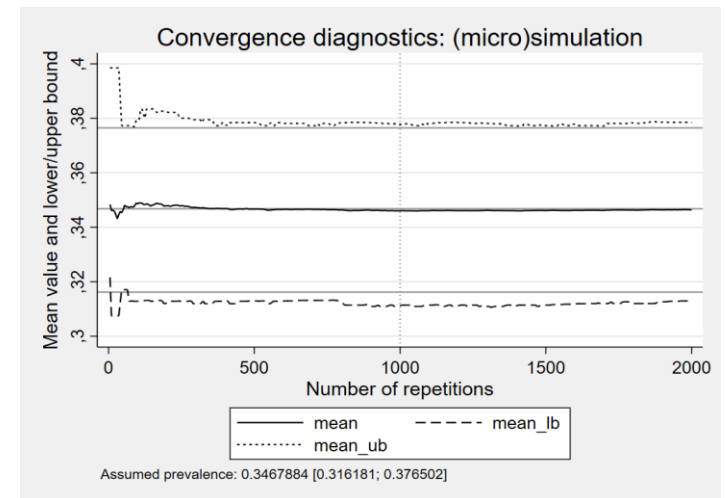| Burden of disease cause (level 3)	$YLD_{unadjusted}$	$YLD_{adjusted}$	Reduction (in %)
ischemic heart disease	212.080,9	202.781,5	-4,4%
lower back pain	1.485.972,0	1.434.132,0	-3,5%
tracheal, bronchus, and lung cancer	35.045,9	33.464,0	-4,5%
stroke	106.608,7	102.268,8	-4,1%
chronic obstructive pulmonary disease	311.586,8	301.819,1	-3,1%
Alzheimer's disease and other dementias	249.555,4	235.566,2	-5,6%
diabetes mellitus	541.972,2	526.822,9	-2,8%
headache disorders	878.128,4	853.028,3	-2,9%
neck pain	486.411,4	473.412,9	-2,7%
depressive disorders	478.367,4	469.767,3	-1,8%
colon and rectum cancer	62.269,5	59.502,2	-4,4%
anxiety disorders	510.356,2	500.130,3	-2,0%
breast cancer	105.120,2	101.444,9	-3,5%
alcohol use disorders	215.066,2	208.714,8	-3,0%
road injuries	65.375,6	64.581,3	-1,2%
lower respiratory infections	13.117,3	13.041,5	-0,6%
prostate cancer	73.377,0	69.976,4	-4,6%
hypertensive heart disease	77.827,6	74.197,5	-4,7%

see Porst et al. 2022b, Table 7

Uncertainty interval (short UI)

Input variables:

p / i	d	j	dw
UI [lb;ub]	UI [lb;ub]	UI [lb;ub]	UI [lb;ub]

YLD
UI [lb;ub]
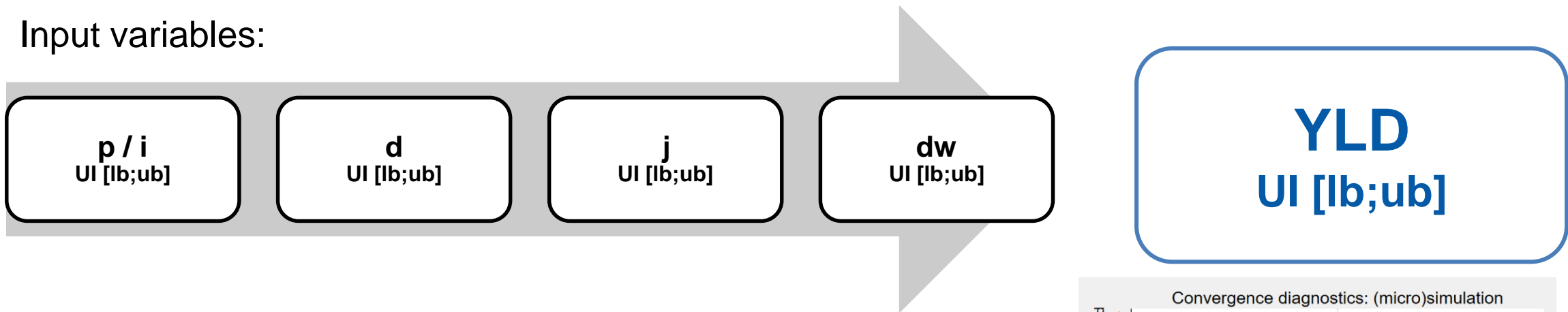
Method (more details see Porst et al. 2022b):

- Distribution of each Input-variable is known (assumption: log-normal distribution) and given by the mean and standard deviation
- Algorithm: draw a random value from a log-normal distribution (1), estimate YLD by each disease model (2) and repeat steps (1) and (2) 1,000 times to obtain a distribution of the outcome
- Estimate UI by the 2.5 and 97.5 percentile

Convergence diagnostics: (micro)simulation

Assumed prevalence: 0.3467884 [0.316181; 0.376502]

see Porst et al. 2022b, Figure 4

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DALY (rates) overall by sex
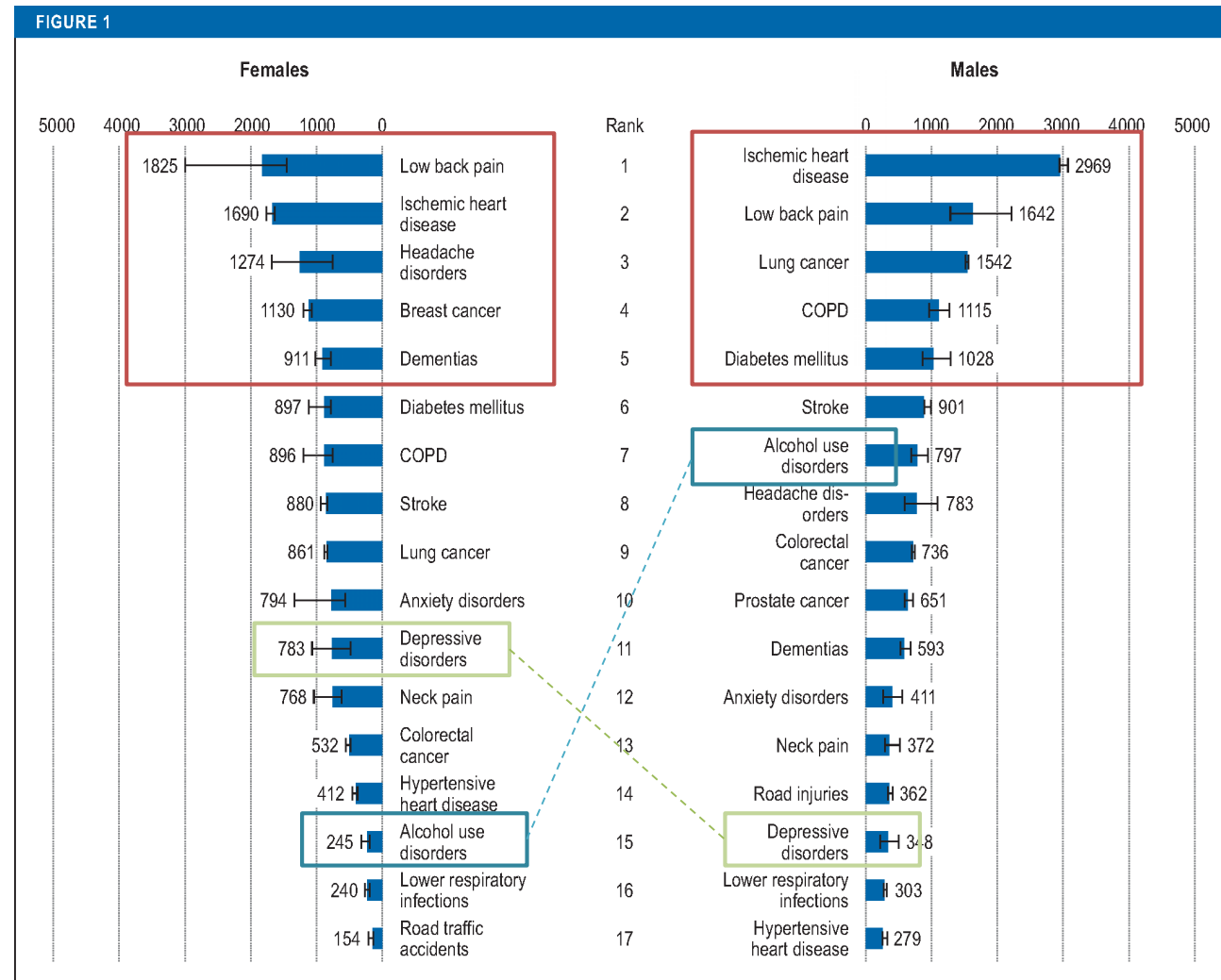
Total burden of disease (DALY per 100 000 population [pop]) for selected causes of burden of disease by sex (Level 3, Germany), error bars correspond to the 95% UI; source: BURDEN 2020; YLL: cause of death statistics 2017 (31), Federal Statistical Office of Germany 2018 (32); YLD: *eTable 3*; our own calculations; only 17 ranks each are presented here since no DALY were calculated for prostate cancer in women and breast cancer in men, and the residual category "Other transport injuries" is not shown (*eTable 1*, *eTable 2*); data limitations must be taken into account when making a direct comparison of DALY (*eTable 3*); COPD, chronic obstructive pulmonary disease; DALY, disability-adjusted life years; RI, road injuries; YLL, years of life lost due to death; YLD, years lived with disability

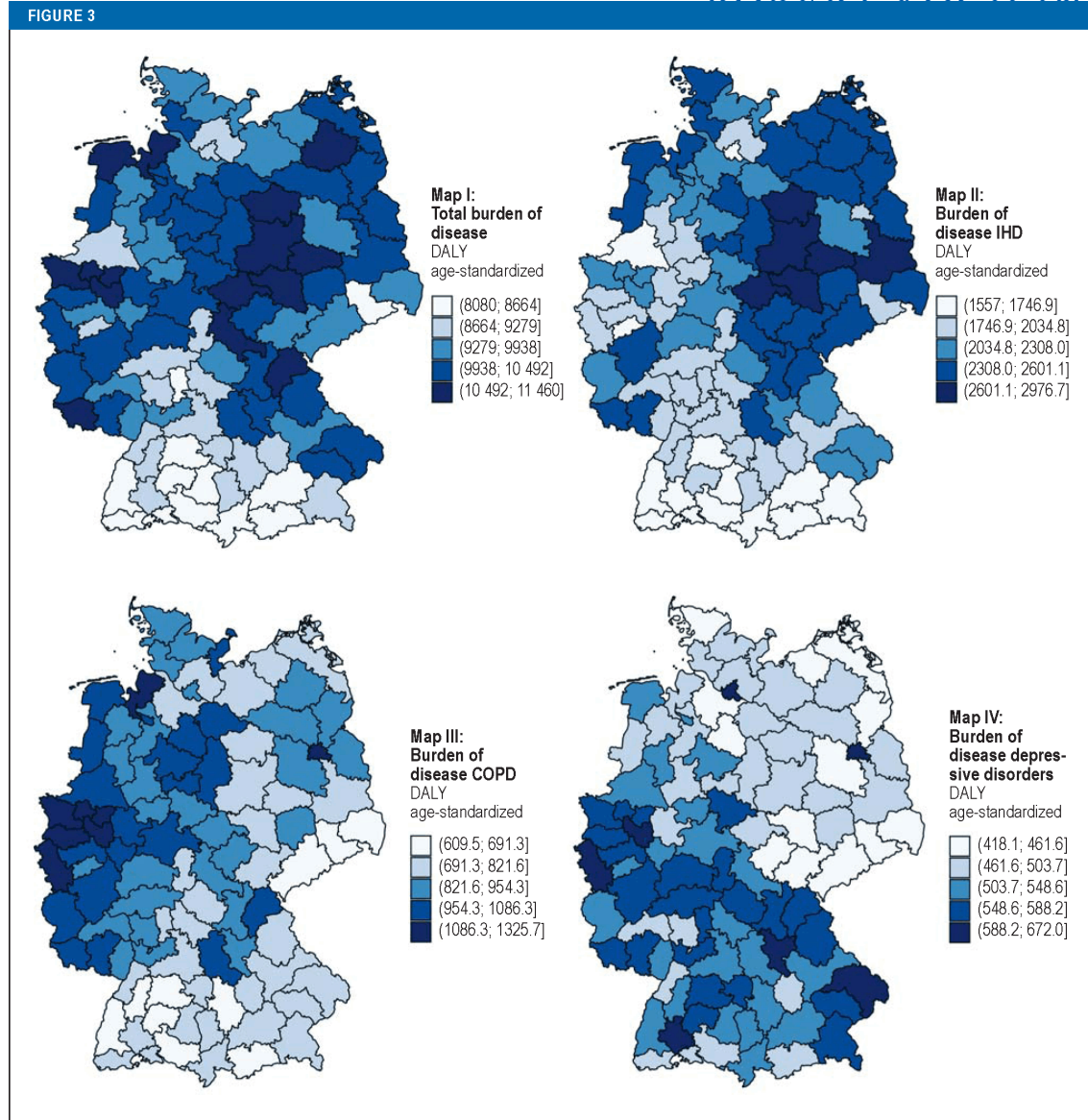Source: Porst et al. 2022a

Share of YLD and YLL by cause

FIGURE 2
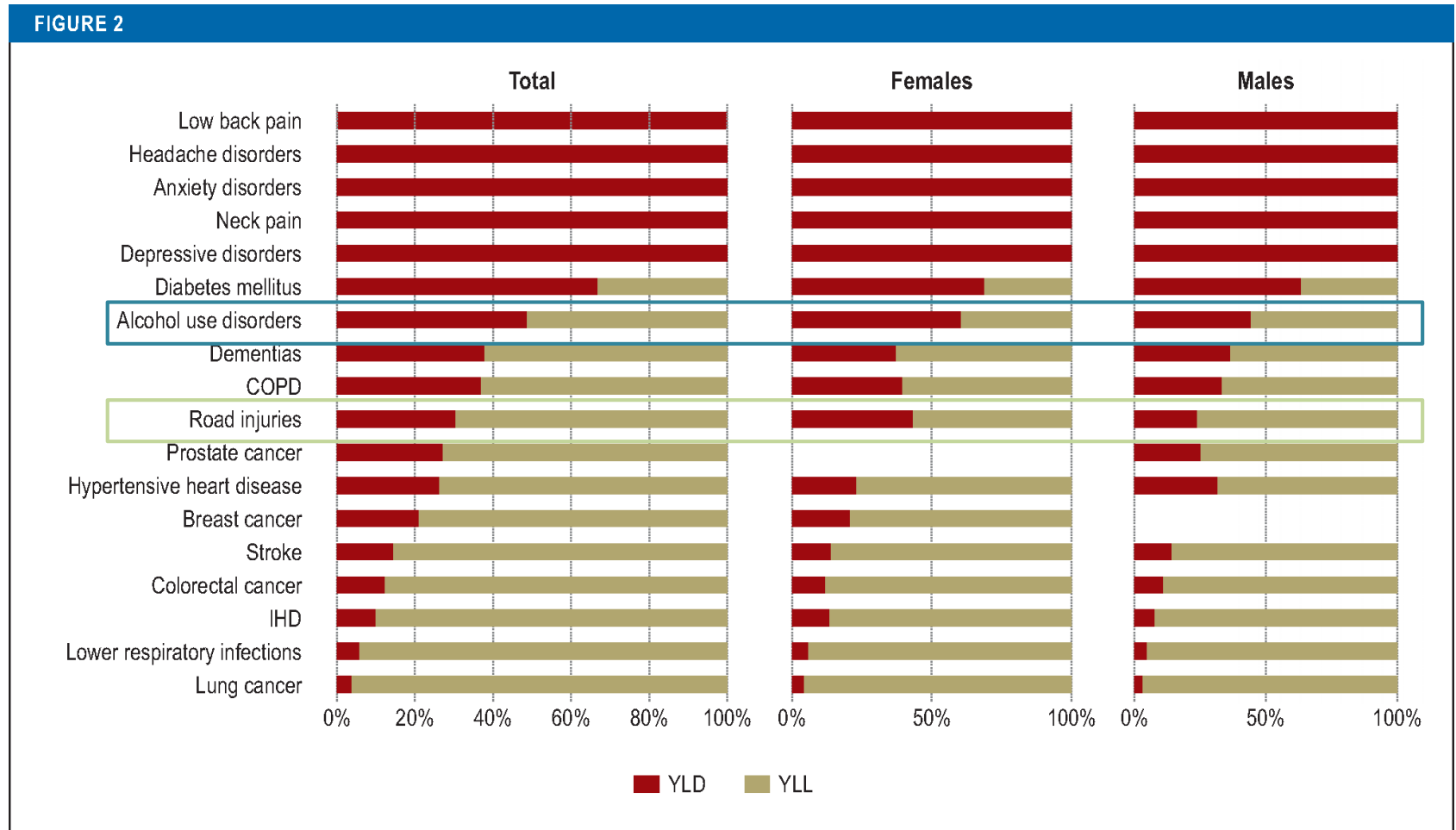
Relative contribution of YLL and YLD to the total burden of disease (absolute DALY) for the selected causes of burden of disease (level 3, Germany, both sexes)
Source: BURDEN 2020; YLL: Cause of death statistics 2017 (31), Federal Statistical Office of Germany 2018 (32); YLD: *eTable 3*; own calculations; the residual category "Other transport injuries" is excluded (*eTable 1*, *eTable 2*); COPD, chronic obstructive pulmonary disease; DALY, disability-adjusted life years; IHD, coronary heart disease; YLL, years of life lost due to death; YLD, years lived with disability

Source: Porst et al. 2022a

DALY (age-standardized) on regional level

Level: 96 spatial planning regions (SPR)

FIGURE 3

Map I:
Total burden of
disease
DALY
age-standardized

(8080; 8664]
(8664; 9279]
(9279; 9938]
(9938; 10 492]
(10 492; 11 460]

Map II:
Burden of
disease IHD
DALY
age-standardized

(1557; 1746.9]
(1746.9; 2034.8]
(2034.8; 2308.0]
(2308.0; 2601.1]
(2601.1; 2976.7]

Map III:
Burden of
disease COPD
DALY
age-standardized

(609.5; 691.3]
(691.3; 821.6]
(821.6; 954.3]
(954.3; 1086.3]
(1086.3; 1325.7]

Map IV:
Burden of
disease depres-
sive disorders
DALY
age-standardized

(418.1; 461.6]
(461.6; 503.7]
(503.7; 548.6]
(548.6; 588.2]
(588.2; 672.0]

Total burden of disease (age-standardized DALY per 100 000 population) at the spatial planning regions level (level 3, both sexes) for the sum of all causes of burden of disease (Map I), and for IHD (Map II), COPD (Map III) and depressive disorders (Map IV); range in brackets
Source: BURDEN 2020; YLL: Cause of death statistics 2017 (31), Federal Statistical Office of Germany 2018 (32); YLD: eTable 3; our own calculations; spatial planning regions, see Federal Institute for Research on Building, Urban Affairs and Spatial Development (BBSR) (34); Map I total burden of disease. Excluded from Map I are pain disorders and alcohol use disorders due to the lack of spatial data resolution (eTable); COPD, chronic obstructive pulmonary disease; DALY, disability-adjusted life years; IHD, ischemic heart disease; YLL, years of life lost due to death; YLD, years lived with disability

Summing up

- Start with a selection of diseases
- Find/collect appropiate data sources depending on disease and input variable (prevalence/incidence, severity distribution, duration)
  - Is the outcome well represented in the data? (bias: underestimation, overestimation)
  - Estimates by age and sex and subnational level possible?
- Setting up data management
- YLD adjustment
  - Method: microsimulation or something simpler/more complex?
  - Independent vs. dependent adjustment (tbd)
- Uncertainty
  - Shape: log-normal distribution? (gamma distribution)
  - DALY: combining UIs of YLL and YLD

RKI   Alexander Rommel, Elena von der Lippe, Annelene Wengler, Michael Porst,
         Janko Leddin, Aline Anton, Caoimhe Cawley & Thomas Ziese

UBA   Dietrich Plaß & Heike Gruhl

WIdO Katrin Schüssel, Gabriela Brückner, Jan Breitkreuz & Helmut Schröder

Literature

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- Hilderink, H. B., et al. (2016). "Accounting for multimorbidity can affect the estimation of the Burden of Disease: a comparison of approaches." Archives of public health = Archives belges de sante publique 74(1): 1 - 16.

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- Murray CJ: Quantifying the burden of disease: the technical basis for disability-adjusted life years. Bull World Health Organ 1994; 72: 429–45.

- Murray CJL, Lopez AD: The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020. Cambridge: Harvard School of Public Health on behalf of the World Health Organization and the World Bank 1996.

- Porst M, von der Lippe E, Leddin J, Anton A, Wengler A, Breitkreuz J, Schüssel K, Brückner G, Schröder H, Gruhl H, Plaß D, Barnes B, Busch MA, Haller S, Hapke U, Neuhauser H, Reitzle L, Scheidt-Nave C, Schlotmann A, Steppuhn H, Thom J, Ziese T, Rommel A: The burden of disease in Germany at the national and regional level—results in terms of disability-adjusted life years (DALY) from the BURDEN 2020 study. Dtsch Arztebl Int 2022a; 119: 785–92. DOI: 10.3238/arztebl.m2022.0314

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Several approaches: combined DW (CDW)

- Additive approach
  - $CDW_{ij} = DW_i + DW_j$

    → Individual burden sums up to more than 1

- Maximum approach
  - $CDW_{ij} = \max(DW_i, DW_j)$

    → Counting the health state with the highest burden

- Multiplicative approach
  - $CDW_{ij} = 1 - ((1 - DW_i) * (1 - DW_j))$

    → Individual burden converges to 1, but it doesn´t reach it

see Hilderink et al. 2016

Example: Major depressive disorder (MDD)

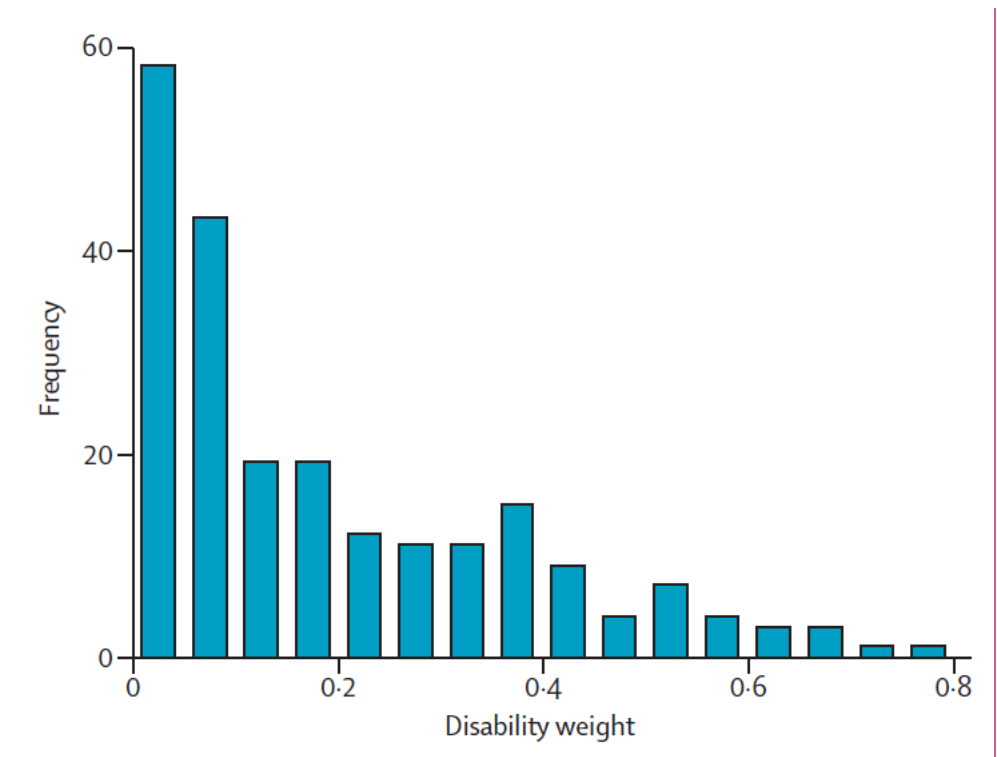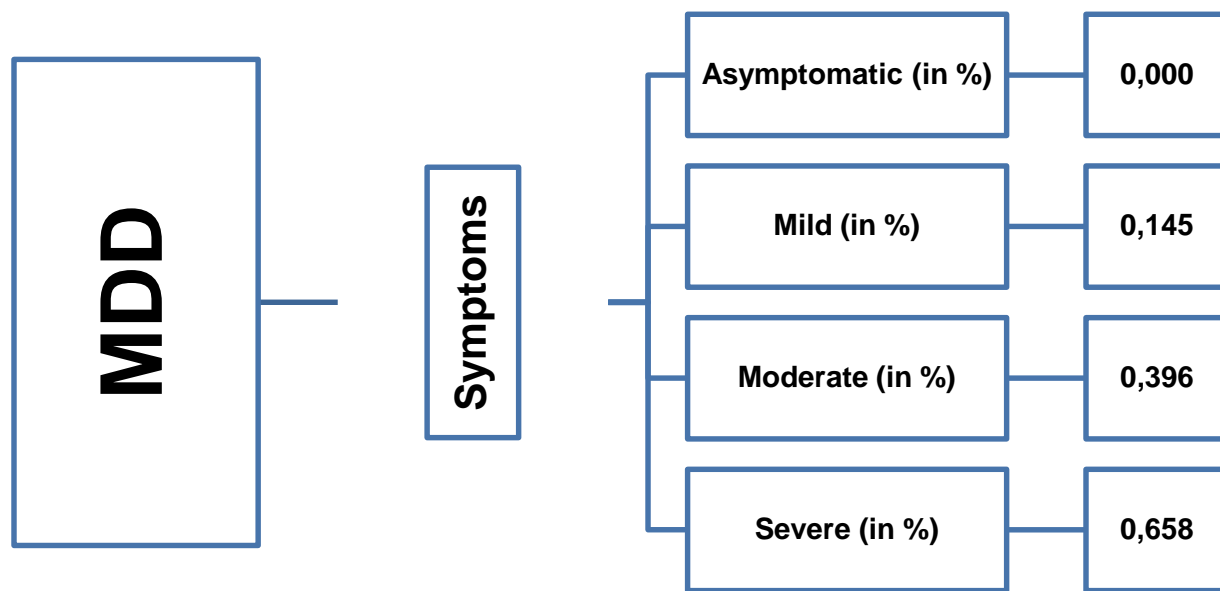Prevalence   Duration   Severity distribution   Disability weights
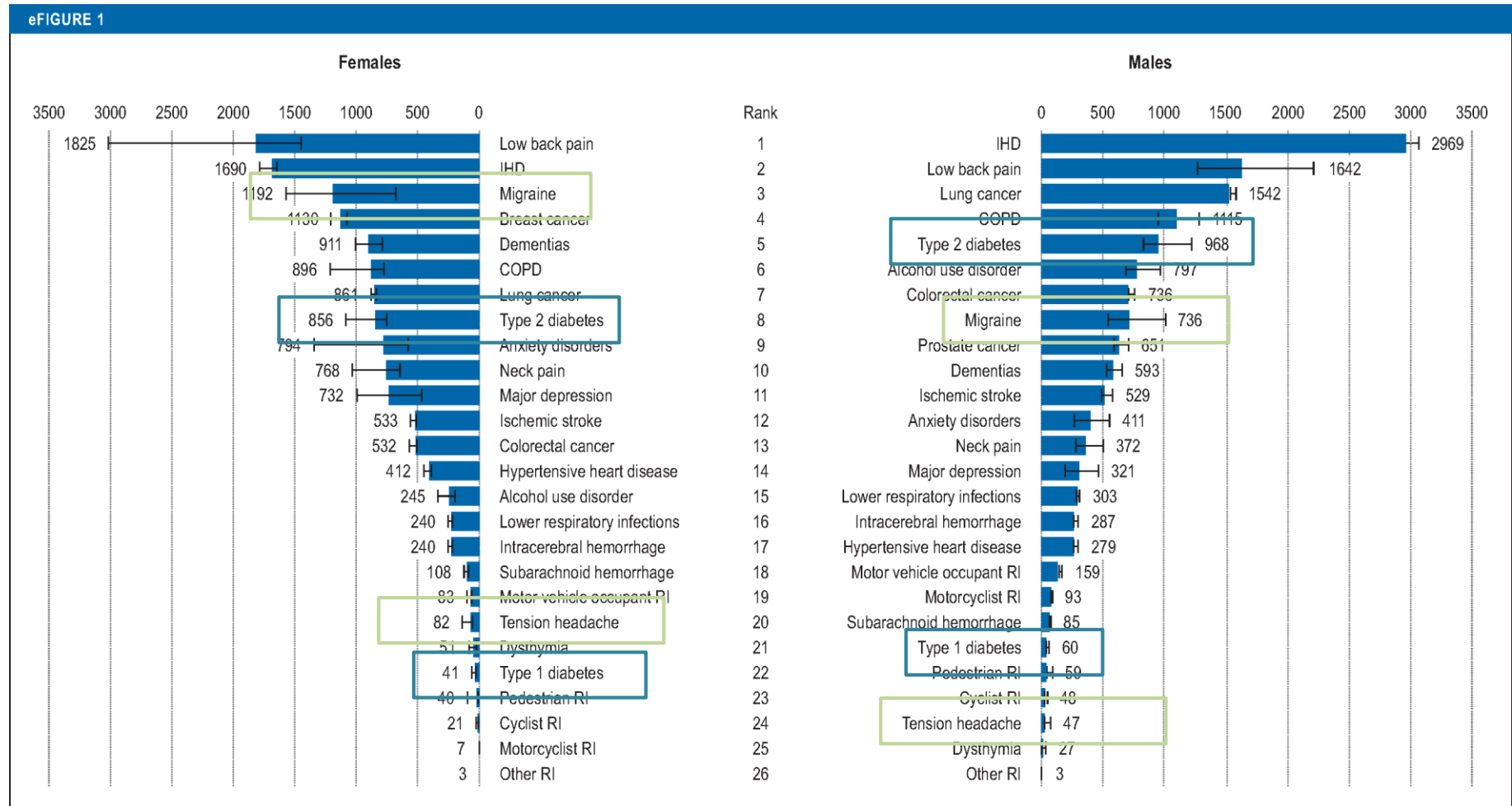

MDD	Symptoms	Asymptomatic (in %)	0,000
		Mild (in %)	0,145
		Moderate (in %)	0,396
		Severe (in %)	0,658

Figure 4: Frequency distribution of disability weights for 220 health states

Salomon et al. 2012, p. 2138

DALY (rates) overall by sex

eFIGURE 1

Total burden of disease (DALY per 100 000 population [pop]) of the selected causes of burden of disease by sex (level 4, Germany), error bars correspond to the 95% UI

Source: BURDEN 2020; YLL: Cause of death statistics 2017 (31), Federal Statistical Office of Germany 2018 (32); YLD: (eTable 3); our own calculations; only 26 ranks each are presented here because no DALY were calculated for prostate cancer in women and breast cancer in men, and the residual category "Other transport injuries" is not shown (eTable 1, eTable 2); data limitations must be taken into account when making a direct comparison of DALY (eTable 3); COPD, chronic obstructive pulmonary disease; DALY, disability-adjusted life years ; RI, Road injuries; YLL, years of life lost due to death; YLD, years lived with disability

Source: Porst et al. 2022a