Amager and Hvidovre Hospital
Clinical Research Department

UNIVERSITY OF COPENHAGEN

Jon Ambæk Durhuus

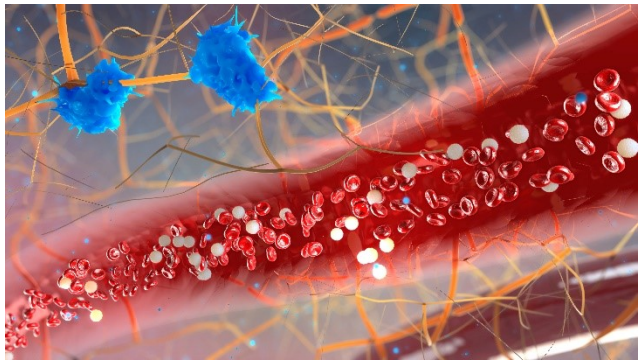
PhD, MSc Biomedicine

Molecular and Clinical Perspectives on Multimorbidity in Elderly Patients

Department of Clinical Research, Copenhagen University Hospital – Amager & Hvidovre Hospital (AHH), Denmark

MSc in Biomedicine (RUC)

DNA repair research



PhD in cellular and genetic medicine (UCPH, CEHA)

Mitochondrial research

"Simvastatin usage Alters Mitochondrial Respiration"

Postdoc (HNPCC register, AHH)

- Hereditary Urothelial Tumour Signature
- Population-based Reflex Testing for Defective MMR in CRC

Clinical Research Department

- Biomarkers of inflammaging in patients with multimorbidity and polypharmacy
- Post-acute sequelae in COVID-19 patients

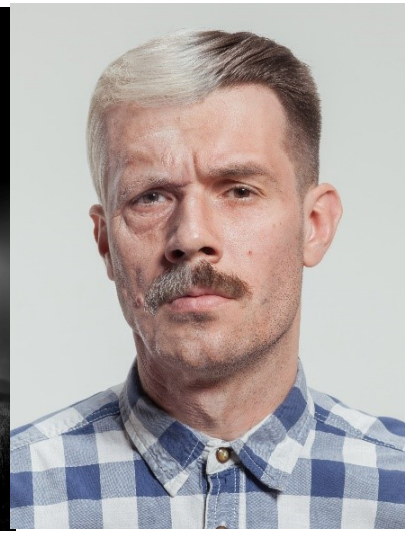
Background - ageing models

House mouse

- Short lived
- 2-year life-span, (max 5 years)
- Cancer prone

Naked mole rat

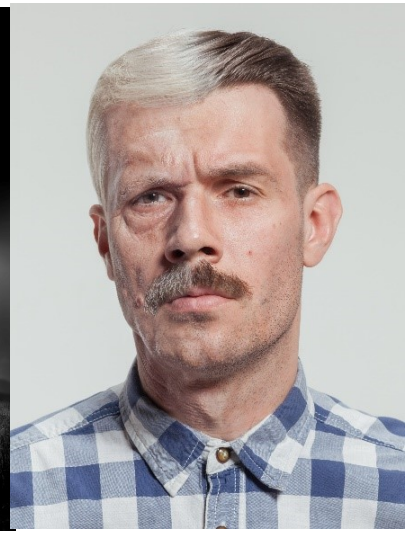
- Long lived
- 30-year life-span, (max 36 years)
- “Never gets cancer” → Carcinogenesis resistant

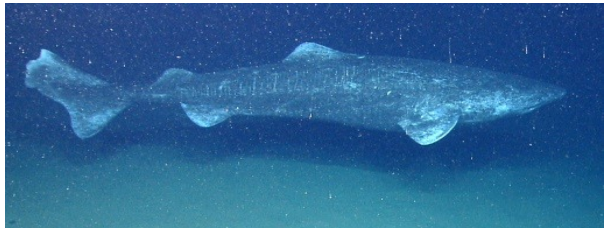


Elephant

- Long lived
- Cancer resistant
- Different strategy to protect against DNA damage than NMR
- >20 copies of the *p53* gene in elephant genome

Background - ageing models



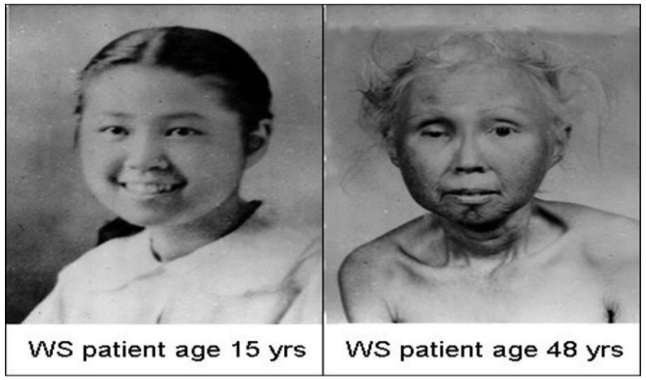


Greenland shark – 512y

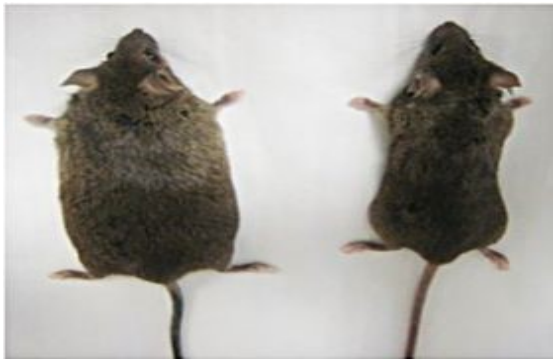
Planarian -15y

Hydra -immortal

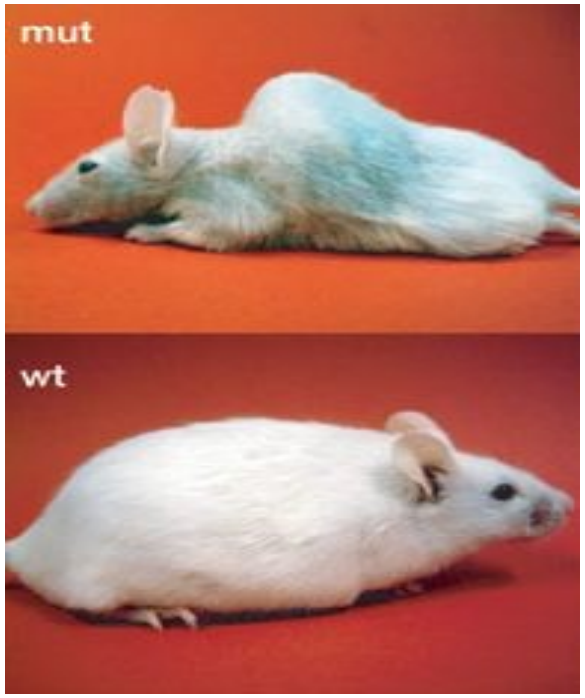
Ageing models



Genes and Disease
Werner syndrome
NCBI (1998)

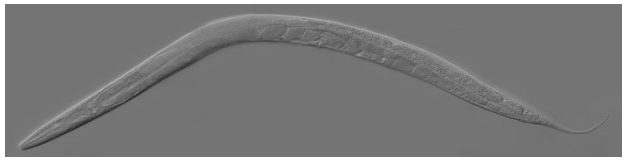


Wu *et al.,*
Development 142 (2015)

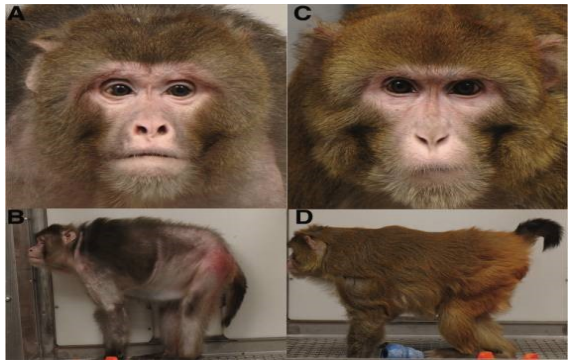


Premature ageing in mice expressing defective mitochondrial DNA POL
Trifunovic *et al.,*
Nature 429 (2004)

Interventions – Caloric restriction



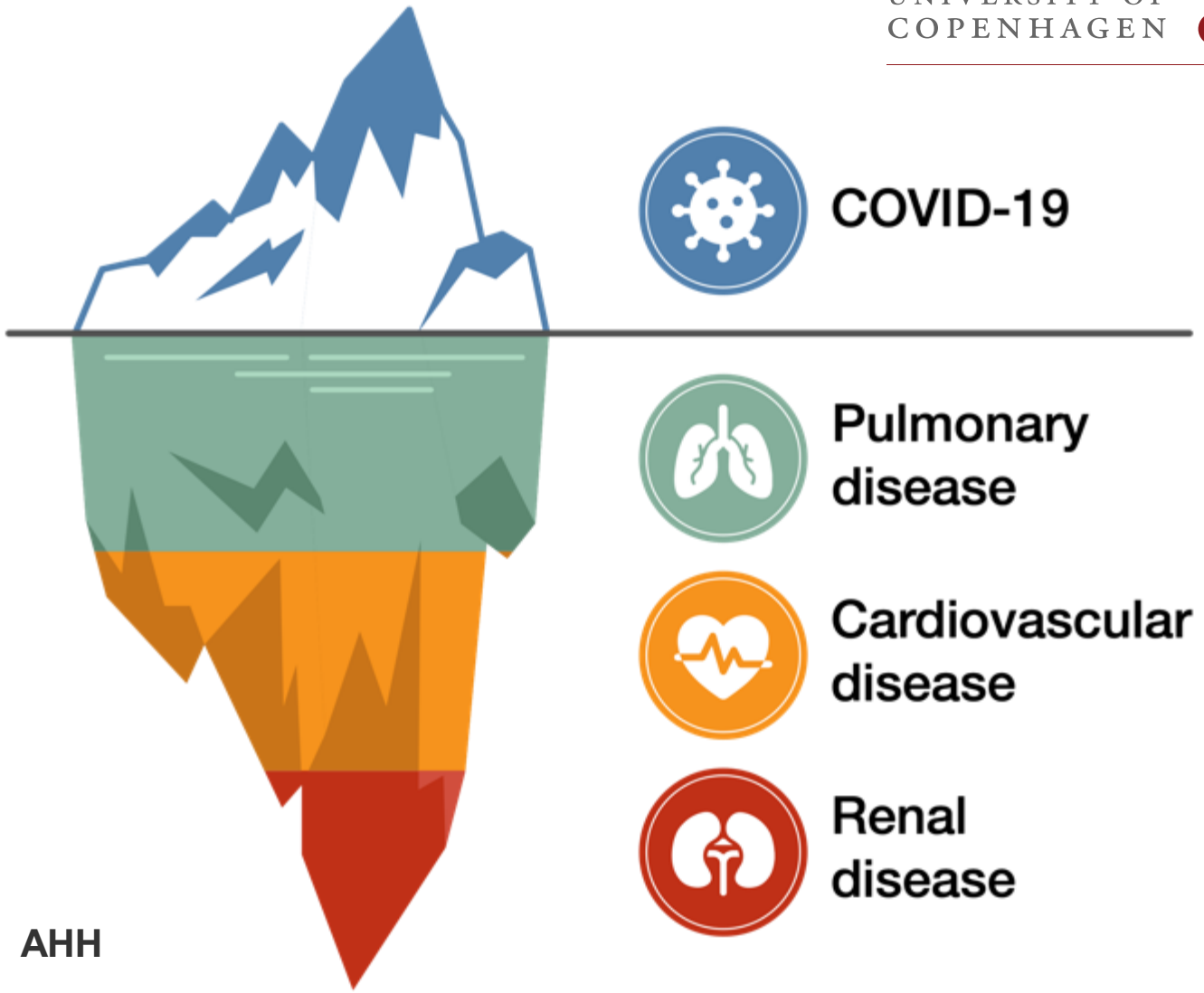
Klass. Mech Ageing Dev. 1983



Colman *et al*., Science 325 (2009)

UCPH

AHH


COVID-19
Pulmonary disease
Cardiovascular disease
Renal disease

Multimorbidity

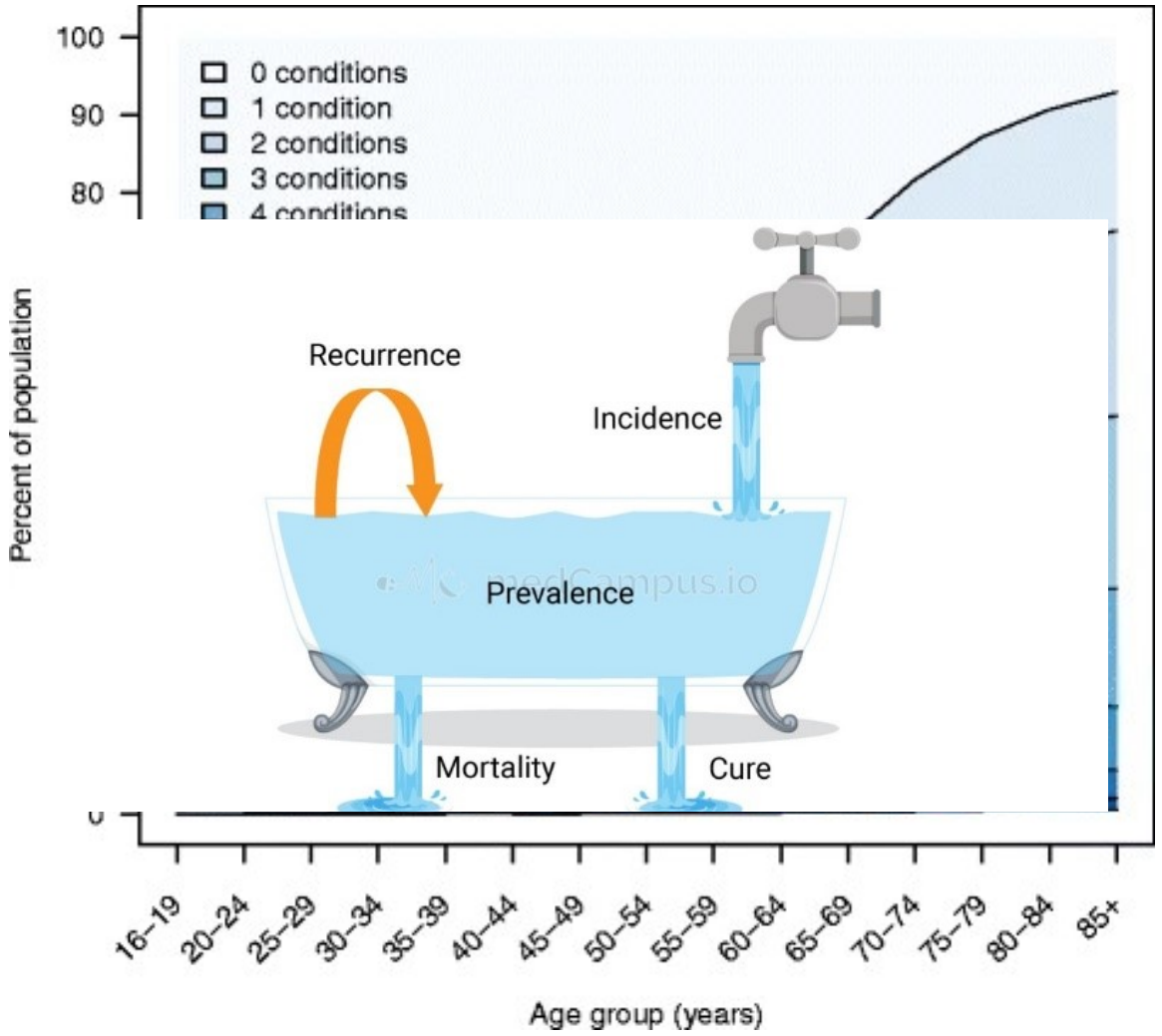
- Co-occurrence of ≥2 long-term medical conditions
- It's a major health and social care challenge.
- Reduces quality of life, physical functioning and life expectancy and increases the risk of psychological distress and the risk of adverse drug events from polypharmacy.
- The prevalence is increasing in the general population and is more common in the elderly population, in females and in individuals from low socioeconomic status.
- Accounts for:
  - 50% of general practice appointments,
  - 64% of outpatient appointments,
  - 70% of inpatient bed days and
  - 70% of the total healthcare expenditure (In UK, Department of Health).

INDLAND

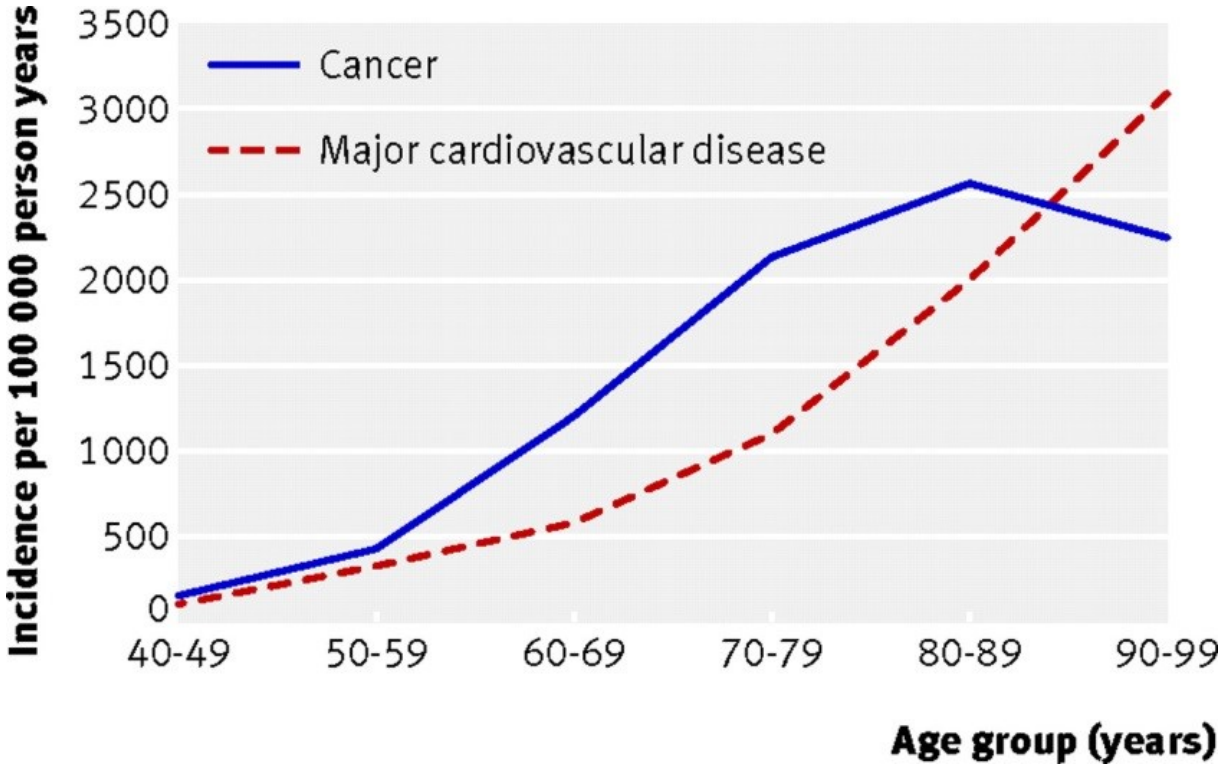
Flere multisyge vil presse sundhedsvæsnet i fremtiden

I 2050 vil 25 procent flere danskere lide af mere end én kronisk sygdom, viser fremskrivninger.

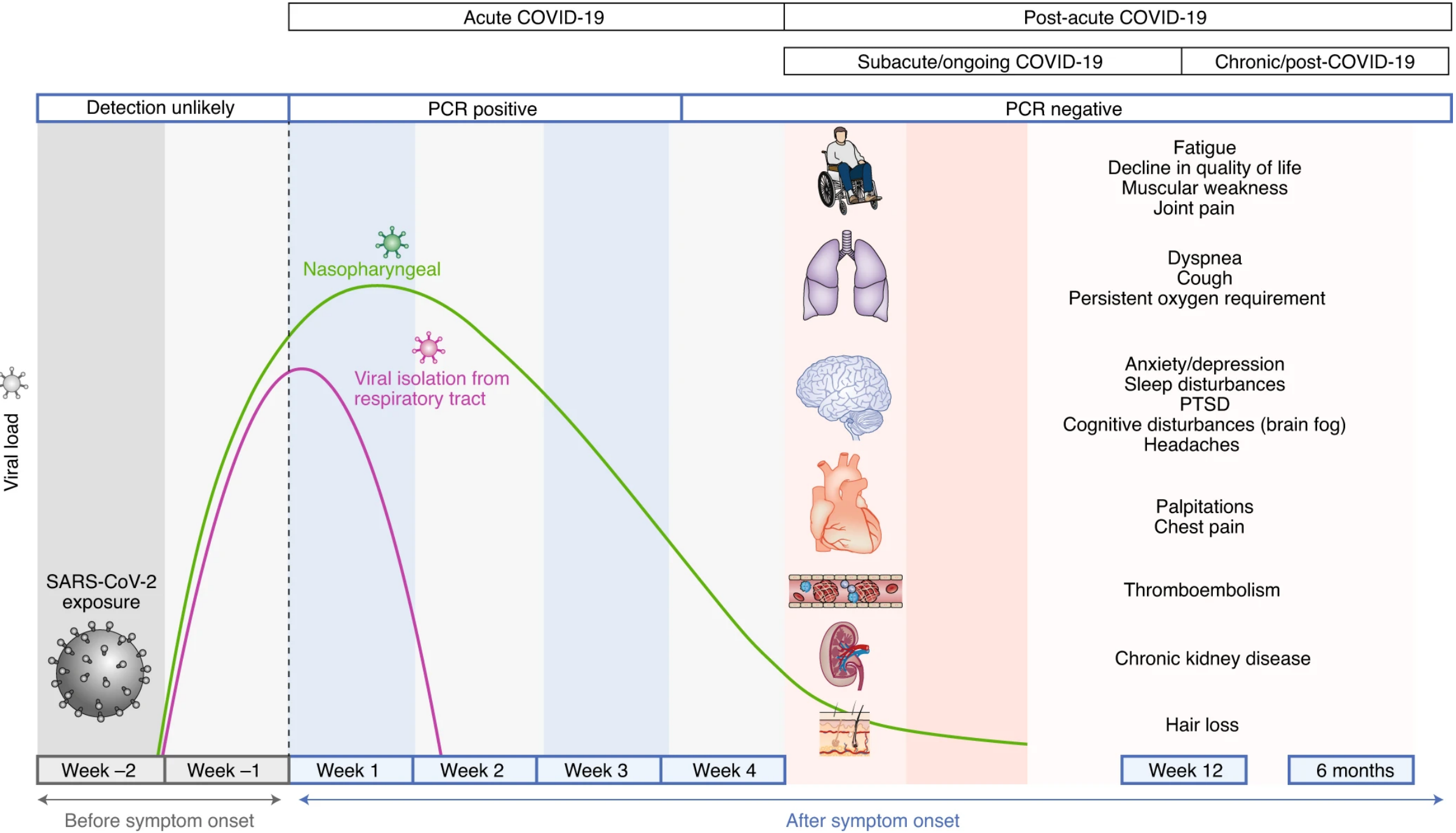
Multimorbidity



Schiøtz et al., BMC Public Health 17 (2017)

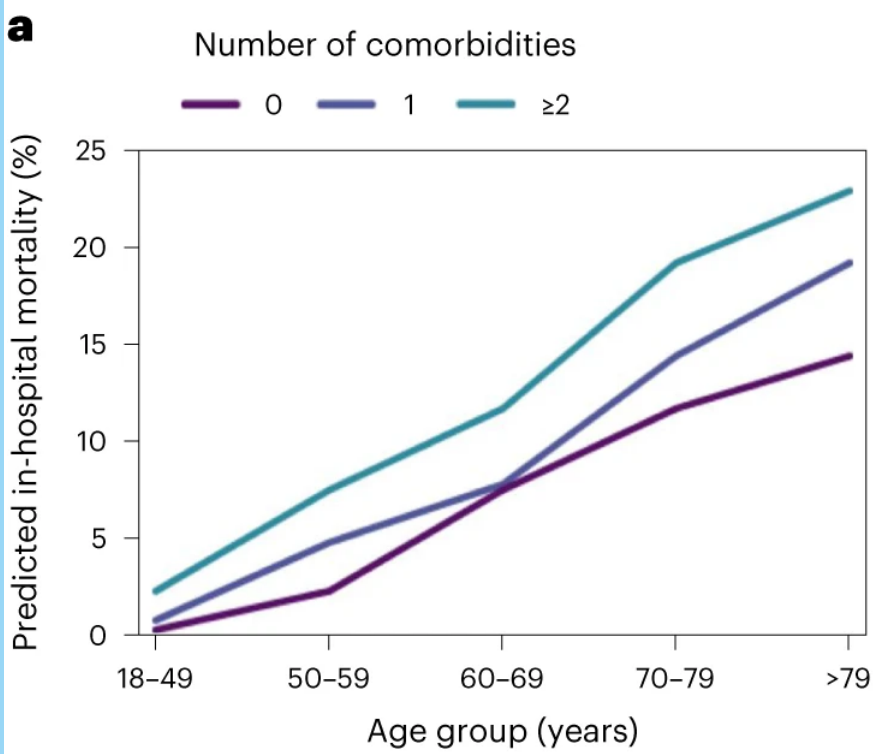


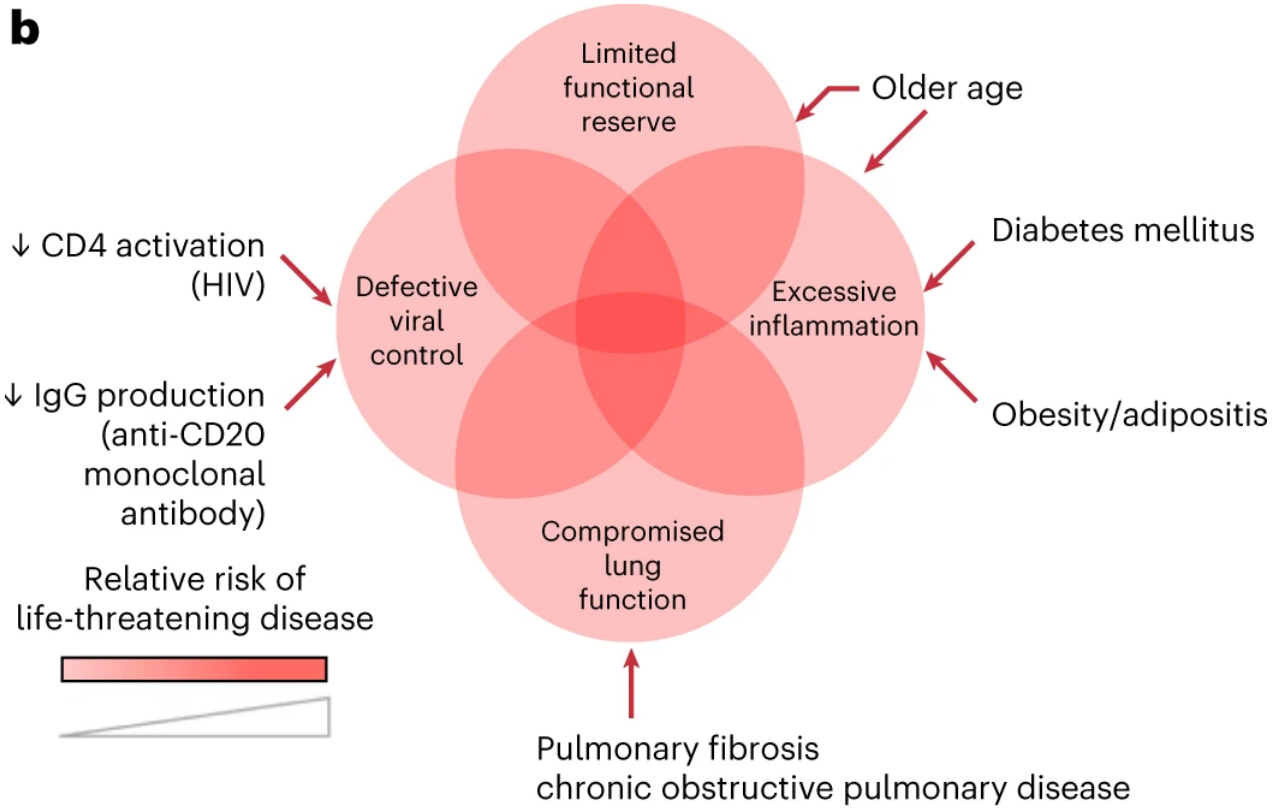
Driver *et al*., BMJ 337 (2008)



Nalbandian et al., (2021) “Post-acute COVID-19 syndrome”

Comorbidities, multimorbidity and COVID-19





Russell et al., Nature Medicine 29 (2023)

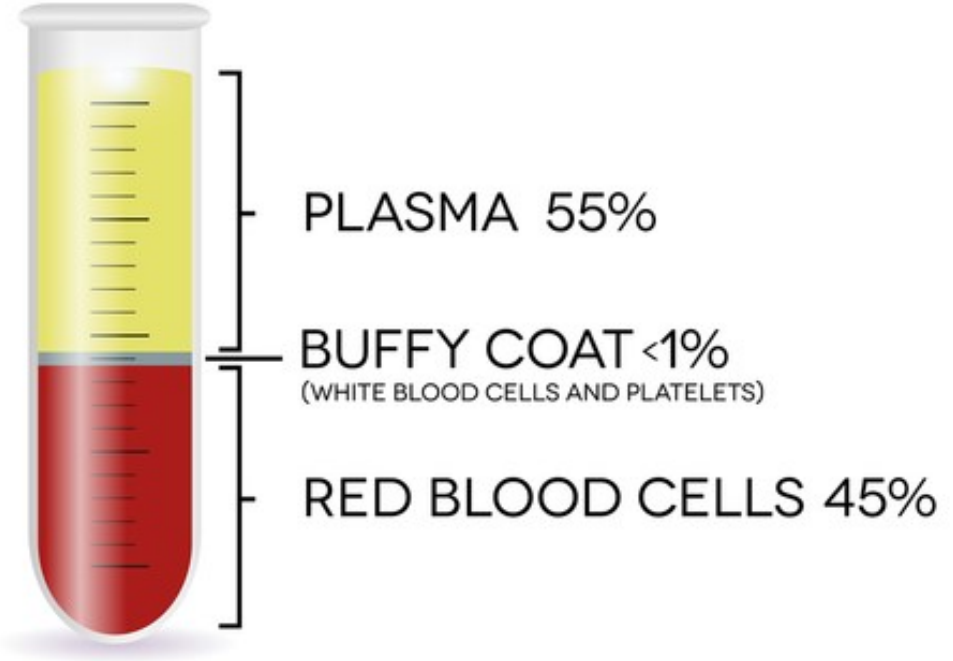
Data

Wet lab biomarkers (blood)

Dry lab biomarkers (registries)

“We do you need that many blood samples?”

As different blood components have different density, sediment rate and size, they can be separated with centrifugal force



1. Red Blood Cells (Erythrocytes)

Function: Oxygen transport and carbon dioxide removal.

Structure: Biconcave discs containing hemoglobin. No mitochondria

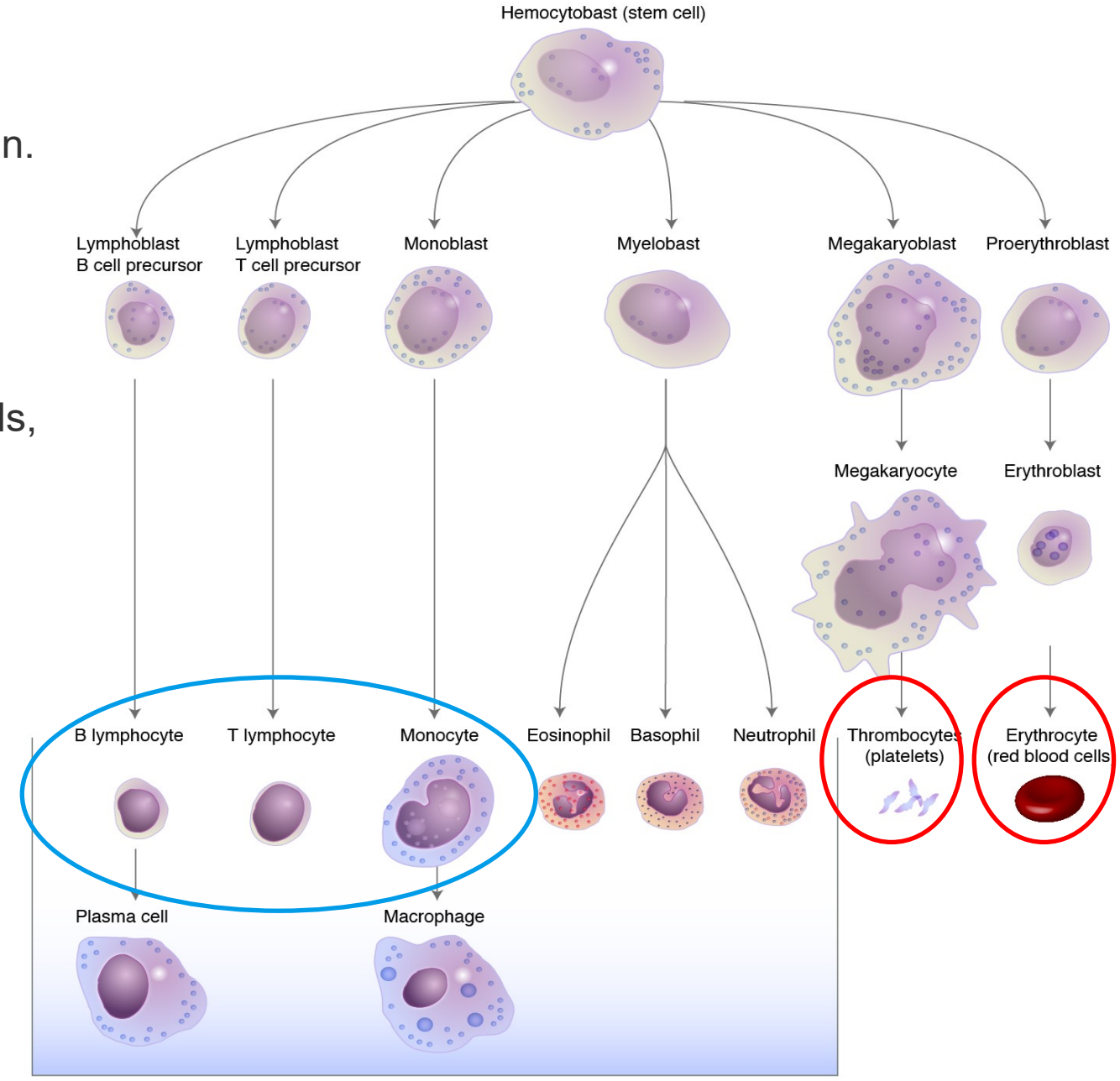
Clinical relevance: Anemia, blood transfusions.

2. White Blood Cells (Leukocytes)

Neutrophils, lymphocytes, monocytes, eosinophils, basophils.

Functions: Immune response, infection control.

Clinical relevance: Leukemia, infections.



Lymphocytes - white blood cells

1. **Platelets (Thrombocytes)**

   Hemostasis and clot formation.

   Structure: Cell fragments. No nuclei.

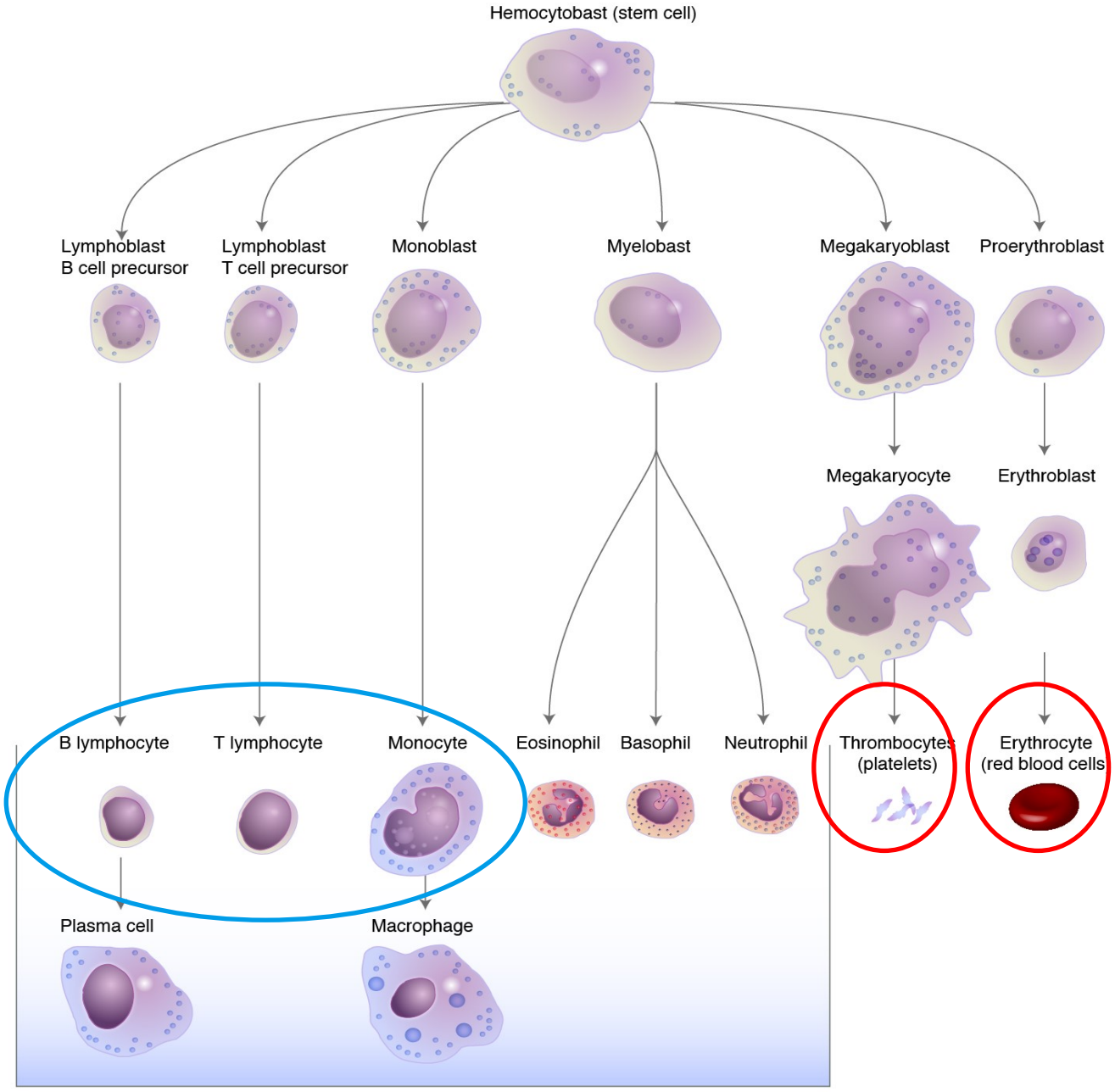
   Clinical relevance: Bleeding disorders, thrombocytopenia.

2. **Plasma**

   Composition: Water, proteins (albumin, globulins, fibrinogen), electrolytes, hormones.

   Functions: Nutrient transport, waste removal, immune response.

   Clinical relevance: Coagulation studies, protein assays.

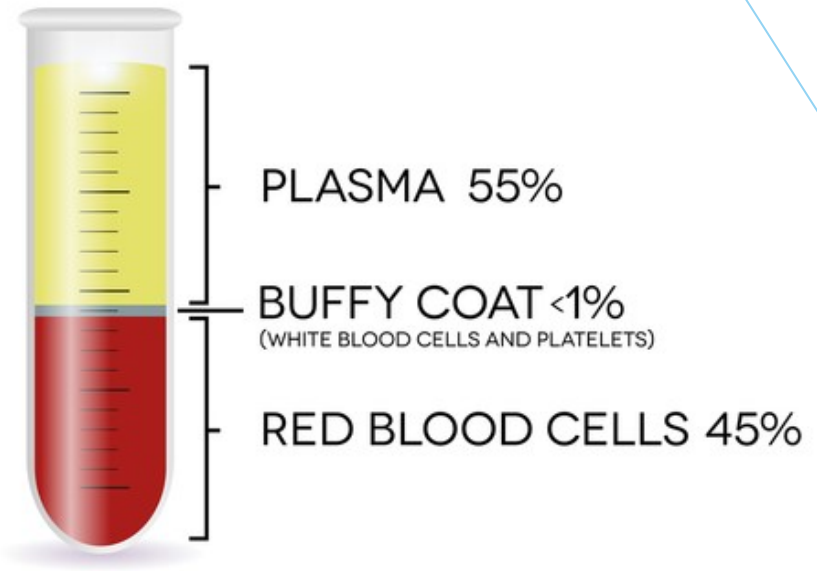


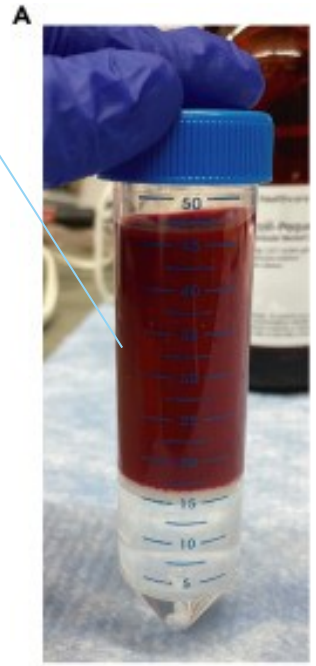
Lymphocytes - white blood cells

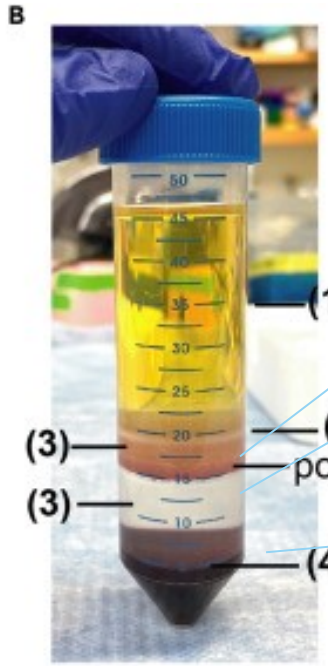
Complete Blood Count

RBC count, WBC count, platelet count, hemoglobin, hematocrit.

General health assessment, anemia diagnosis.







Plasma

WBC - mononuclear blood cells

WBC - polynuclear blood cells

RBC

Cui *et al.*, STAR Protocols 2, 2021

Biochemistry lab:
alanine amino transferase,
albumin,
basic phosphatase, bilirubin,
blood urea nitrogen (BUN),
carbamide,
creatinine,
C-reactive protein (CRP),
D-dimer, potassium,
coagulation factor II+VII+X (KF2710),
high-, very low- and low-density lipoproteins,
sodium,
cholesterol, and
triglycerides.

Automated Hematology Systems

Data

Wet lab biomarkers (blood)

Dry lab biomarkers (registries)

REGISTERS	DATA
Danish Civil Registration System	Sex, age, marital status, household type
National Patient Register	Somatic, psychiatric, and private hospital admissions, diagnosis codes, outpatient visits, hospital procedures
National Prescription Register	Information on all prescription drugs dispensed at Danish pharmacies
Danish Register of Causes of Death	Date and cause of death
Danish National Health Service Register for Primary Care	Health services from general practitioners, practicing medical specialists, physiotherapists, dentists, psychologists, chiropractors, chiropodists ect.
Danish Education Register	Highest obtained education
Migration Register	Dates for emigration and immigration.
Register for Income	Personal and family income
DREAM database: public benefits	Pension, maternity leave, benefits (illness, unemployment ect.)
Socio economic classification	Determined based on information regarding the individual's primary source of income or employment.
Employment Register	Main employment
Laboratory Information System for Hospital Laboratories, Clinical Biochemistry Departments (LABKA)	Laboratory results and dates

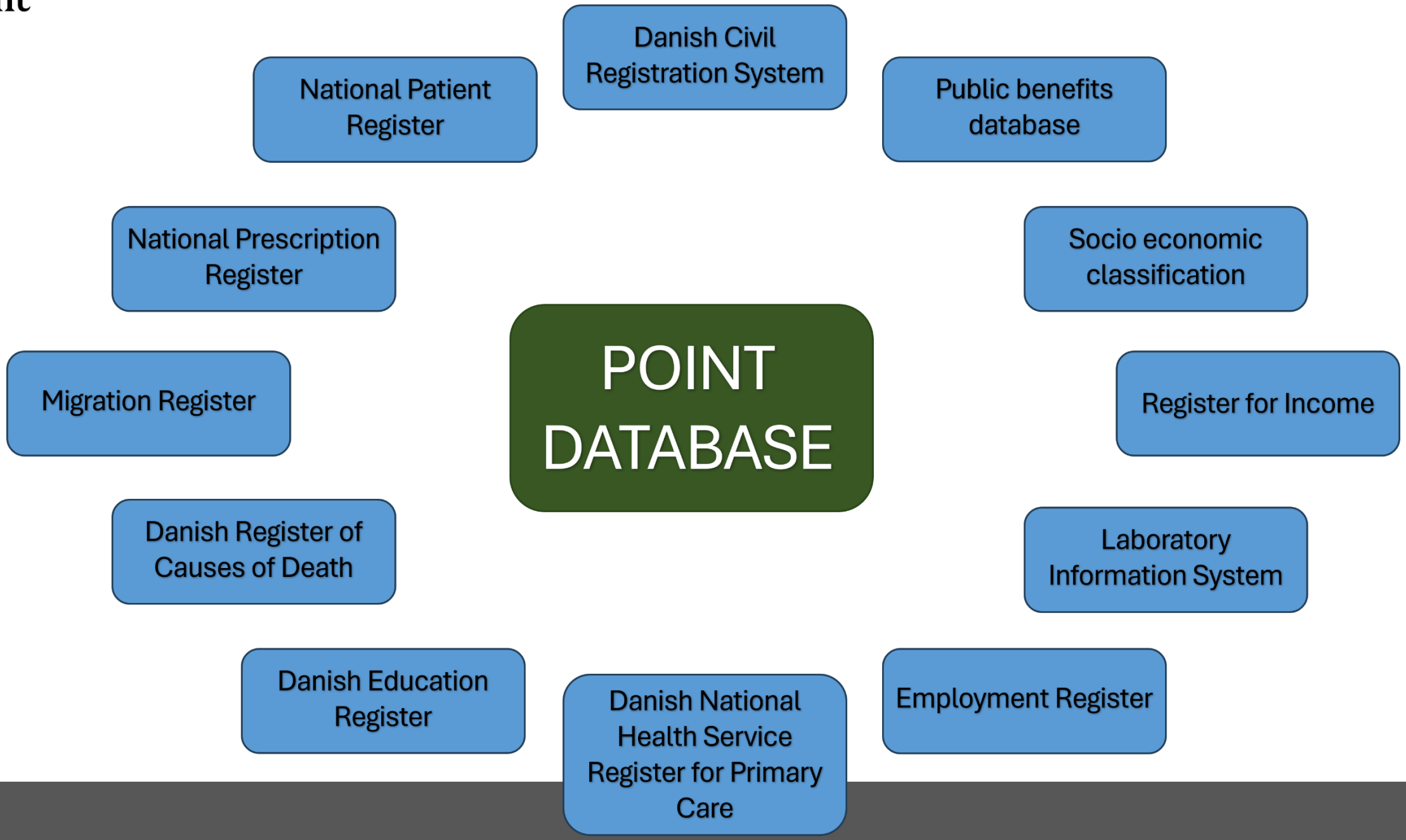
Multimorbidity

Table 1 Algorithms used to define the 16 conditions

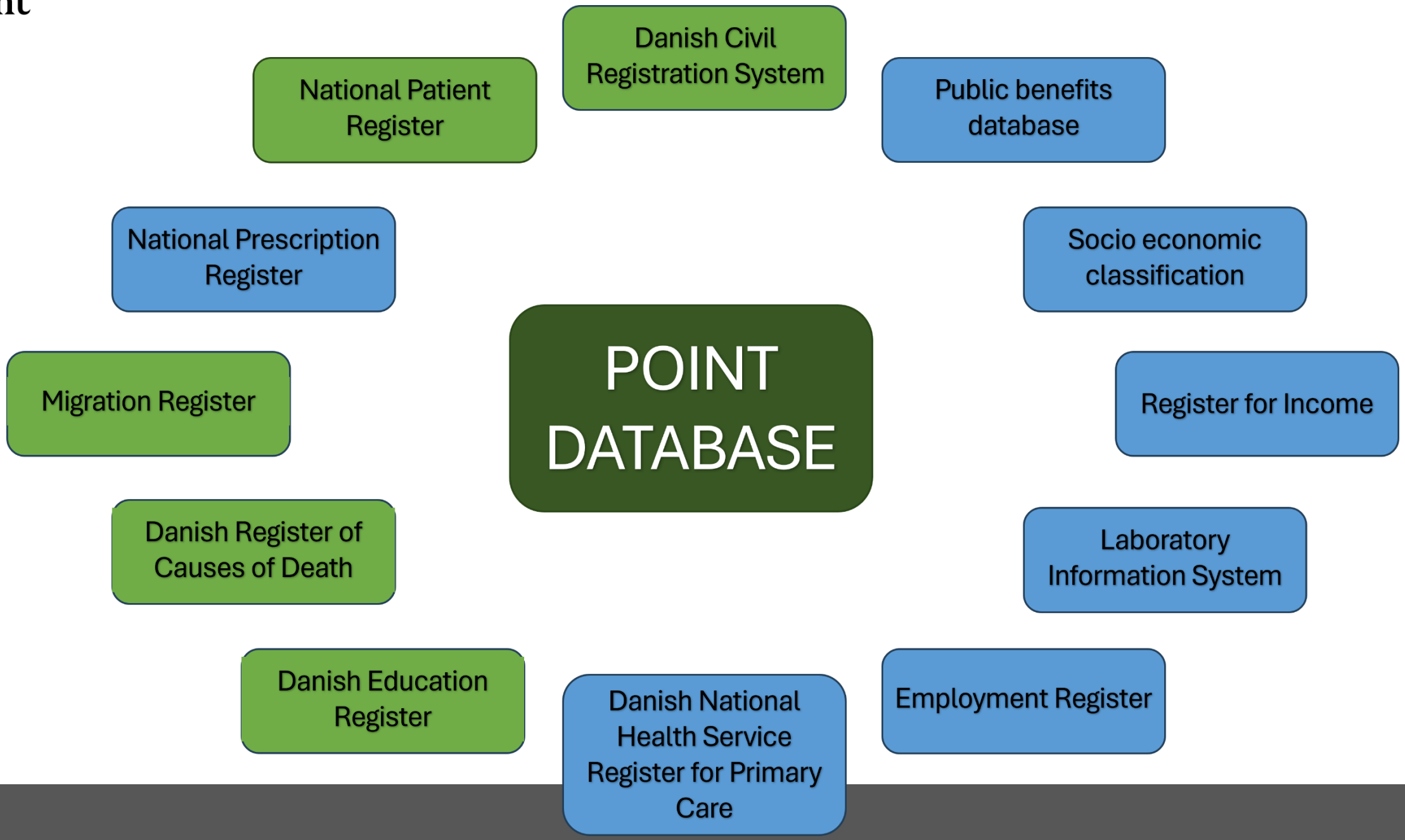
No.	Condition	Defined as a physical or mental health condition in the study	ICD-10 from the Danish National Patient Register	Definition
1	Diabetes	Physical		All persons included in the Danish Diabetes Register where the inclusion date is before the population date (1/1 2012) [22]
2	Cancer	Physical	C00-C43 or C45-C97	(DIAG) [a]
3	Back pain	Physical	M40–54	(DIAG) [a]
4	Osteoarthritis	Physical	M15-M19	(DIAG) [a]
5	Osteoporosis	Physical	M80-M82and/or for persons aged 45 years and older contacts with the ICD-10 codes S22.0, S22.1, S32.0, S32.7, S32.8, S42.2, S42.3, S42.4, S42.7, S42.8, S42.9, S52.5, S52.6, S52.7, S52.8, S52.9, S62.0, S62.1, S72	(DIAG) [a] and/or (MEDICINE) [b] all medicine prescriptions with either ATC: M05B, G03XC01, H05AA02, H05AA03

Schiøtz et al., BMC Public Health 17 (2017)

point


Danish Civil Registration System
National Patient Register
Public benefits database
National Prescription Register
Socio economic classification
POINT DATABASE
Migration Register
Register for Income
Danish Register of Causes of Death
Laboratory Information System
Danish Education Register
Danish National Health Service Register for Primary Care
Employment Register

point


Danish Civil Registration System
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POINT DATABASE
Migration Register
Register for Income
Danish Register of Causes of Death
Laboratory Information System
Danish Education Register
Danish National Health Service Register for Primary Care
Employment Register

point

COPD

Arrhythmia

Kidney disease

Heart failure (left-sided)

Heart failure (right-sided)

Ischemic heart disease

Study population

Pre-covid population

Individuals who are:

- 18 years old
- living in Denmark on **February 26, 2017**

Study period

Feb. 26, 2017 – Dec. 31, 2019

Peri-covid population

Individuals who are:

- 18 years old
- living in Denmark on **February 26, 2020**

Study period

Feb. 26, 2020 – Dec. 31, 2022

Collaborators

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Thank you for your attention

Jon Durhuus