Danish Clinical
Quality Program

The Danish Clinical Quality Program– National Clinical Registries (RKKP)

Access to Real-World Data: New Opportunities

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Webinar on Personal Medicine
June 9th 2021

Agenda

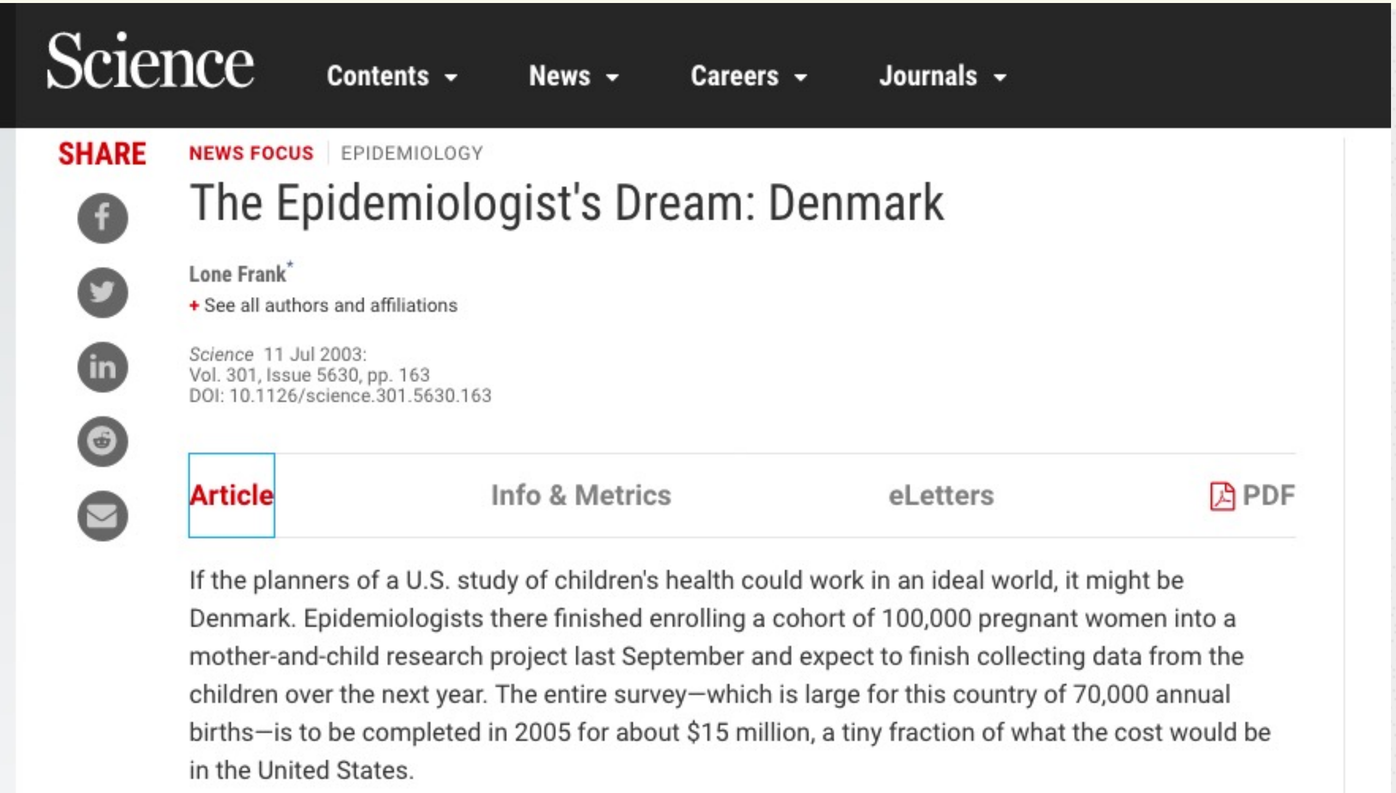
1. Introduction
2. Overview of the clinical data available in RKKP health data registries
3. Services and opportunities for collaboration
4. How to proceed - whom to contact - and general requirements for getting access to data
5. *Examples*

THE EPIDEMIOLOGIST'S DREAM: **DENMARK**

(Science, 2003)

(Science, 2000)

When an Entire Country is a Cohort



NEWS FOCUS | EPIDEMIOLOGY

The Epidemiologist's Dream: Denmark

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If the planners of a U.S. study of children's health could work in an ideal world, it might be Denmark. Epidemiologists there finished enrolling a cohort of 100,000 pregnant women into a mother-and-child research project last September and expect to finish collecting data from the children over the next year. The entire survey—which is large for this country of 70,000 annual births—is to be completed in 2005 for about $15 million, a tiny fraction of what the cost would be in the United States.

EPIDEMIOLOGY

When an Entire Country Is a Cohort

Denmark has gathered more data on its citizens than any other country. Now scientists are pushing to make this vast array of statistics even more useful

For years, any woman who got an abortion had to accept more than the loss of her fetus: For some unknown reason, she also faced an elevated risk for breast cancer. At least that was what several small case-control studies had suggested before Mads Melbye, an epidemiologist at the Statens Serum Institute in Copenhagen, undertook the largest effort ever to explore the link. He and his colleagues obtained records on 400,000 women in Denmark's national Abortion Register, then checked how many of the same women were listed in the Danish Cancer Register. Their foray into the two databases led to a surprising result: As they reported in *The New England Journal of Medicine* in 1997, there appears to be no connection between abortion and breast cancer.

Their success underscores the value of a trove of data the Danish government has accumulated on its citizenry, which today totals about 5 million people. Other Scandinavian countries have created powerful database systems, but Denmark has earned a preeminent reputation for possessing the most com-

digit personal identification number, called the CPR, that follows each Dane from cradle to grave. According to Melbye, "our registers allow for instant, large cohort studies that are impossible in most countries."

Beauty in numbers. These Danish twins starred in a variety show at the turn of the 20th century; now it's their medical records, part of a database, that are in demand.

But Melbye and other scientists think they

by the Danish Board of Health and public hospitals, their use of 120 demographic databases overseen by the agency Statistics Denmark is tightly restricted. Statistics Denmark won't allow researchers to remove from its premises data coded by CPR, and the procedures for accessing information at all are unwieldy and expensive.

Statistics Denmark officials are reluctant to release data tied to CPRs, citing privacy concerns. "The public should have confidence that information identifying them as individuals does not reside outside of this institution," says the agency's Otto Andersen.

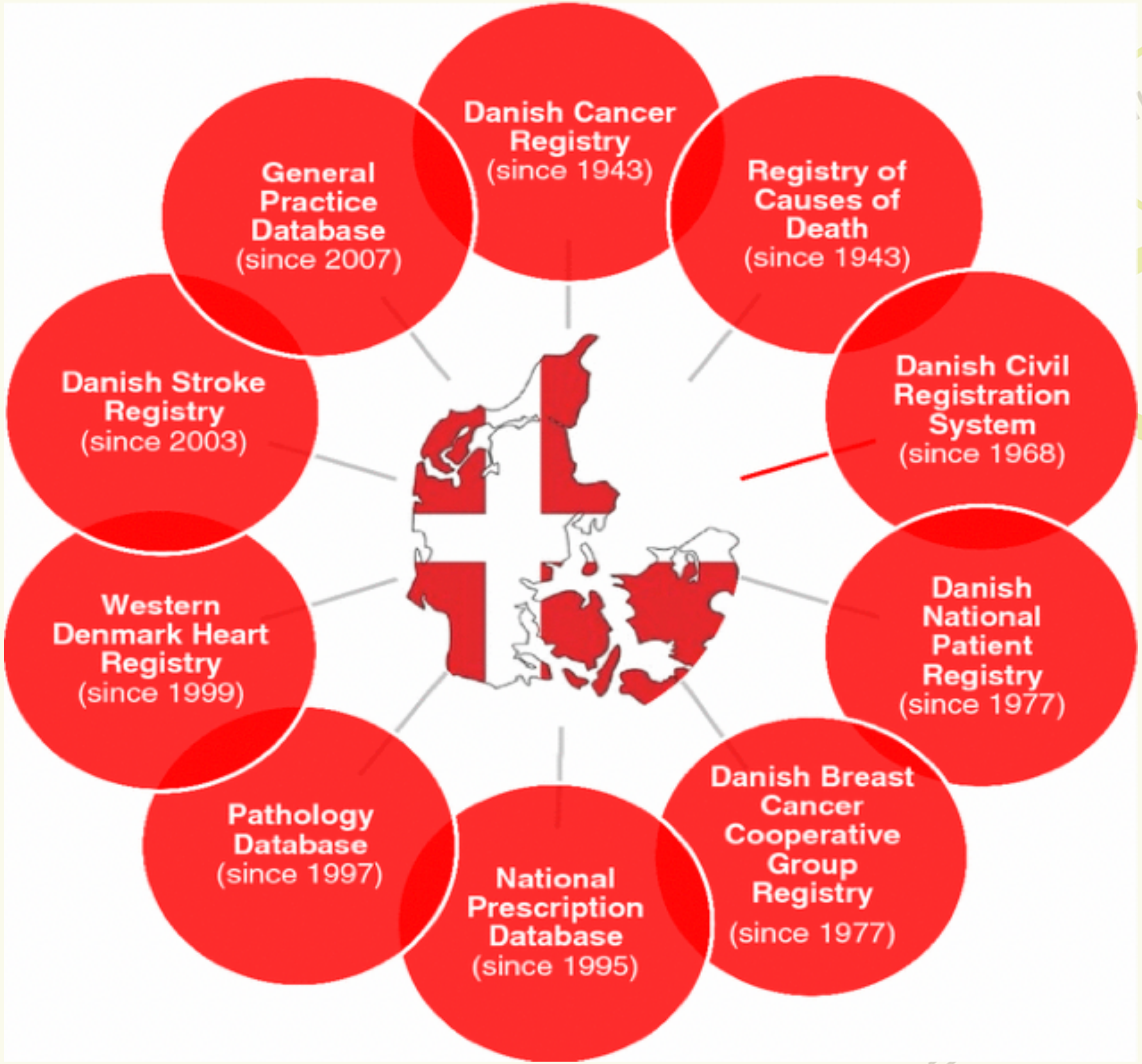
Last month, Danish research minister Birte Weiss formed a committee to break the impasse. Denmark's databases are "a resource which can be used more optimally," she told *Science*. "This should be a scientific flagship."

Working the health databases can yield powerful results. For years the U.S. National Institutes of Health has supported a study following twins, hoping to tease out the relative contributions of genes and lifestyle to aging. Led by University of Southern Denmark gerontologist Kaare Christensen, the project has tapped the Danish Twin Register, which includes 110,000 pairs of twins born since 1870. After following more than 2000 pairs of twins aged 70 or

SH TWIN REGISTER, UNIVERSITY OF SOUTHERN DENMARK

THE RIGHT CONSTELLATION

- Universal tax-funded, income-independent healthcare
- Extensive long-term record-keeping
- Individual-level linkage
- Lifetime follow-up



Danish Cancer Registry
(since 1943)

Registry of Causes of Death
(since 1943)

Danish Civil Registration System
(since 1968)

Danish National Patient Registry
(since 1977)

Danish Breast Cancer Cooperative Group Registry
(since 1977)

National Prescription Database
(since 1995)

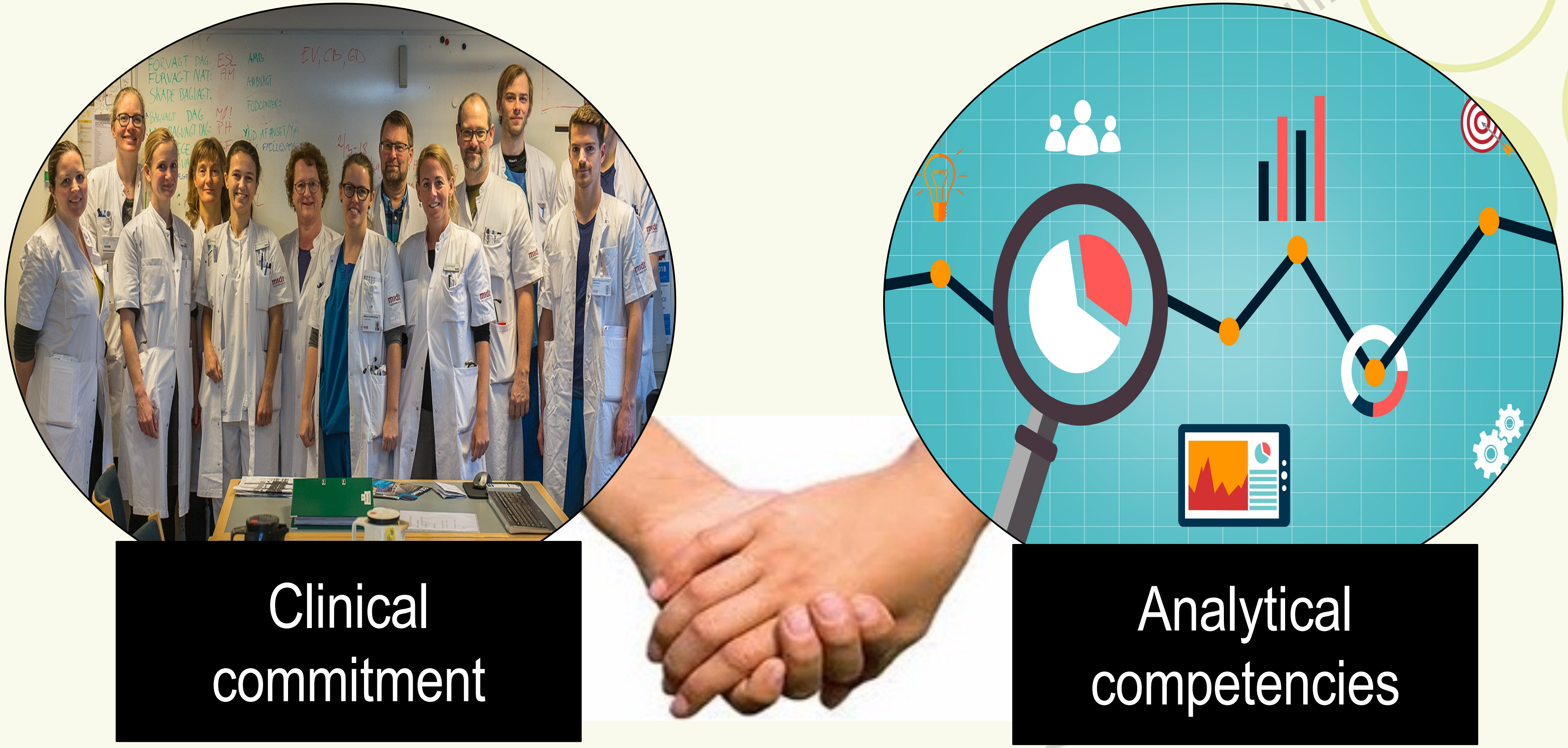
Pathology Database
(since 1997)

Western Denmark Heart Registry
(since 1999)

Danish Stroke Registry
(since 2003)

General Practice Database
(since 2007)

National Clinical Registries



Clinical commitment

Analytical competencies

“An organized system that uses observational study methods to collect uniform clinical data to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves a predetermined scientific, clinical, or policy purpose(s)”

Gliklich R, Dreyer N. Registries for Evaluating Patient Outcomes: A User’s Guide. Rockville, MD: Agency for Healthcare Research and Quality; 2010. AHRQ Publication No. 10-EHC049.

National Clinical Registries

- **Clinical ownership** and **responsibility for content** and **analysis** and **interpretation** and **ACTION**
- Founded through the professional societies
- Mandated by law
- Exempt from patient consent to data collection
- Mandatory national coverage (Record completeness)
- Funded by healthcare providers

Clinical data available

- 86 National Clinical Registries
- Oldest: 1978. Youngest: to be established in 2022
- Examples:
    - Danish Ocular Oncology Database – 75 patients a year
    - The Danish Database for Acute and Emergency Hospital Contacts - 1,8 mio. hospital contacts
    - The Danish Adult Diabetes Registry - GP and hospital care
    - Danish Cardiac Rehabilitation Database - primary and secondary care
    - Some with focus on implantation safety (The Danish Pacemaker and ICD Register) - others on a procedure (Danish Anesthesia Database) – most disease specific (stroke, depression, lung cancer)

Clinical data available

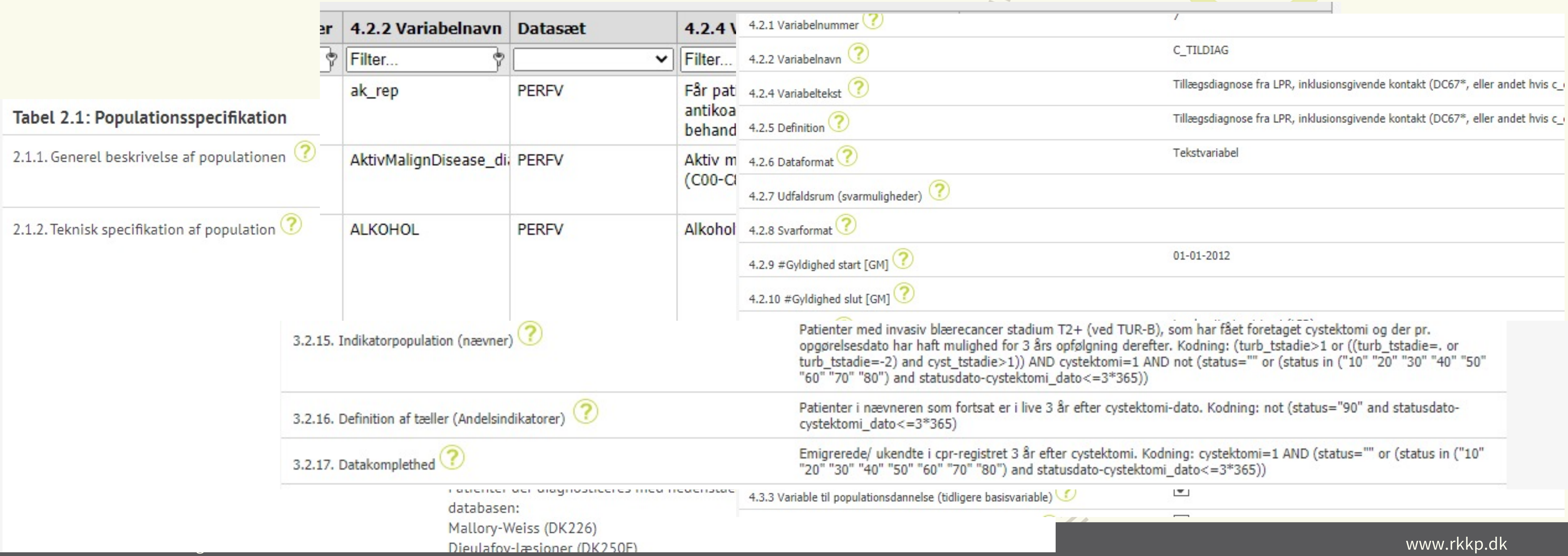
- 28 cancer registries, including quality of palliative care and national screening programmes
- 13 chronic diseases (excluding cardiovascular and psychiatric registries)
- 11 cardiovascular diseases
- 8 non-neoplastic elective surgery/orthopaedic surgery, gynaecology
- 6 emergency/acute surgical and medical care (excluding cardiovascular and psychiatric registries)
- 6 psychiatry, including dementia care
- 4 obstetrics
- 10 misc.

Clinical data available

- Patient characteristics
- Disease characteristics
- Information on the intervention
- Information on outcome
- <10 registries: patient reported data
- Unique patient identifer
- Longitudinal follow-up

The registries **fully** documented (in Danish)

www.rkkp-dokumentation.dk/



Tabel 2.1: Populationsspecifikation

2.1.1. Generel beskrivelse af populationen	
2.1.2. Teknisk specifikation af population	

databasen:
Mallory-Weiss (DK226)
Dieulafoy-læsioner (DK250E)

er	4.2.2 Variabelnavn	Datasæt	4.2.4 V
Filter...	Filter...		Filter...
	ak_rep	PERFV	Får pat antikoa behand
	AktivMalignDisease_di	PERFV	Aktiv m (C00-C
	ALKOHOL	PERFV	Alkohol

4.2.1 Variabelnummer	7
4.2.2 Variabelnavn	C_TILDIAG
4.2.4 Variabeltekst	Tillægsdiagnose fra LPR, inklusionsgivende kontakt (DC67*, eller andet hvis c_
4.2.5 Definition	Tillægsdiagnose fra LPR, inklusionsgivende kontakt (DC67*, eller andet hvis c_
4.2.6 Dataformat	Tekstvariabel
4.2.7 Udfaldsrum (svarmuligheder)	
4.2.8 Svarformat	
4.2.9 #Gyldighed start [GM]	01-01-2012
4.2.10 #Gyldighed slut [GM]	
4.3.3 Variable til populationsdannelse (tidligere basisvariable)	☑

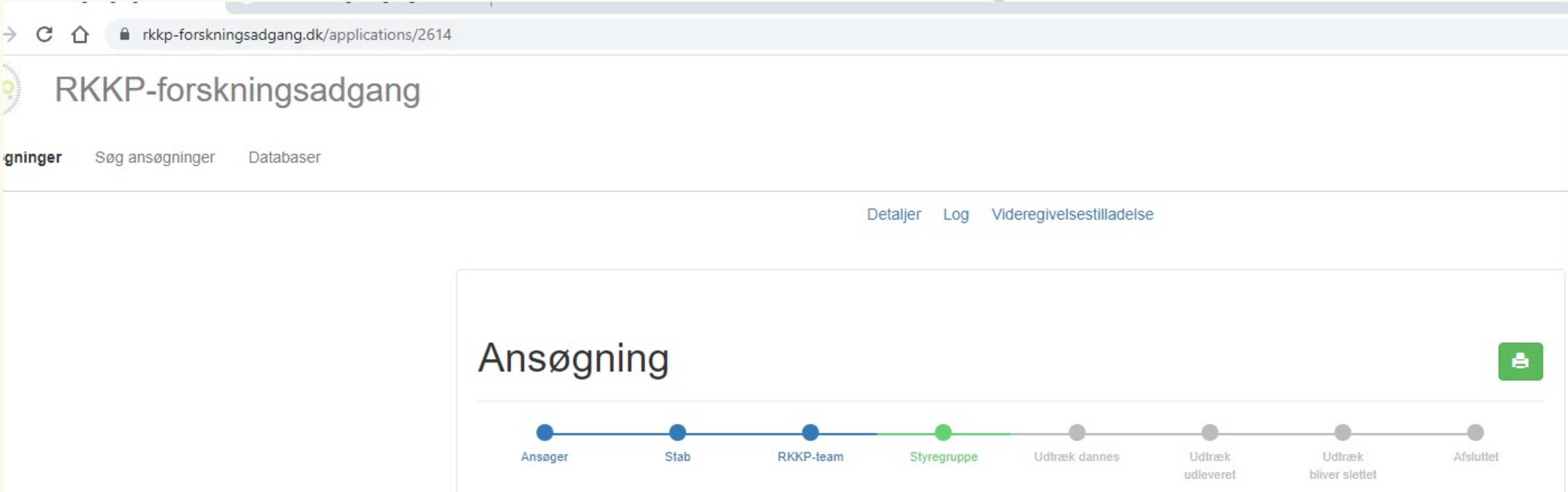
3.2.15. Indikatorpopulation (nævner)	Patienter med invasiv blærecancer stadium T2+ (ved TUR-B), som har fået foretaget cystektomi og der pr. opgørelsesdato har haft mulighed for 3 års opfølgning derefter. Kodning: (turb_tstadie>1 or ((turb_tstadie=. or turb_tstadie=-2) and cyst_tstadie>1)) AND cystektomi=1 AND not (status="" or (status in ("10" "20" "30" "40" "50" "60" "70" "80") and statusdato-cystektomi_dato<=3*365))
3.2.16. Definition af tæller (Andelsindikatorer)	Patienter i nævneren som fortsat er i live 3 år efter cystektomi-dato. Kodning: not (status="90" and statusdato-cystektomi_dato<=3*365)
3.2.17. Datakomplethed	Emigrerede/ ukendte i cpr-registret 3 år efter cystektomi. Kodning: cystektomi=1 AND (status="" or (status in ("10" "20" "30" "40" "50" "60" "70" "80") and statusdato-cystektomi_dato<=3*365))

How to proceed

- Data can be passed on to research purposes
    - Approved projects in EU/Nordic countries
    - Can document GDPR-compliance
    - Can document that data is necessary for the project

How to proceed

- Online - https://www.rkkp-forskningsadgang.dk/
- 261 data sets passed on to research in 2020

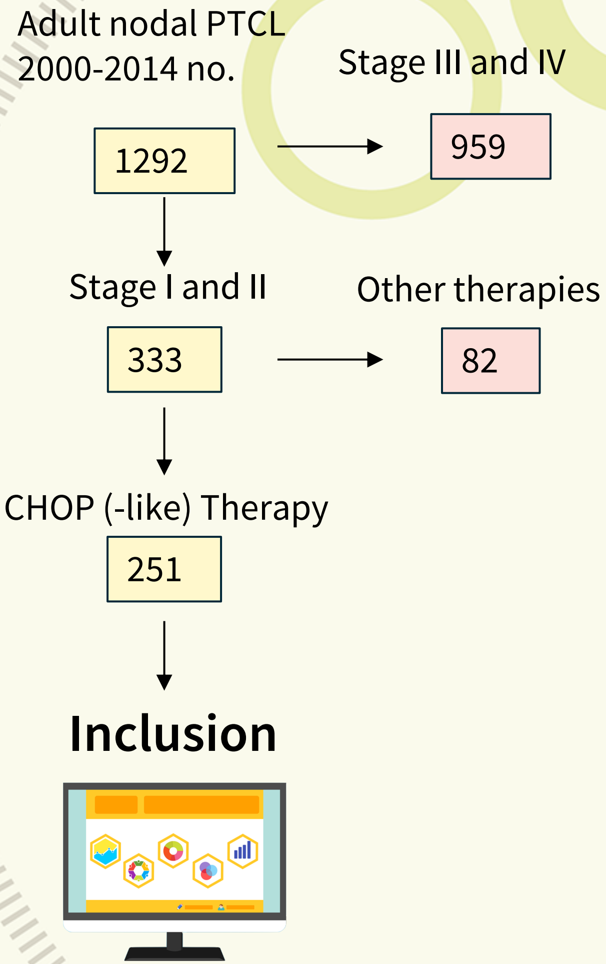


Possible roles in the R&D chain

- Characterization of of patients with high unmet needs
- Benchmark of response/survival observed in early trials
- Complex innovative trial designs in late development
- Post-marketing studies
- Decision support tools and digital diagnostics

Limited stage T-cell lymphoma
Unmet needs and benchmarking of early trial results

- Rare disease with high unmet needs – very few patients with limited stage disease
- Characterization of outcomes in a real-world setting to obtain benchmark for novel therapies therapies
- 251 well-characterized patients with long (and complete) follow-up for survival analyses obtained from Nordic population-based registries, including RKKP



Adult nodal PTCL
2000-2014 no.
1292

Stage III and IV
959

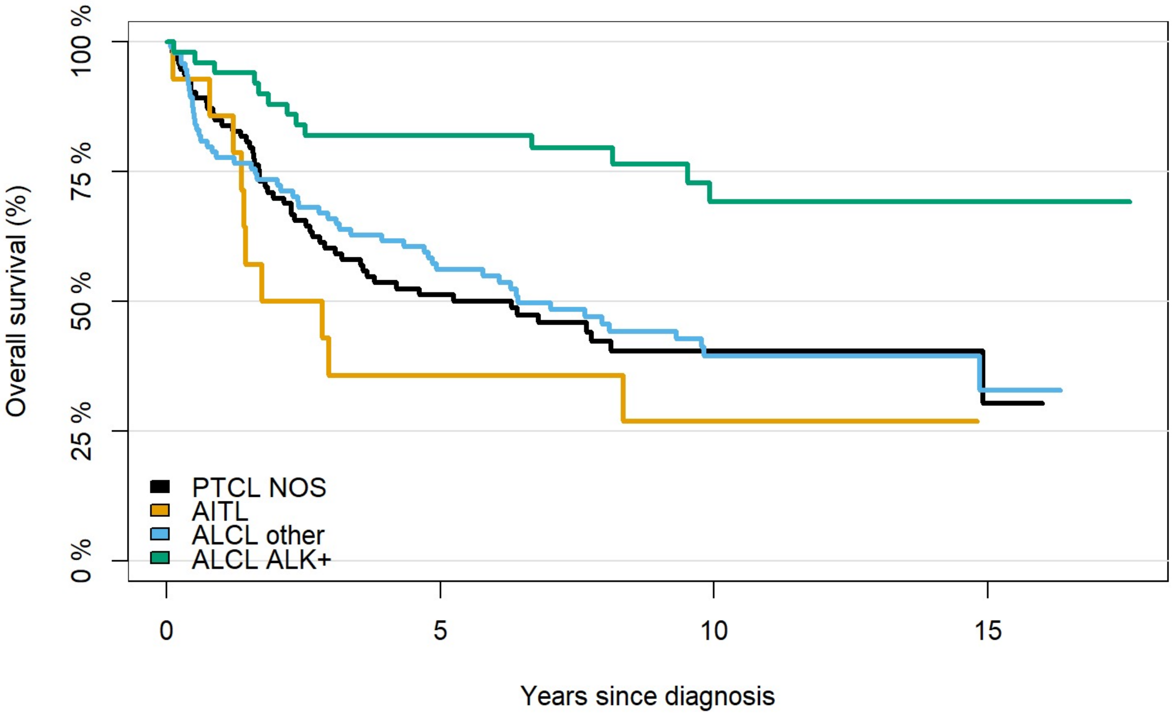
Stage I and II
333

Other therapies
82

CHOP (-like) Therapy
251

Inclusion

Limited stage B-cell lymphomas
Outcomes poorer than other more common



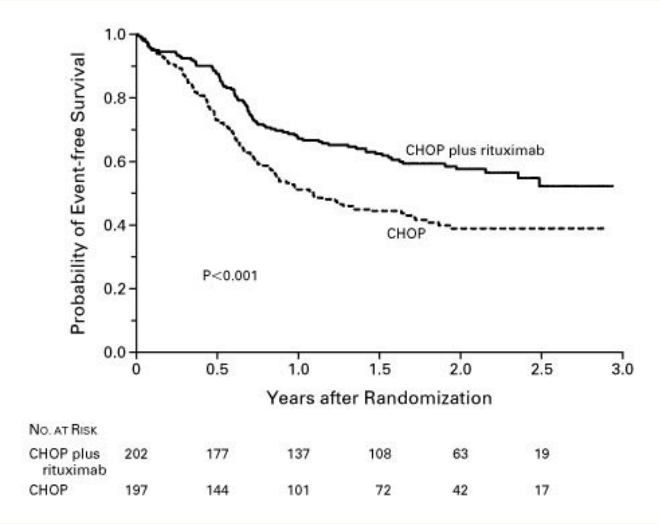
93	68	52	41	27	21	17	10	5	1	0
14	7	5	5	4	3	2	1	1	0	0
94	69	59	48	37	32	18	14	8	1	0
50	45	41	35	31	24	19	13	7	3	1

- With exception of a single subgroup, outcomes are clearly poorer than for corresponding B-cell lymphomas
- Important to have precise outcomes data when assessing efficacy of novel therapies for selected patient population
- The population-based setting is a strength and ensures data on an unselected (more unbiased) populations reflective of the real-world patients
- **Similar analyses can be done for various cancers and other diseases**

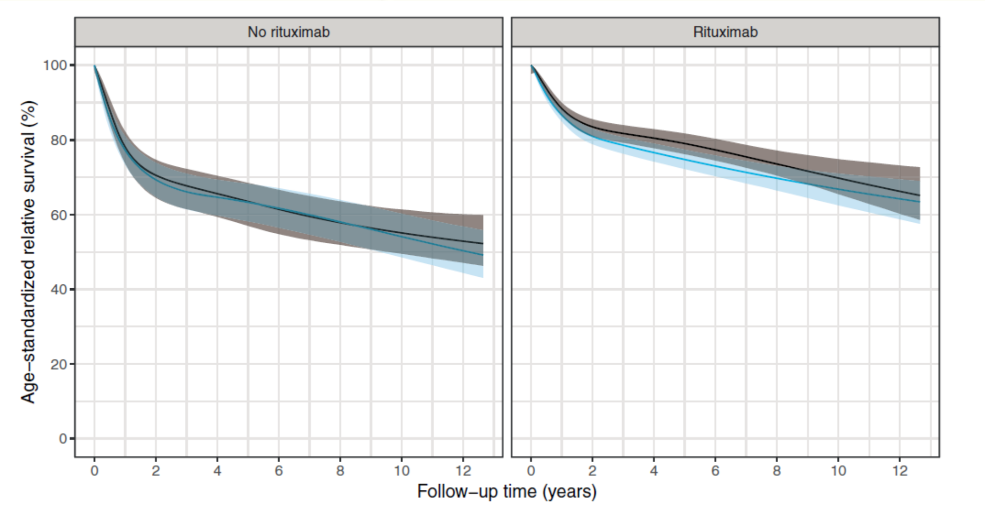
Post-marketing studies

Real-world effectiveness of new cancer drugs

- Effect may differ in the real-world setting with frail, elderly patients being prevalent
- Value to new drugs to society can be explored in nationwide RW data
- For example, we can document the effectiveness of rituximab in a nationwide real-world setting where all inhabitants have equal access to health care



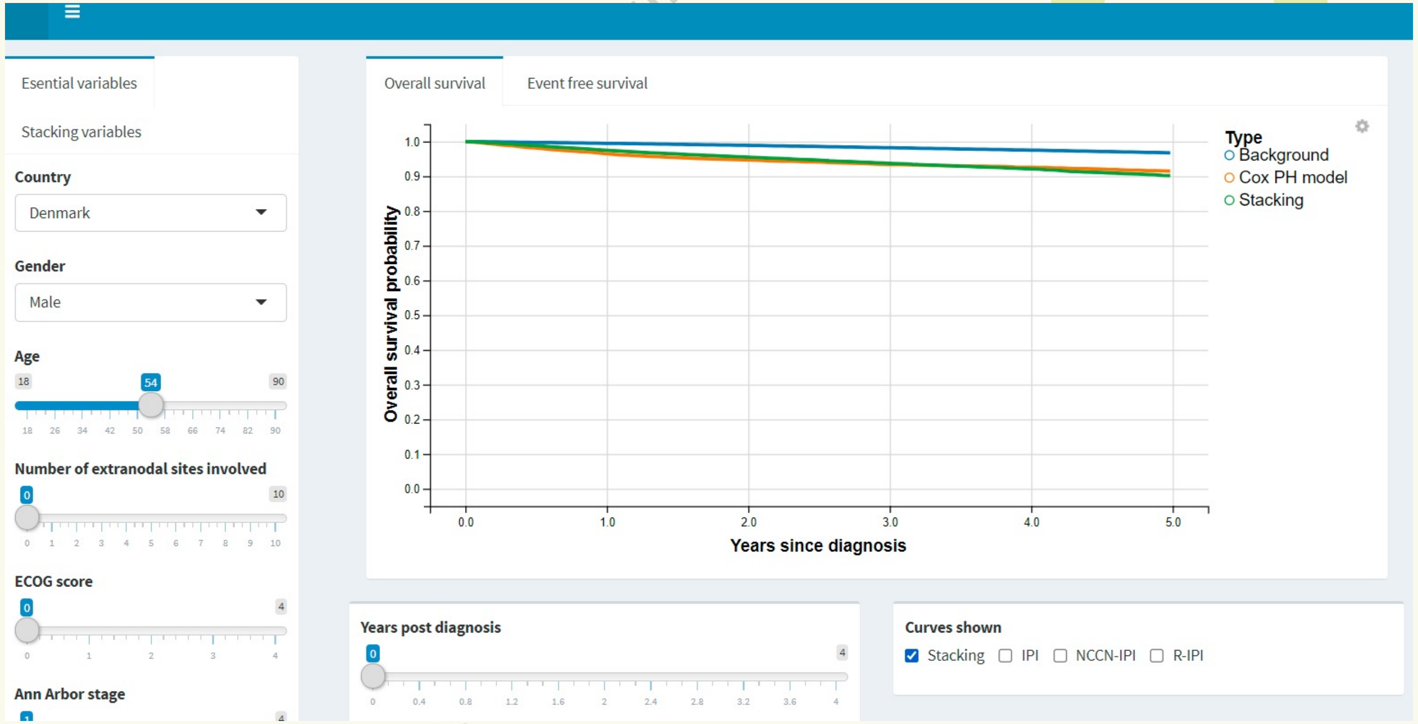
Coiffier et al. NEJM (2002)



Jakobsen et al. Leuk & Lymp (2019)

Decision support tools

- R&D funding to development of decision support tool
- Decision support tools *must* work in a RW setting
- RW patients have to be included in the development process
- In the example, we can provide highly accurate information on outcomes in lymphoma using simple clinical information for personalized outcome predictions – in contrast to the typically used group based outcome prediction



Country
Denmark

Gender
Male

Age
18 54 90

Number of extranodal sites involved
0 10

ECOG score
0 4

Ann Arbor stage
1 4

Years post diagnosis
0 4

Curves shown
☑ Stacking ☐ IPI ☐ NCCN-IPI ☐ R-IPI

Biccler et al. Journal of clinical cancer informatics 2018


THANK
YOU

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