Muligheder for registerbaseret forskning i Danmark.

Mette Søgaard, seniorforsker, Klinisk Epidemiologisk Afdeling

A historical view

1645 Church files

1769 The first census of the Danish Kingdom

1856 The first disease registry -*The Leprosy Registry in Norway*

1924 National population registry

1925 The registry of cerebral palsy

1937 The registry of tuberculosis

1943 Cancer registry

1943 Registry of causes of death

1953 The central Psychiatric registry

1968 CPR registry

1973 The Medical Birth Registry

1977 The Hospital Discharge Registry

"Perhaps the best population-based data sources are

the extensive data linkage networks in the

Scandinavian countries. The availability of such

registries for the virtually entire population is an

invaluable resource for epidemiologic investigation"

Michael S. Kramer Clinical Epidemiology and Biostatistics 1988

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 complete and interwoven collection of statistics touching on almost every aspect of life. The Danish government has compiled nearly 200 databases, some begun in the 1930s, on everything from medical records to socioeconomic data on jobs and salaries. What makes the databases a plum research tool is the fact that they can all be linked by a 10-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 can extract even more from this data gold mine. They argue that not enough money is being spent on maintaining and expanding existing databases, and they say that red tape is hampering studies that require correlation of health and demographic data. The problem is that, while they have unfettered access to more than 80 medical databases maintained 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 older, Christensen's group has so far tied to genes about a quarter of the variation in human longevity. "The project is made possible by the unmatched age and completeness of the Danish Twin Register," he says.

The health databases have proven invaluable for probing contradictions raised by smaller studies and following disease pro-

When the entire…..

"Access to more than 80 medical databases maintained by the Danish Board of Health and public hospitals…..(available from Statens Serum Institut)"

"120 demografic databases maintained by Statistics Denmark"

+ 60 clinical quality databases

Why is Denmark a cohort?

- Establishment of the Danish Civil Registration System in 1968

- Long tradition for registration

- Public health care system

The Danish Health Care System

♦ Population 5.5 million

♦ Free tax-supported health care for

- Visits at general practitioner
- Visits at specialist
- Admissions to hospital and outpatients visits, and
- A part of the costs to drugs is paid

The Civil Registration System

- Period: 1 April 1968

- Main variables:
  - Civil Registration Number
  - Civil status
  - Civil Registration Number of father/mother/children
  - Death data
  - Immigration
  - Emigration

- Updated daily

The civil registration number is used in all Danish registries

STATENS SERUM INSTITUT

Aktuelt | **Sundhedsdata og -it** | **Smitteberedskab** | **Diagnostik** | **Vaccination** | **Forskning** | **Produkter**

- National Sundheds-it
- Sundhedsøkonomi og -finansiering
- Sundhedsvæsenet i tal
- Indberetning og patientregistrering
- Registre og kliniske databaser
- Lægemidler
- Forskerservice

Forside > Sundhedsdata og -it > Forskerservice

Forskerservice

- Forskerservice Klassisk
- Forskermaskinen
- Ansøgningsskema
- Priser
- Service
- Datasikkerhed

Forskerservice

Forskerservice under Statens Serum Institut arbejder for at understøtte registerforskningen i Danmark. Er du forsker og har brug for data i forbindelse med din forskning, kan du via Forskerservice søge om registerdata på sundhedsområdet.

Frem til september 2014 har forskere kunnet søge dataudtræk via Forskerservice, men da Forskerservice nu har udvidet sin service med en ny måde at få data, har den tidligere mulighed for at få tilsendt data skiftet navn til Forskerservice Klassisk, mens den nye service har fået navnet Forskermaskinen.

Forskerservice giver nu adgang til sundhedsdata på to måder
Afhængigt af dine konkrete behov kan du vælge at søge om adgang til data via Forskerservice Klassisk eller via Forskermaskinen.

Forskerservice Klassisk

Forskerservice Klassisk leverer dataudtræk, som er nøje tilpasset til det enkelte forskningsprojekt. Præcis som Forskerservice altid har gjort.

Forskerservice Klassisk er især relevant for forskere, der enten har behov for at koble data fra Statens Serum Institut med andre data eller har behov for adgang til journaler og lignende.

Læs mere om Forskerservice Klassisk

Forskermaskinen

Forskermaskinen giver online adgang til de individbaserede pseudonymiserede data, som er nødvendige for et forskningsprojekt.

Forskermaskinen er især relevant for forskere, der har behov for større mængder af data, men ikke umiddelbart har behov for journaladgange og lignende.

Læs mere om Forskermaskinen

Kontakt Forskerservice

Statens Serum Institut
Artillerivej 5
2300 København S

Tlf.: 3268 5116

Telefonen er åben alle hverdage fra 9.30-15

Spørgsmål om ansøgningsskema:
Forskerservice@ssi.dk

Spørgsmål om registre og Forskermaskinen:
UdtraekForskerservic@ssi.dk

Find medarbejdere i Forskerservice

Overblik over Forskerservice

I vores vejledende beskrivelse kan du få - og printe - et samlet overblik over, hvad Forskerservice tilbyder og hvordan vi arbejder.

Se beskrivelse af Forskerservice

Følg din sag

Hvis du har søgt om data via Forskerservice, kan du bruge dit sagsnummer til at se status på din ansøgning.

Se din ansøgningsstatus (Excel)

De nationale sundhedsregistre

SSI's registre indeholder data om befolkningens sundhedstilstand og sundhedsvæsenets ydelser.

Læs om de nationale sundhedsregistre

Gl. journalnummer

Registre

- ☐ Landspatientregistret
- ☐ Det Psykiatriske Centrale Forskningsregister
- ☐ DRG- og DAGS-grupperet Landspatientregister
- ☐ Dødsårsagsregistret
- ☐ Cancerregistret
- ☐ Sygesikringsregistret
- ☐ Medicinsk fødselsregister
- ☐ Misdannelsesregistret
- ☐ Abortregistret
- ☐ IVF registret
- ☐ Patologiregistret
- ☐ Registret over stofmisbrugere i behandling
- ☐ Registret over anvendelse af tvang i psykiatrien
- ☐ Familiedatabasen
- ☐ Sessionsregistret
- ☐ Det Nationale Diabetes Register
- ☐ CPR-registret
- ☐ Nationalt Alkoholbehandlingsregister (NAB)
- ☐ Bevægelsesregisteret (BVR)
- ☐ Yderregisteret (YDR)
- ☐ Løn og beskæftigelsesregisteret (LBR)
- ☐ Autorisationsregisteret (AUT)
- ☐ Vævsanvendelsesregisteret VAR
- ☐ Kun tilladelse

Marker om

- ☐ Oplysninger videregives
- ☐ Data ønskes samkørt med data fra Danmarks statistik
- ☐ Projektet er anmeldt til datatilsynet

Bilag til ansøgning

Statistics Denmark

- Social registries:
  - Education
  - Job
  - Tax
  - Type and size of housing

Principles for use:

1. All data are stored in Statistics Denmark

2. Analysis must be done in Statistics Denmark;
   - or by modem

3. Statistics Denmark links the registries and deletes the civil registration number

4. No access to the civil registration number and paper records an thus no possibilities for validation

5. The procedure for getting access to the data might take up to six months

6. Only get data access to projects

Department of Clinical Epidemiology

Report no. 37

Use of Medical Databases in
Clinical Epidemiology

Henrik Toft Sørensen, Tina Christensen, Hanne Kjeldahl Schlosser,
Lars Pedersen, eds.

Aarhus University Hospital

AARHUS
UNIVERSITY

Statens Serum Institut

Overvågning i tal, grafer og kort

Her kan du udtrække overvågningsdata og få dem præsenteret som søjlediagrammer, tabeller og kort.

Sådan bruger du "Overvågning i tal og grafer - Individuelle anmeldelser og Laboratorieanmeldelser" (pdf)

Vejledning til "Vaccinationstilslutning" (pdf)

Individuelle anmeldelser

Vælg venligst en sygdom på listen nedenfor

Vælg sygdom   OK

Laboratorieanmeldelser

Vælg venligst en sygdom på listen nedenfor

Vælg sygdom   OK

Vaccinationstilslutning

Vælg venligst en vaccination på listen nedenfor

Data opgjort per 16. april 2012

Vælg vaccination   OK

Faste oversigter

Seneste sygdomsopgørelse

Tarminfektionsmonitor

Overvågning af dødelighed

De individuelt anmeldelsespligtige sygdomme

- Aids
- Anthrax
- Botulisme
- Creutzfeldt-Jakob
- Difteri
- Fugleinfluenza hos mennesker
- Hepatitis:
  - A akut
  - B akut
  - B kronisk
  - C akut
  - C kronisk
- Hæmolytisk uræmisk syndrom (HUS)
- Hæmorrhagisk feber (Lassa, Marburg, Ebola)
- Kolera
- Kongenit rubella
- Kopper
- Legionella pneumoni
- Lepra
- Leptospirose
- Levnedsmiddelbåren sygdom
- Meningokoksygdom
- Morbilli
- Neuroborreliose
- Ornitose
- Pandemisk influenza (i den præpandemiske alarmperiode, efter udmelding fra Sundhedsstyrelsen)
- Paratyfus
- Parotitis
- Pertussis hos børn < 2 år
- Pest
- Plettyfus (typhus exanthematicus)
- Polio
- Purulent meningitis
- Rabies
- Rubella i graviditeten
- SARS
- Shigella dysenteri
- Tetanus
- Tuberkulose
- Tyfus
- Vandbåren sygdom
- Verotoksinproducerende E. coli (VTEC)

Laboratoriebaseret overvågning

For nogle mikroorganismer og sygdomme er der obligatorisk indberetningspligt fra det diagnosticerende laboratorium

Følgende mikroorganismer eller sygdomme er omfattet af obligatorisk indberetningspligt fra det diagnosticende laboratorium:

- Okulo-genital klamydia
- Gonoré
- Tarmpatogene bakterier
- Listeriose
- Malaria
- Invasiv pneumokoksygdom
- Invasiv Haemophilus influenzae-sygdom (Hib-sygdom)
- Kighoste
- Methicillin-resistent staphylococcus aureus (MRSA)
- Hiv

Endvidere skal der indsendes bakterieisolater til Statens Serum Institut i følgende tilfælde:

- Invasiv pneumokoksygdom
- Invasiv Haemophilus influenzae-sygdom (Hib-sygdom)
- Methicillin-resistent staphylococcus aureus (MRSA)
- Clostridium difficile-infektion
  - C. difficile-isolater med resistens over for de nyere fluorkinoloner (fx moxifloxacin)
  - C. difficile-isolater fra patienter med svære manifestationer af C. difficile-associeret infektion
  - C. difficile-isolater indsamlet i forbindelse med udbrudsmistanke

Den danske mikrobiologidatabase

Projekter

> HAIBA

> MiBa II

MiBa II

En begrænsning for brug af den nuværende version af MiBa til overvågningsformål er at det kun er oplysninger indeholdt i "det almindelige prøvesvar", der overføres til MiBa. Dette prøvesvar er målrettet den kliniske bruger, til brug for behandling af patienten.

MiBa II projektet har to hovedelementer:

1. Differentieret visning af MiBa data med udvikling af en målrettet visning af data til forskellige typer af MiBa brugere.
2. Udvikling af "det udvidede mikrobiologiske prøvesvar" som vil give mulighed for overførsel af oplysninger vedrørende mikrobielle egenskaber og subtyper ved hjælp af en fælles national datamodel.

Målet for MiBa II projektet er at tilgodese forskellige behov for visning af oplysninger fra MiBa, for henholdsvis den kliniske bruger, mikrobiologen og den nationale overvågning på Statens Serum Institut. Disse oplysninger kan være specielle resistensdata, der er nødvendige i overvågningssammenhæng, men som er irrelevante for behandling af patienter.
Målet er endvidere at gøre det muligt at registrerer og overfører oplysninger vedrørende mikrobielle egenskaber og subtyper med en fælles datastruktur og udvikle fælles terminologier til dette brug.

MiBa data-flow diagram
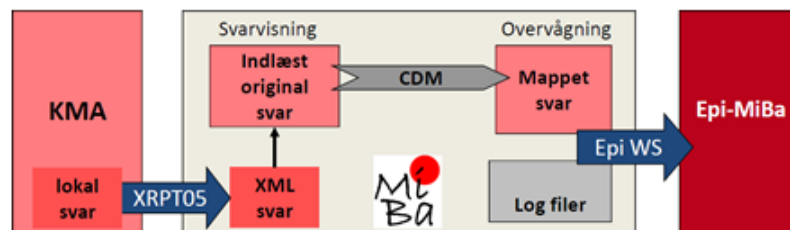
MiBa

- Contains electronic reports from departments of clinical microbiology (DCM) in Denmark since 2010.

- Data is owned by the DCMs and use of data must be approved by each DCM and the executive committee.

- MiBa is a joint national collaboration and the applicant is expected to cooperate with all relevant persons in relation to the data.

- The applicant will be appointed a contact person from each DCM that will help interpret the data.
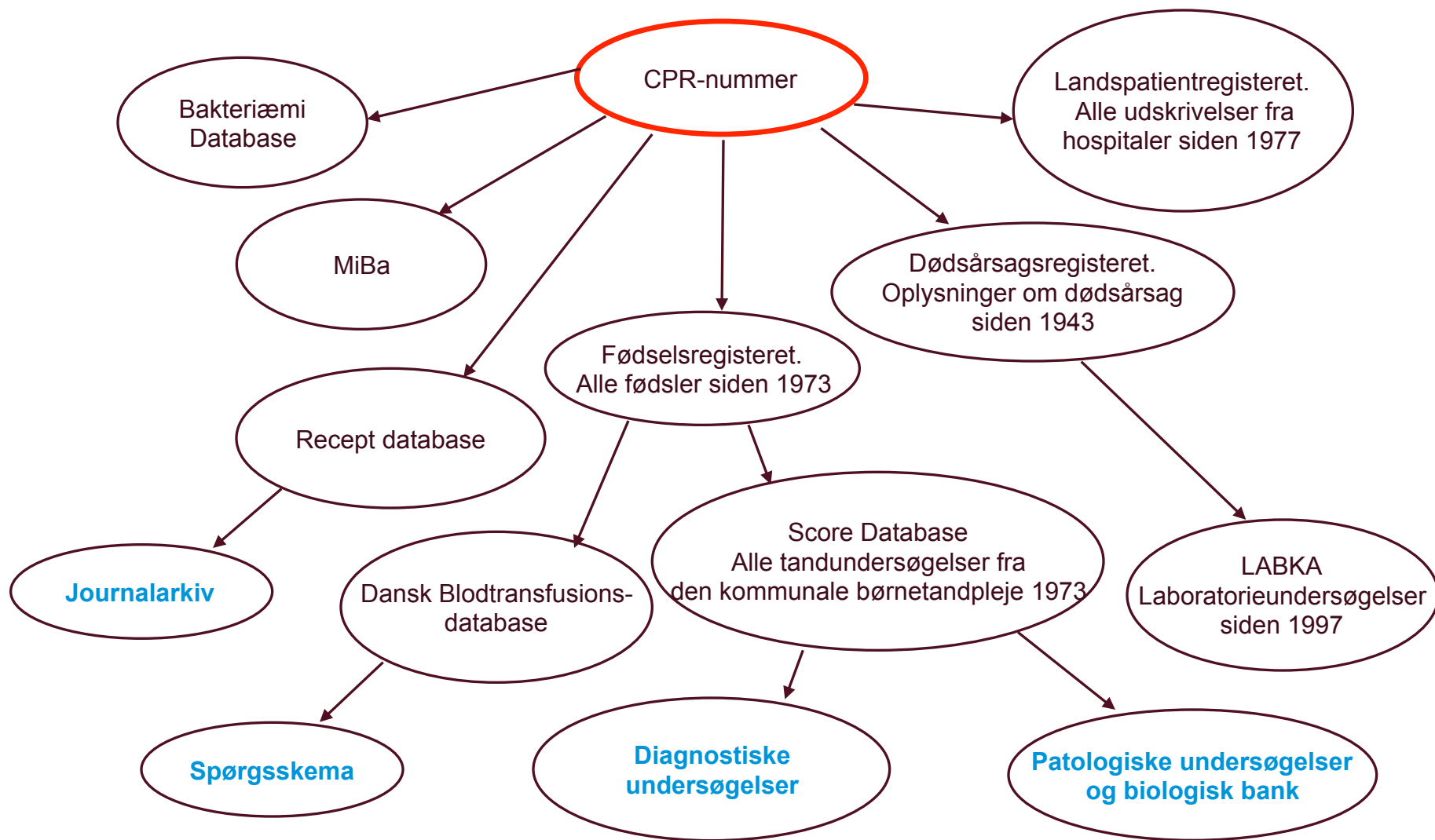
"Are they gaining, Huxley?"

Risiko, prognose og komplikationer for resistent infektion

| 5.000 med resistent E.coli | 20.000 med følsom E.coli | 50.000 populations kontroller |

JAC

Risk of resistance related to antibiotic use before admission in patients with community-acquired bacteraemia

Gitte Pedersen[a], Henrik Carl Schønheyder[b], Flemming Hald Steffensen[c] and Henrik Toft Sørensen[c,d]

[a]*Department of Medicine M and* [b]*Department of Clinical Microbiology, Aalborg Hospital, Aalborg;* [c]*The Danish Epidemiology Science Centre at theDepartment of Epidemiology and Social Medicine, University of Aarhus, Aarhus;* [d]*Department of Medicine V, Aarhus University Hospital, Aarhus, Denmark*

We analysed the association of antibiotic therapy before admission and antibiotic resistance of blood isolates in a total of 1717 community-acquired bacteraemias in the County of Northern Jutland during 1992–96. Antibiotics had been prescribed to 14% of the patients during the 30 days before admission and to 37% during the 6 months. The most frequently prescribed antibiotics within 30 days were ampicillin (28%), penicillin G (27%), sulphonamides and/or trimethoprim (16%) and macrolides (14%). The most frequent blood isolates were *Escherichia coli* (33%), other Enterobacteriaceae (8%), *Streptococcus pneumoniae* (23%) and *Staphylococcus aureus* (10%). Of the 575 isolates of *E. coli*, 425 (74%), 432 (75%) and 518 (90%) were susceptible to ampicillin, sulphonamides and trimethoprim, respectively. Previous antibiotic prescriptions were strongly associated with resistance to ampicillin, sulphonamides and trimethoprim in *E. coli*. The association was less pronounced for *S. aureus* and enteric rods other than *E. coli*. Antibiotic prescriptions within the last 3 months predicted antibiotic resistance, and this should be taken into account when selecting empirical antibiotic therapy of severe community-acquired infections.

High Prescribers of Antibiotics Among General Practitioners – Relation to Prescribing Habits of Other Drugs and Use of Microbiological Diagnostics

FLEMMING HALD STEFFENSEN[1,2], HENRIK CARL SCHØNHEYDER[3] and HENRIK TOFT SØRENSEN[1,4]

From the [1]Danish Epidemiology Science Centre at the Department of Epidemiology and Social Medicine, University of Aarhus, and [4]Department of Internal Medicine V, Aarhus University Hospital, Århus, and the Departments of [2]Internal Medicine M, and [3]Clinical Microbiology, Aalborg Hospital, Aalborg, Denmark

General practitioners' (GPs') prescriptions of antibiotics have shown large variations and may not always be rational. We analysed GPs' prescriptions and use of microbiological diagnostics in Viborg County during a 6-month period in 1992 based on Danish Health Service data. In a logistic regression model we tried to identify potential predictors for a high prescriber of antibiotics, i.e. the GPs with the highest number of prescriptions per patient (upper quartile). Two categories were calculated for the predictor variables, dividing the distribution by the median value. The most liberal GP wrote 15 times as many prescriptions for antibiotics per patient as the most restrictive GP. A strong predictor for high prescribing of antibiotics was the number of prescriptions for other drugs per patient [odds ratio (OR) 12.3, 95% CI: 2.8–54.4] after adjustment for age and sex. High use of throat swabs was a strong negative predictor of high prescribing of antibiotics (OR 0.2, 95% CI: 0.1–0.8) while high use of cultures (OR 2.4, 95% CI: 0.8–6.9) and of urinary susceptibility tests (OR 3.1, 95% CI: 1.1–9.3) were positive predictors. The GP's general attitude to pharmacotherapy seems important for antimicrobial chemotherapy, and if use of antibiotics should be reduced, targeted strategies should be aimed at high prescribers.

F. H. Steffensen, The Danish Epidemiology Science Centre, Høegh-Guldbergs Gade 10, DK-8000 Aarhus C, Denmark

Aarhus University Hospital

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# The "How are you?" public health survey
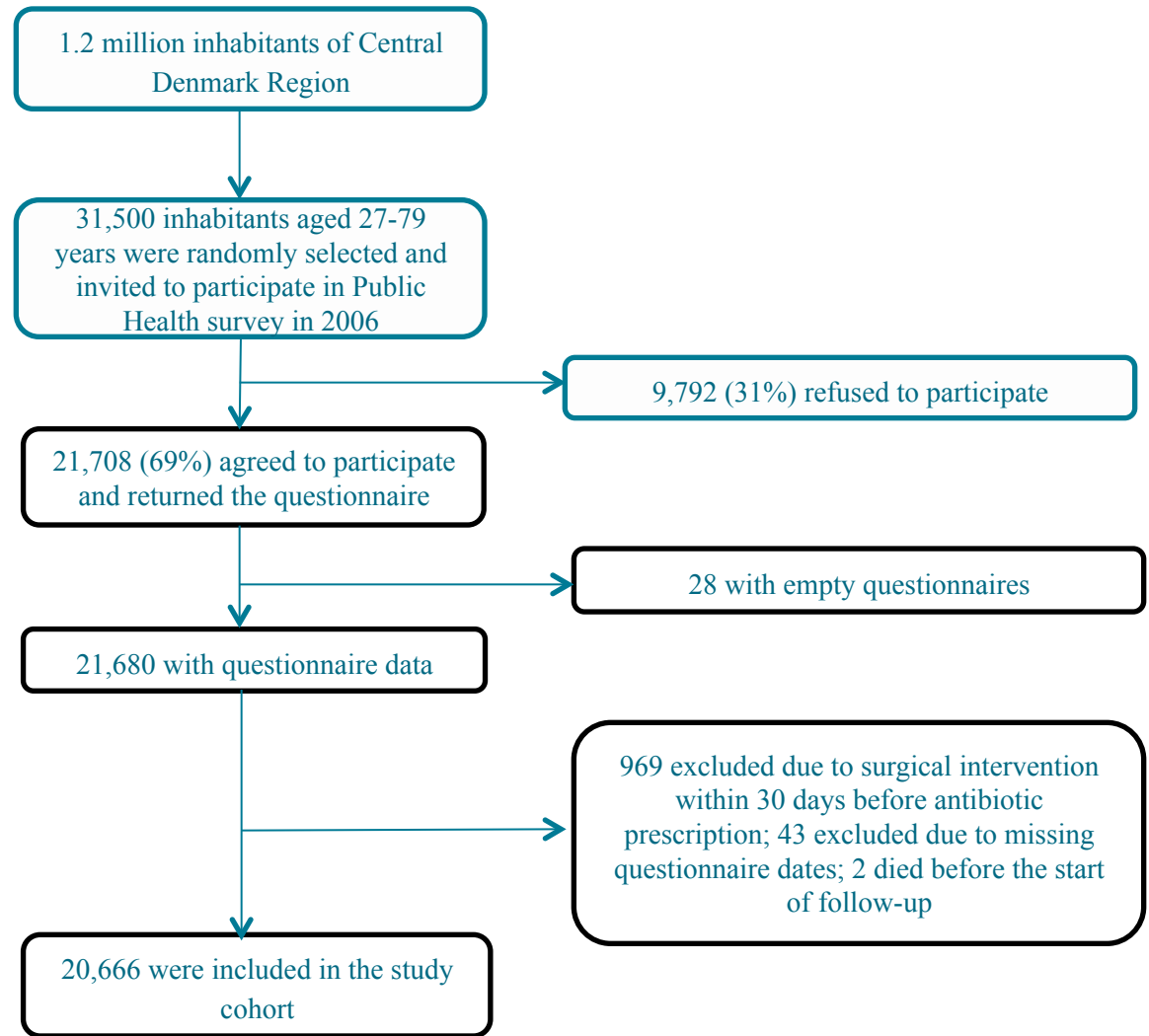
Antibiotic use according to lifestyle factors among participants in the "How are you?" public health survey

	N=20,666	Two-year rate ratio	
		Crude	Adjusted
Smoking$^\delta$			
Non-smoker	15,772	1.00 (Referent)	1.00 (Referent)
Smoker	4695	1.19 (1.13 – 1.25)	1.23 (1.17 – 1.29)
Diet*			
Healthy	4337	1.00 (Referent)	1.00 (Referent)
Unhealthy	15,862	0.92 (0.87 – 0.97)	1.01 (0.95 – 1.06)
Physical exercise#			
No exercise	2150	1.15 (1.06 – 1.24)	1.16 (1.08 – 1.25)
One day per week	1619	0.90 (0.82 – 0.98)	0.89 (0.82 – 0.98)
Two days per week	2243	0.95 (0.88 – 1.03)	0.97 (0.90 – 1.04)
Three days per week	2122	0.89 (0.82 – 0.96)	0.91 (0.84 – 0.98)
Four days per week	2493	0.90 (0.84 – 0.97)	0.93 (0.86 – 1.00)
Five days per week	1262	0.80 (0.73 – 0.89)	0.82 (0.74 – 0.91)
Six days per week	2314	0.86 (0.80 – 0.93)	0.86 (0.79 – 0.93)
Daily exercise	5961	1.00 (Referent)	1.00 (Referent)
Alcohol intake†			
Low	16,716	1.00 (Referent)	1.00 (Referent)
Moderate	2226	0.96 (0.89 – 1.03)	0.97 (0.90 – 1.04)
High	1214	1.03 (0.94 – 1.12)	1.09 (1.00 – 1.19)
BMI			
Underweight	781	1.21 (1.07 – 1.36)	1.14 (0.96 – 1.35)
Normal weight	9738	1.00 (Referent)	1.00 (Referent)
Overweight	7351	1.00 (0.95 – 1.05)	1.07 (1.02 – 1.13)
Obese	2796	1.24 (1.16 – 1.32)	1.27 (1.19 – 1.35)

Anil et al, Epidemiology (in press)

Antibiotic Use Varies Substantially Among Adults: a Cross-national Study from Five European Countries in the ARITMO project
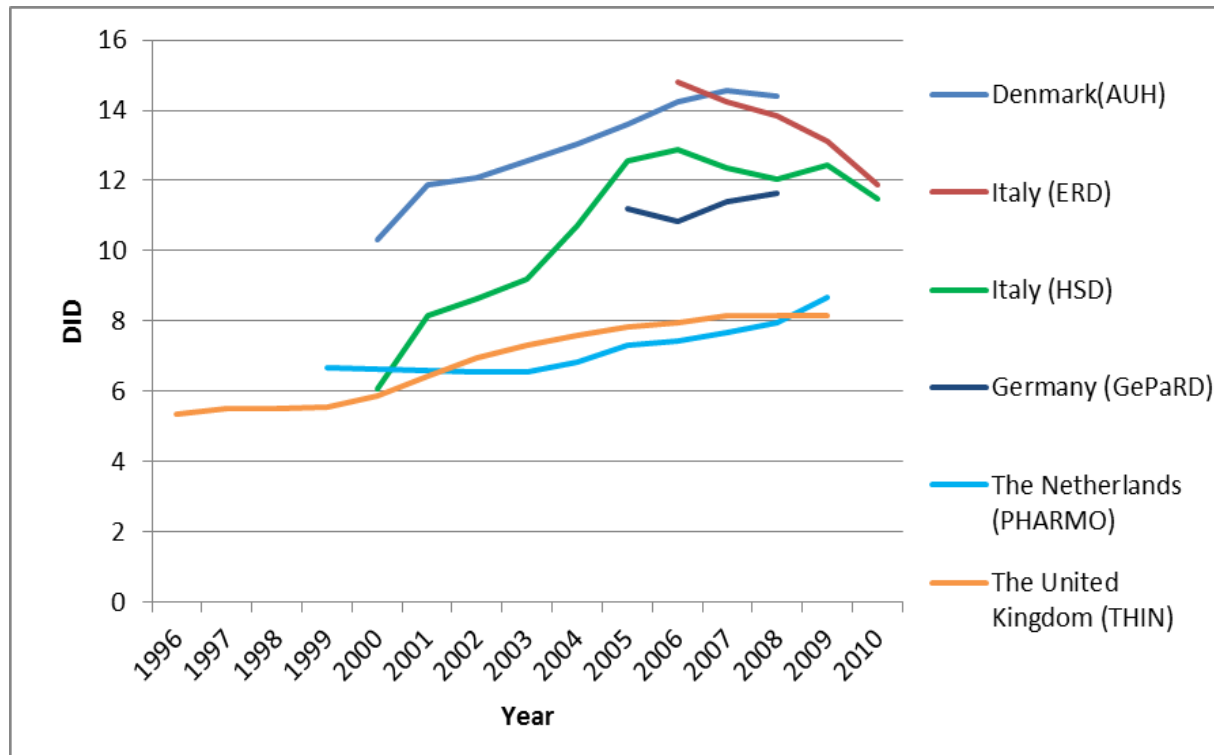
Anil et al, submittet

Strengths and limitations of databases as data source

Strengths

- Can be based on already available data

- Quick, feasible, less expensive
  - May be the only ethical or affordable solution

- Large sample sizes and long follow-up
  - May study rare exposures
  - May study rare or delayed outcomes

- Population-based data
  - Reduce the risk of selection bias and drop-outs
  - Measure usual clinical practice

- Data collected independently of the research project
  - Reduce the risk of recall or non-response bias, or investigator bias

- Do include disadvantaged populations

- May give results similar to primary data-based research if conducted rigorously

Limitations

"Epidemiologists have become so enamoured with statistical analysis of the data that they pay too little attention to the <u>validity of the raw data</u>"

Gordis Am J Epi. 1979

Limitations

- Possibly lack of completeness and validity
  - Variation or errors in coding
  - Incompleteness in coding, especially comorbidities
  - Limits in the specificity of the available codes
  - Errors and variation in clinical diagnosis
  - → The validity of registered data often have to be evaluated

- Possibly lack of data on confounder variables related to lifestyle, patients' and doctors' decision making, etc.
  - Smoking, alcohol, BMI
  - Socioeconomic variables
  - Confounding by indication
  - Healthy user bias

- Possibly lack of clinical details since not controlled by researcher
  - Lab tests, disease location, cancer staging, <u>travel to foreign countries</u>, etc.

Lancet 2004;363:1728-31