Big data and the use in drug development

Steinar Thoresen MD PhD Strategic Lead Oncology
The Nordics and Netherland, Merck Group

Oslo, 19. November 2019

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Agenda

0 1 **Disclosure**

0 2 **Big Data/RWE - a buzz word?**

0 3 **Registry data**

0 4 **Conclusion**

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Steinar Thoresen

Head of Election Committee
Oslo Cancer Cluster (OCC)

Head R&D
Norwegian Pharma-Trade Association

Board Member
Bergen Biomedical

Blog
www.dagensmedisin.no

2019-now	***Medical Strategy Lead Oncology Merck, Nordics and Netherlands***
2013-19	Medical Director Abbvie
2006-13	Head of Clinical Research, Medical Director GSK
1990-2013	Professor University of Bergen
1991-2006	Director National Cancer Screening Norway
1990-91	Visiting professor Harvard Medical School
1984-90	The Cancer Registry of Norway
1983-84	Forensic medicine University of Oslo
1979-83	Pathologist PhD Haukeland University-Hospital

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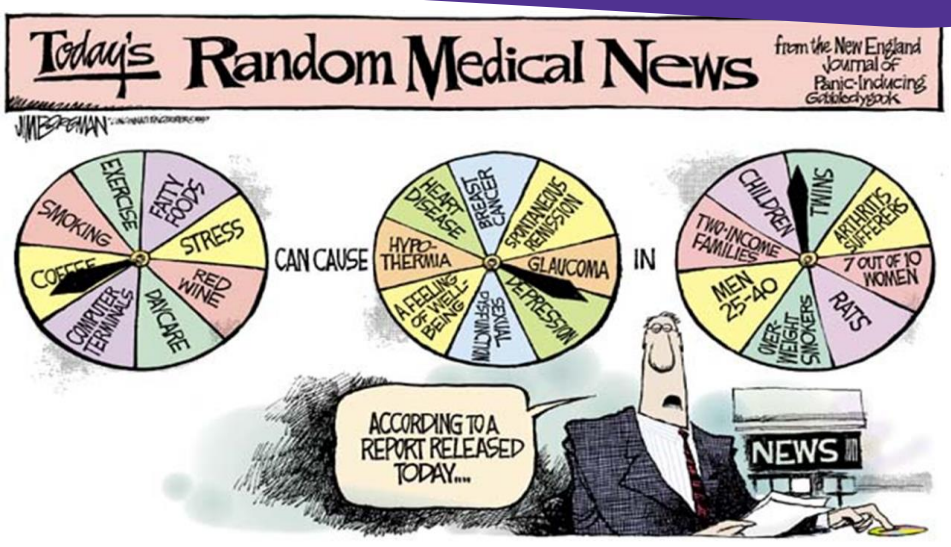
Epidemiology
is the study of the determinants of disease distribution and frequency



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Clinical studies as of yesterday?

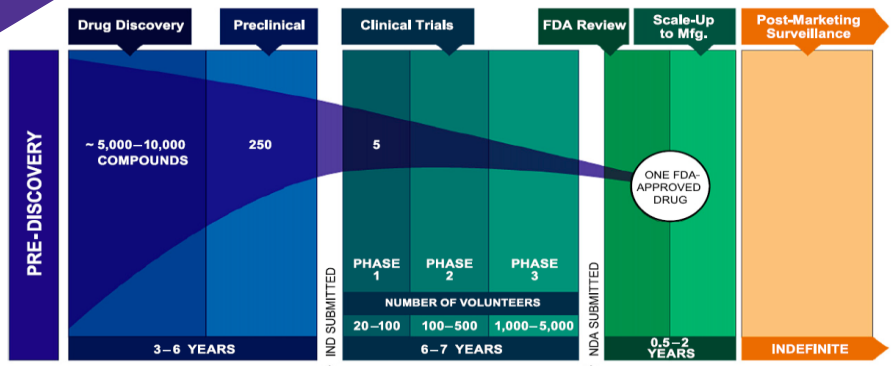

Figure 1. The research and development process. IND = Investigational New Drug Application; Mfg. = manufacture; NDA = New Drug Application. Adapted by permission from Reference 21.

Pharmaceutical Research and Manufacturers of America. Drug discovery and development: understanding the R&D process [accessed 2012 Jul 26]. Available from: http://www.lnovation.org

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Industry and academia clinical studies

Status

Industry is serving the market:

Close to 100 % of all drugs and vaccines are developed and brought to the patients **by the industry** (often in collaboration with academia)

Time & costs to market are high:

Around **10-15 years** with cost of **~1-2 bil€** to bring a molecule to the patients

Trends

More R&D collaborations:

Industry cuts in-house R&D and **develop molecules in collaboration with academia**

Shifted study focus to later stage:

Phase 2 and 3 studies tend to have shorter follow-up and include fewer patients than previous

Rising importance of **Phase 4 studies** in the future (real-life data, HEOR and bio-markers)

Nordic countries to play important role

- **11-digit unique ID**
- **large national registries**
- **several high-standard biobanks**

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~3,4 %

Success rate of oncology drug development from 2001-2015

bil$ 2+

Average cost per oncology drug development from bench to patient

17,368

Oncology drug clinical trials conducted 2001-2015

2X

Success rate doubled for trials that included patient stratification

7%

Of oncology trials utilized a biomarker in 2015

Wong, Chi Heem, Kien Wei Siah, and Andrew W. Lo. "Estimation of clinical trial success rates and related parameters." *Biostatistics* 20.2 (2019): 273-286.

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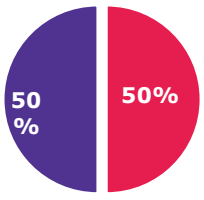
The RCT based model

The analysis of recent failures during phase III (late stage attrition) is supportive of the new R&D model:

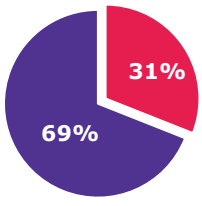
RCTs

Efficacy



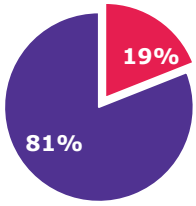
Failure rate

Safety



- **8%** through confirmation of **known safety** concerns
- **23%** through **other safety** issues

Lack of differentiation



- **16%** on lack of differentiation **in efficacy**
- **3%** on lack of differentiation **in safety**

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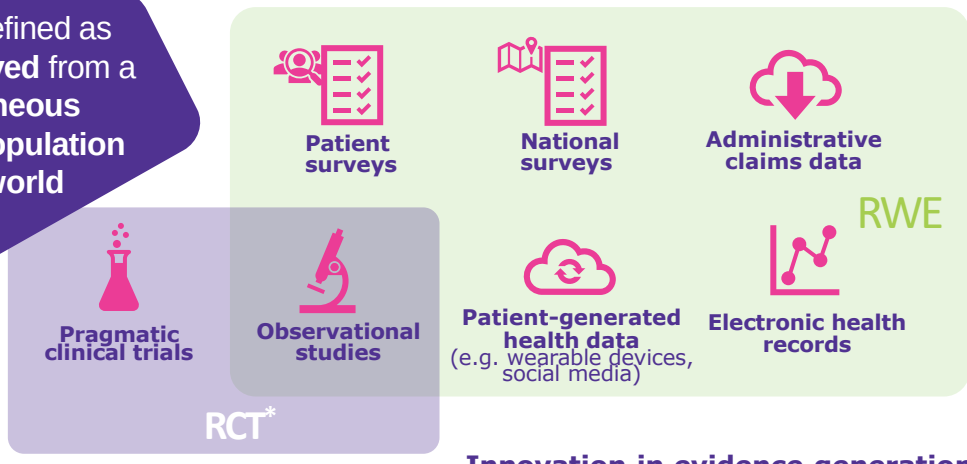
What is RWE?

RWE is defined as **data derived** from a **heterogeneous patient population** in a **real-world setting**



Innovation in evidence generation

*RCT = Randomized controlled trials

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RCTs and real-world studies provide different information and both are required to describe the value of a drug therapy

RCTs

- Gold standard for assessing the **efficacy** of a drug
- **Strict inclusion/exclusion** criteria as well as **consistent drug administration** create an ideal environment to isolate the effect of a drug

- However, these **conditions are seldom replicated** in everyday clinical practice
- The effectiveness/safety of drugs in the **real-world often differ** from efficacy/safety results from RCTs

Real world studies

- Required to assess the **long-term safety of drugs** to detect rare adverse events that are not detected by RCTs
- Effectiveness and safety profiles are likely to be different in **heterogeneous groups of patients** compared with patients in RCTs

- However, the downside is that real-world studies are **vulnerable to biases** and confounders
- A good grasp of epidemiologic principles are required to **deal with these biases**

Having a **more nuanced view of the strengths and limitations** of RCTs and real-world studies can **facilitate creative thinking** around evidence generation

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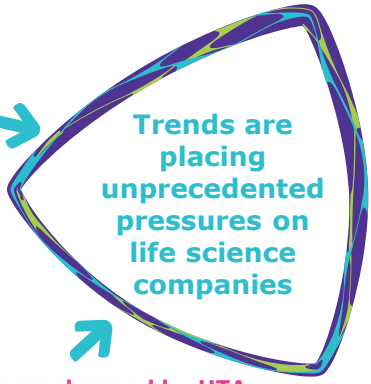
The world is changing – a new era?

Drug prices are on the increase due to both development costs and the increase in personalised treatments meaning R&D investment must be recouped across fewer patients.

Higher cost allocation per drug



Aging population with multiple comorbidities

Ageing populations are increasingly living with multiple comorbidities due to both improved survival from previously fatal diseases such as cancer, and the impact of modern lifestyles, evident from the prevalence of diabetes and obesity.

Increased evidence demand by HTA

Health Technology Assessment (HTA) agencies and payors are becoming more sophisticated in their demands for evidence which they require for product reimbursement.

Deloitte: Real World Evidence – Transforming patient care, 2014

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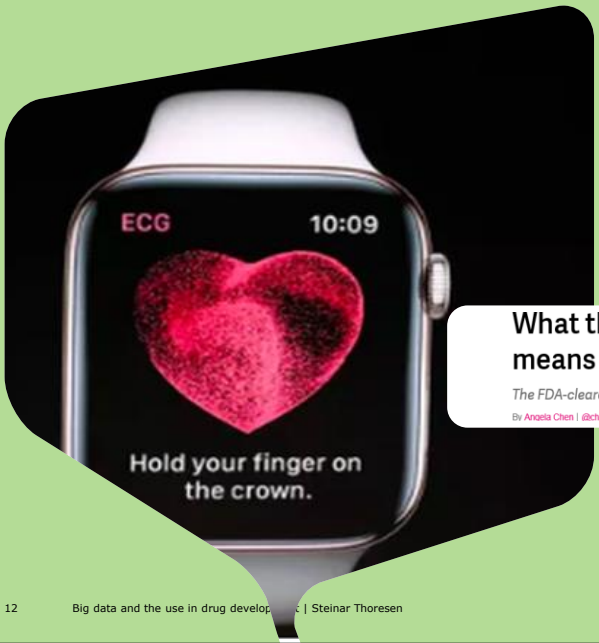

RWE and BIG DATA

What the Apple Watch's FDA clearance actually means

The FDA-cleared features aren't supposed to be used by those under 22

By Angela Chen | @chenqela | Sep 13, 2018, 12:23pm EDT

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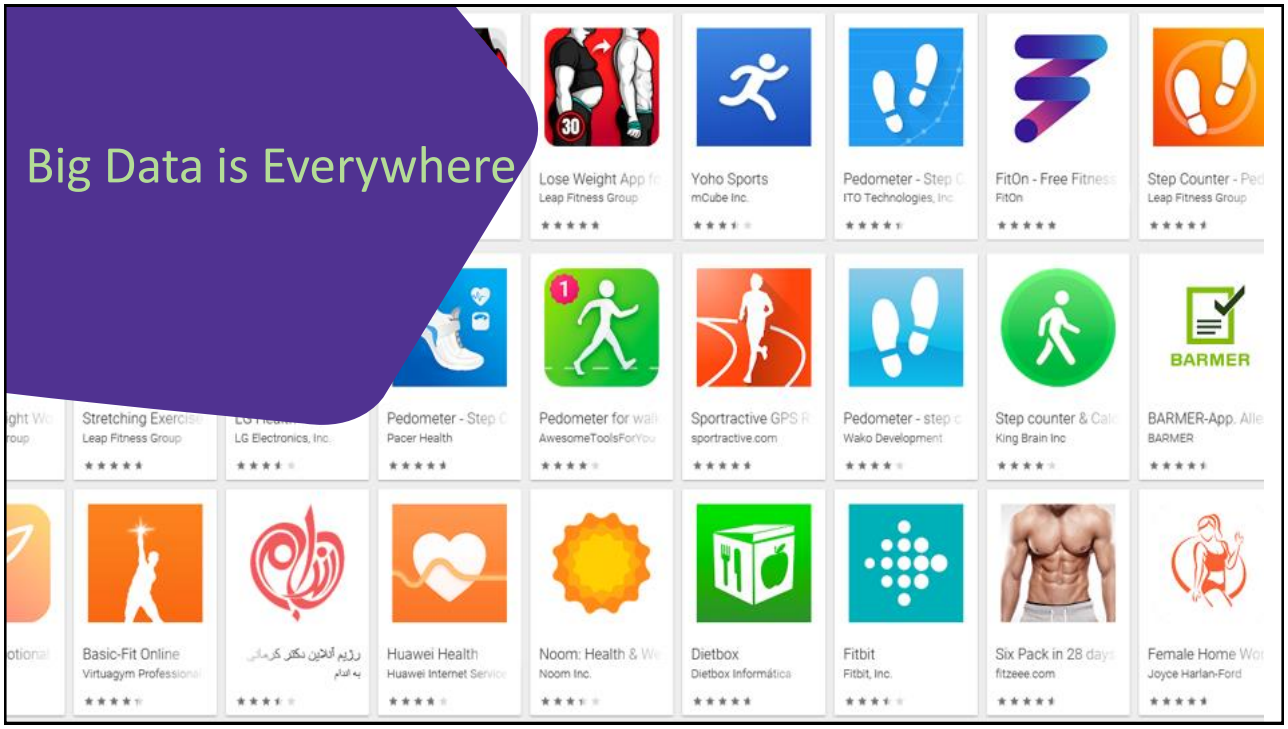
Big Data is Everywhere
Lose Weight App
Leap Fitness Group
Yoho Sports
mCube Inc.
Pedometer - Step
ITO Technologies, Inc.
FitOn - Free Fitness
FitOn
Step Counter - Ped
Leap Fitness Group
Stretching Exercise
Leap Fitness Group
LG Electronics, Inc.
Pedometer - Step
Pacer Health
Pedometer for wall
AwesomeToolsForYou
Sportractive GPS
sportractive.com
Pedometer - step
Wako Development
Step counter & Calo
King Brain Inc
BARMER
BARMER-App. Alle
BARMER
Basic-Fit Online
Virtuagym Professional
Huawei Health
Huawei Internet Service
Noom: Health & We
Noom Inc.
Dietbox
Dietbox Informática
Fitbit
Fitbit, Inc.
Six Pack in 28 days
fitzeee.com
Female Home Wor
Joyce Harlan-Ford

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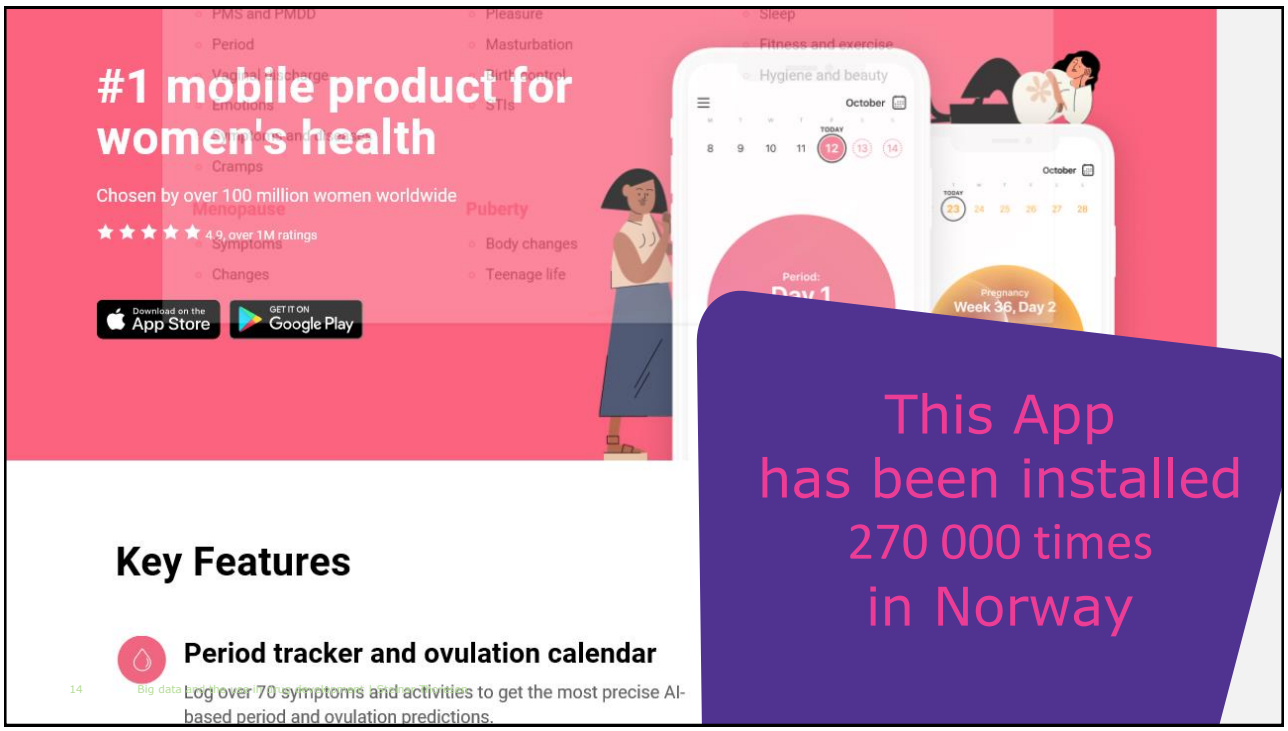
#1 mobile product for women's health
Chosen by over 100 million women worldwide
4.9, over 1M ratings
Download on the App Store
GET IT ON Google Play
PMS and PMDD
Period
Cramps
Menopause
Symptoms
Changes
Pleasure
Masturbation
Puberty
Body changes
Teenage life
Sleep
Fitness and exercise
Hygiene and beauty
October
Period:
Pregnancy
Week 36, Day 2
Key Features
Period tracker and ovulation calendar
Log over 70 symptoms and activities to get the most precise AI-based period and ovulation predictions.
This App has been installed 270 000 times in Norway

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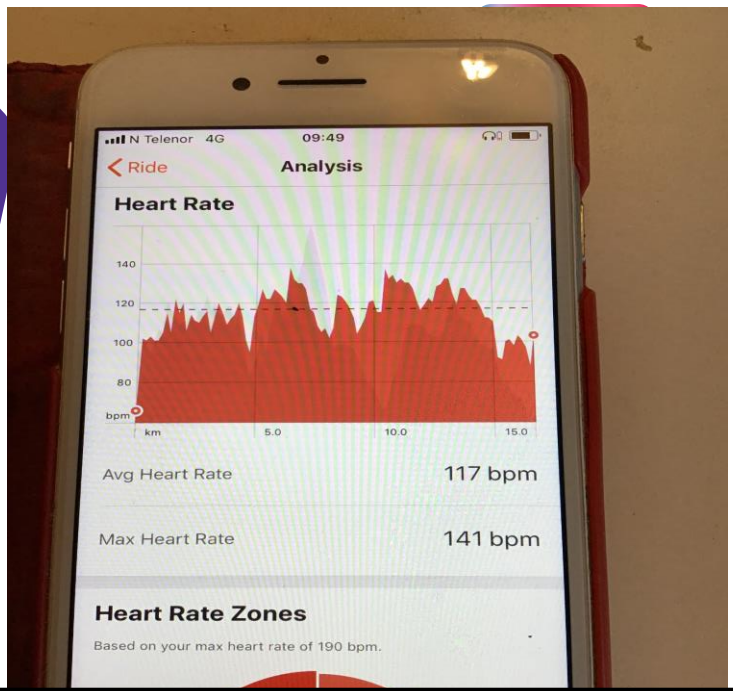
My last bike-ride



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News Network For Journalists Mayo Clinic Radio

By Duska Anastasijevic

Mayo Clinic selects Google as strategic partner for health care innovation, cloud computing

September 10, 2019

ROCHESTER, Minn. — Mayo Clinic and Google announced a 10-year strategic partnership on Tuesday, Sept. 10. This partnership will redefine how health care is delivered and accelerate the pace of health care innovation through digital technologies.

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UCSF

About Patient Care Re

Home > UCSF News Center > Public-Private Consortium Aims to Cut Preclinical Cancer Drug Discovery f

Public-Private Consortium Aims to Cut Preclinica
Cancer Drug Discovery from Six Years to Just One

Lawrence Livermore National Laboratory, Frederick National Laboratory for Cancer Research, GSK, and UCSF Partner on Effort

By Laura Kurtzman on October 27, 2017

A supercomputer in the Lawrence Livermore National Laboratory, which will be used in a new public-private project to speed disco new drug therapies. *Photo by Lawrence Livermore National Laboratory*

Scientists from two U.S. national laboratories, industry, and academia on Oct. 27 launched an unprecedented effort to transform the way cancer drugs are discovered by creating an open a

American preclinic initiative

Goal:
from 6
to 1 year

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Helsedataprogrammet Norway

The aim of the Health Data Program is to **improve the utilization** of Norwegian **health data** from health registers, population-based surveys and research biobanks. The program will **simplify access, compilation and analysis of health data** across registers.

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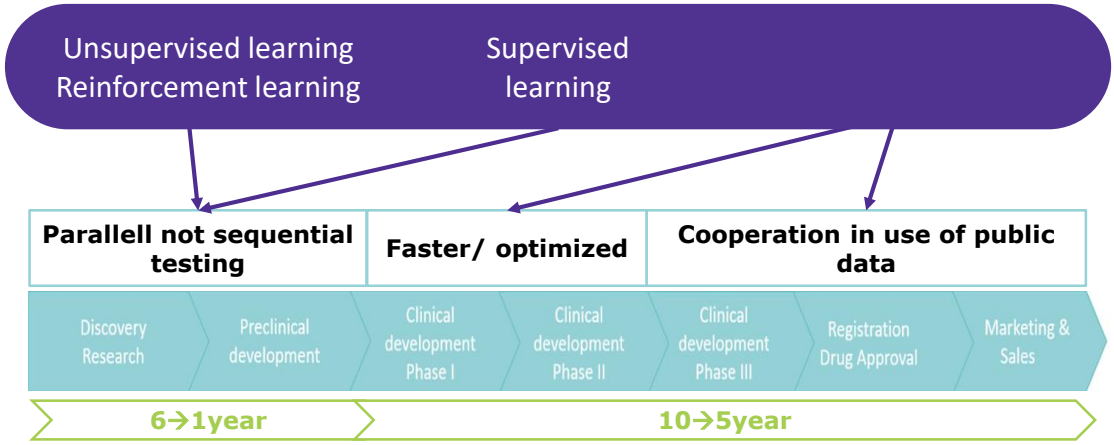
Artificial intelligence in medicine



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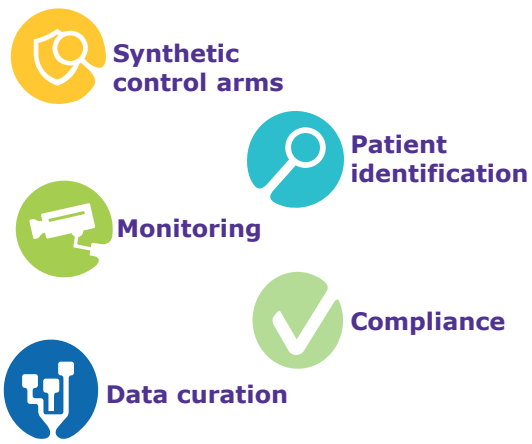
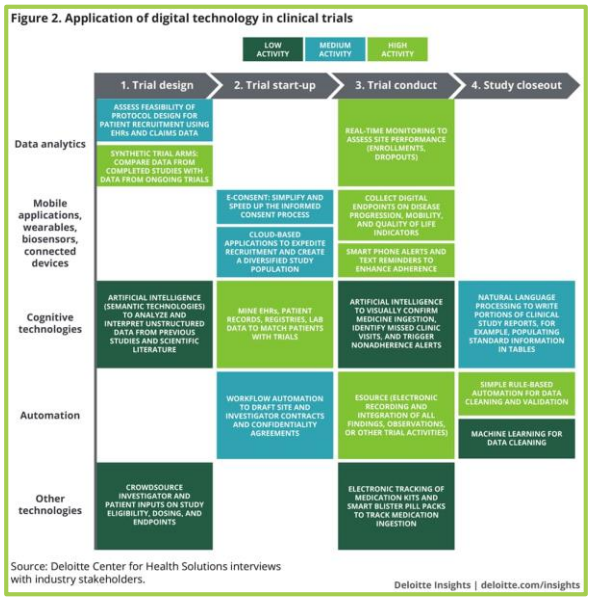
Clinical Trials using big data; RWE and digital





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Biobanks

A unique study has been launched in Finland that will deepen our understanding about the origins of diseases and their treatment. The FinnGen study plans to tap into 500 000 unique blood samples collected by a nation-wide network of Finnish biobanks.

Registries

FinnGen will boost the activities of Finnish biobanks by speeding up sample collection and enabling enrichment of samples with genomic data. The aim is to get up to 500 000 Finnish individuals to participate in the study. The FinnGen will manage anonymous health registry and genomic data without compromising the privacy and integrity of participants.

FINNGEN project Finland Public Private partnership

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Developing diagnostics for the early detection of age-related diseases.

AGELABS

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AgeLab

A simple blood test

We are developing a novel blood-test that predicts all-cause mortality risk and risk of developing specific age-related diseases.

Aging is the predominant risk factor for most diseases and conditions that limit health span. Due to the exponentially increasing proportion of the world's elderly population, developing novel and effective therapies for treating and preventing age-related diseases has become essential.

We can help reduce the cost and the duration of clinical trials.

Learning from history

By applying 21st century machine learning techniques on large epigenetic datasets spanning 45 years back in time.

We create the prediction algorithm by combining genome wide microarrays, high-performance computing, statistics and machine learning.

At the core of our approach lies an algorithm trained on the DNA methylation patterns from thousands of people where lifespan and cause of death is known. We train our algorithm on large unique datasets from Norwegian and international biobanks.

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AgeLab

Molecular diagnostics for clinical trials

Shortening trial duration's and lowering the number of patients needed.

The problem: The cost of developing a new drug roughly doubles every nine years. The average cost of developing a new cancer drug is €556m, the median time to approval is 7.3 years and only 10% pass all three phases and receive approval. The main drivers of time and costs are the number of patients, the trial duration and the low likelihood of success.

The solution: Using our blood-test in clinical trials can help reduce cost, trial duration or the number of patients needed through:

- Better patient selection (inclusion or exclusion criteria)
- Earlier termination of failing clinical trials (biomarker in e.g. interim analysis)
- Earlier understanding of overall therapy effects (biomarker in e.g. interim analysis)
- Improving adaptive clinical trials (biomarker in e.g. interim analysis)
- Shorter survival studies (surrogate endpoint for mortality)
- Adding new indications (surrogate endpoint for mortality or age-related disease)

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INSPIRE

INcreaSe PharmaceutIcal REporting

Pilot project to capture cancer medication data from hospitals

A public-private partnership

Cancer Registry of Norway
INSTITUTE OF POPULATION BASED CANCER RESEARCH

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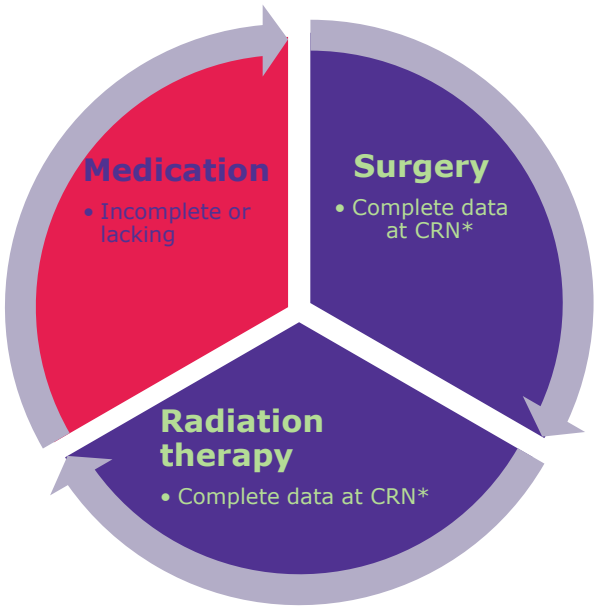
Cancer treatment and data availability today



*CRN = Cancer Registry of Norway

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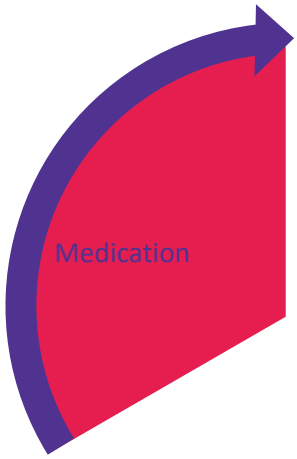
We need cancer medication now



Overview /Statistics

- *Who gets treated, with what drug(s), for what condition?*
- *Prognosis? Survival?*

Quality assessments

- *Adherence to national guidelines?*
- *Regional differences?*

Research

- *Who benefits from new cancer drugs and who doesn't?*

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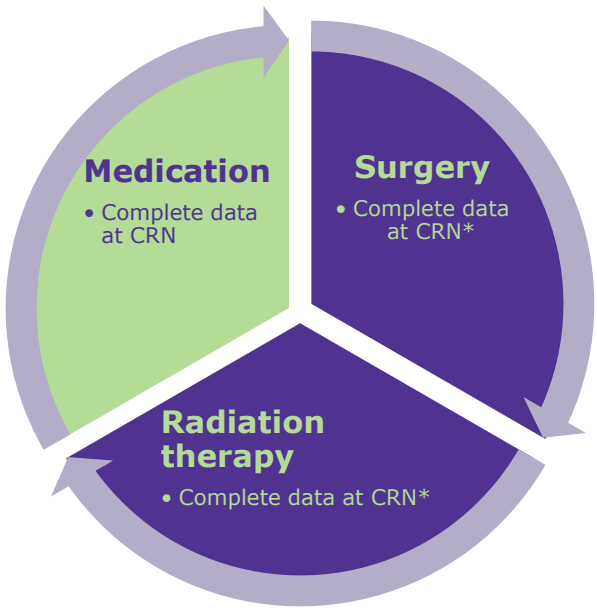
Inspire gives us:

1. Knowledge on cancer drug treatment

2. Knowledge on the complete courses of treatment for all cancer patients



***CRN** = Cancer Registry of Norway
****Complete data for participating hospitals**

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The research question before and after launch

Before:

What is the current disease burden and current treatment effects?

- Incidence/prevalence including subgroups with biomarkers
- Survival/mortality based on current treatment options (historical data)
- Outcome with current standards of care

After:

How does a new treatment option look in a population outside a clinical trial, and what are the new treatment effects including costs?

- «real-life phase 4»: treatment effects (changes) based on recurrence and survival by region/hospital.
- Compare new treatment options and track real-world use of different treatment options by tumor-type/mutations and by regions/hospitals
- Adaptive licensing/Market access in Nordic countries
- Costs and HEOR-data
- Pay for performance

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Status

Big data is already here and will change the way we do clinical studies

Nordic registries/biobanks are world class, but access and linkage to registry data is too slow and our Nordic advantage will not last

Key questions

The key question is: will Nordic authorities and payors accept the new area? They still have a hang-up on old-fashion trials

Privacy issues must be solved. Who owns the data?

Conclusion on big data and drug development

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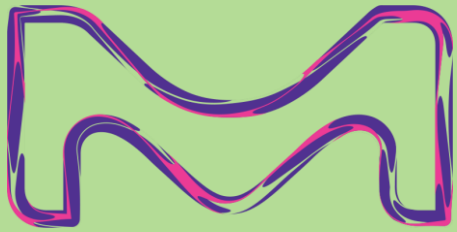

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