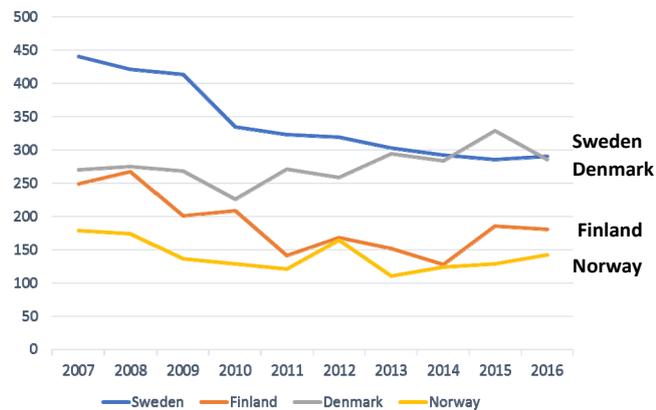


Recruiting Patients from Other Nordic Countries

*Steinar Aamdal, Professor em., Head of Section for
Clinical Cancer Research and Resource Development,
Oslo University
Oslo University Hospital*



The total number of Clinical Trial Applications to Regulatory Authorities in the Nordics



Declining number of clinical trials

Pharma side

- Nordic countries expensive compared to Eastern Europe, Baltic states and Asia ?
- Emerging Asian markets with huge populations (India and China)
- Pharmaceutical companies scaling down in the Nordic region



Declining number of clinical trials

Causes

Pharma side

- Nordic countries expensive compared to Eastern Europe, Baltic states and Asia ?
- Emerging Asian markets with huge populations (India and China)
- Pharmaceutical companies scaling down in the Nordic region

• Hospital side

- Low trial interest from leadership: “production” rather than research and a general negative attitudes towards pharma collaboration
- Clinical trials regarded as costly to the institution ? (Reports: Copenhagen Economics, Menon Economics)
- No financial incentives for doing clinical trials
- Dwindling physician interests in clinical trials:
 - Insufficient trial infrastructure
 - Merits
 - Time



Declining number of clinical trials

Consequences

- **Delayed access for patients to new drugs (up to 5-6 years..)**
- **Delayed implementation of new drugs**
- **Quality of care offered to patients is closely related to clinical research and clinical trial participation**

- **Missed opportunities for translational research**
- **Missed opportunities for international research collaboration**



Nordic countries

attractive partners for clinical trials

- **Very good healthcare systems at all levels providing services for all patients**
- **Homogeneous, stable and well educated population**
- **Excellent Cancer Registries (100% of the cases)**
- **All individuals identified by a 11 digit id number i.e.very few patients lost to follow-up**
- **High patient compliance in trials**
- **Trials performed rapidly and with high quality**
- **English speaking professionals**
- **A general positive attitude to clinical research in the population**



Clinical trials in the Nordics

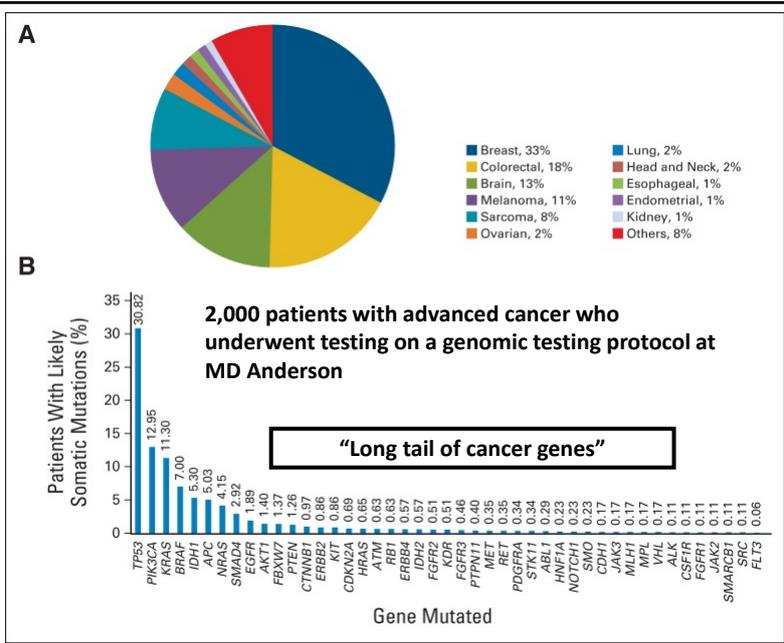
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- English speaking professionals
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- ---
- ***But small populations in each country!***



Changing landscape of cancer trials

Personalized cancer therapy
Precision cancer medicine
Genomics-driven cancer therapy

- Patient selection based on mutational status in tumor rather than tumor type
- Low number of patients in each trial due to mutation rarity (1-5%)
- Phase I trials expands to randomized phase II
- Much more labour-intensive trials – sampling of tumor before, during and after therapy etc..
- Few eligible patients in each Nordic country



Nordic Region



Populations (August) 2017 (Worldometers)

**Sweden: 9.9
Denmark: 5.7
Finland: 5.5
Norway: 5.3
Iceland: 0.3
Total: 26.7**

• Similar treatment cultures



Why Nordic Collaboration?

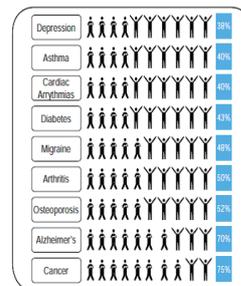
Nordic Cross Border Patient Mobility in Clinical Trials

Maiken Engelstad
 Ass. Dir General, *PH.D. MPH*

NRI conference May 19th 2017

Because we have to!

- **Added value for patients**
 - Better & safer treatments
 - Increased access
 - Cost-efficient; treat more patients
- **Better research** – faster results
- **Attract industry**



FDA Paving the way for personalized medicine, 2013

**26 mill
inhabitants**

Ways of increasing the number of clinical trials in the Nordic Region

- **Simplified approval procedures**
 - Mutual recognition of Medicine Authorities approvals among the Nordic countries
 - Harmonized Ethical trial approvals in Nordics ?
- **Creating clinical trial networks – Nordic Trial Alliance (NTA), Nordic NECT...**
- **Simplify cross-border procedure for patients participation in clinical trials**



Directive 2011/24/EU on patients' rights in cross-border healthcare



- EU Cross Border Directive 2011/24/EU allows patients to receive treatments in other countries within the EU,
- *but does not apply to patients participating in clinical trial.*



A screenshot of the NRI-CONFERENCE 2017 program page. The page features the NRI NETWORKS logo in the top left corner. A navigation menu includes links for HOME, ABOUT NRI, NRI-CONFERENCE, NORDIC SUMMIT, NETWORKS, and CONTACT US. The main content area is titled "Program NRI-Conference 2017" and includes a "Download program here" link. A sidebar on the left lists menu items: Conference registration, About, Program (highlighted), Speakers, Practical information, and Past conferences. The main content area shows the date "Friday 19. May 2017" and a schedule starting at 08:30 with "Registration". The "Main Session 1: Personal genomics - the future of healthcare?" is moderated by an unnamed person. The first session at 09:00 is "Welcome" by speakers Anne Sirethe Erlandsen and Jari Partanen. The second session at 09:15 is "The Genetics of Common Human Traits" by an unnamed speaker.

PARALLEL SESSIONS

02

NORDIC CROSS BORDER PATIENTS FOR CLINICAL TRIALS

Venue: Kaare Norum Auditorium, Oslo Cancer Cluster Innovation Park

Moderator: Steinar Aamdal, Head of Department,
Early Cancer Trials and Research Support, Oslo University Hospital

12:40 - 12:50

Introduction

12:50 - 13:00

Why Nordic Collaboration?

Maiken Engelstad, Ministry of Health and Care Services, Norway

13:00 - 13:55

Sending patients cross border for clinical trial participation - What are the challenges in each country?

- DENMARK - Morten Mau-Sørensen, Head of Phase I unit, Department of Oncology, Rigshospitalet - Copenhagen University Hospital
- SWEDEN - Jeffrey Yachnin, Section Head Early Clinical Trial Unit at Karolinska University Hospital
- FINLAND - Katrīna Peltola, Head of Early Phase, Clinical Trial Unit at Helsinki University Hospital
- NORWAY - Steinar Aamdal, Head of Department, Early Cancer Trials and Research Support, Oslo University Hospital

Nordic Cross Border Trial Collaboration Challenges

- Legal hurdles ?
 - Denmark
 - Sweden
 - Finland
 - Norway
- Costs?
 - Drugs in clinical trial are provided by Pharma free of charge
 - Travel costs
 - Today's drugs commonly have low frequency of toxicity, administered ambulatory
- Risks?
 - Who will carry incurring extra cost in case of complications - intensive care treatment ?



Nordic Cross Border Trial Collaboration

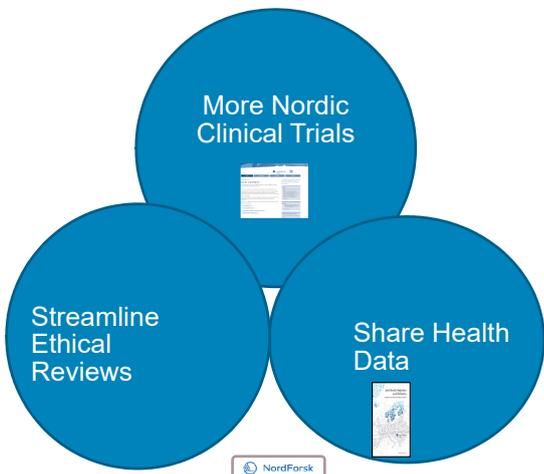
- **Denmark** implemented in 2003 paragraph 23: Expert panel, 5 members, appointed by National Board of Health, may refer patients to experimental treatments in other countries (costs covered by each Amt)
- **Sweden** have no established system, for sending patients to other countries for trial participation , “21 rather independent landsting are challenging” (“Kliniska Studier i Sverige” - collaboration between Vetenskapsrådet og 6 de sjukvårds regioner : web page listing trials, marketing and contact point nationally and internationally..)
- **Finland** have no established system for sending patients to other countries for trial participation
- **Norway** have as, of 2017, no established system for sending patients to other countries for trial participation
-

Minister of Health in Norway

New action plan to increase patients access to clinical trials in Norway

- 1. Clinical research and clinical trials are *integrated parts of patient treatment***
- 2. Creating a website with information about all clinical trials in Norway**
- 3. Allow patients access to clinical trials in countries outside Norway!**
- 4. Establishing an expert panel advising patients on clinical trial participation (“second opinion” system in Denmark as template) up and running from 2018**
- 5. Increase Nordic trial collaboration - Nordic Trial Alliance Multicenter studies...**
- 6. Develop financial incentives**

Project "Nordic Research For Better Health"



THE NORWEGIAN
PRESIDENCY
2017



Nordic Council
of Ministers

Norwegian Ministry of Health and Care Services

Nordic Collaboration in health research



“Proposal for a joint Nordic initiative on ethical reviews of clinical trials”

Nordic Region



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- **Similar treatment cultures**



Thank you !





VERDIEN AV INDUSTRIFINANSIERTE KLINISKE STUDIER I NORGE

Department of Cancer Treatment 2012, Clinical Cancer Research Unit



Verdien av kliniske forsøk i Danmark

- **Hvorfor flere kliniske studier til Danmark:**

- Økt tilgang til for pasienter til utprøvende behandling
- Kompetanseheving og kvalitet i helsetjenesten
- Endring i klinisk praksis
- Arbeidsplasser
- Generer flere studier på sikt
- Styrker internasjonalt forskningsnettverk

- *Besparelser i det offentlige: 22 000 DKK i legemiddelutgifter per forsøksperson (88 mill. DKK for de 175 industri-initierte studiene i 2015).*
- *Legemiddelindustrien bruker 248 millioner DKK (2015) på kliniske studier i Danmark*
 - *Frikjøp av leger, sykepleiere og innkjøp av utstyr til sykehusene*



Copenhagen Economics,
Feb 2017





VERDIEN AV INDUSTRIFINANSIERTE KLINISKE STUDIER I NORGE



277 millioner kroner overføres til sykehusene årlig



<i>Gjennomsnittlig overføring per studie</i>	2,9 mill. kr
<i>Gjennomsnittlig overføring per pasient som deltar</i>	156 000 kr
<i>Årlige totale overføringer til Norske behandlingstilstander*</i>	277 mill. kr

*Justert for gjennomsnittlig studieledd (2,6 år), samt antall studier som pågår hvert år (243 stk.)



Kliniske studier gir arbeidsplasser og verdiskaping



- Sysselsetter om lag **456 årsverk** i Norge
- Gir **2,7 mrd. kroner** i verdiskaping (2015)

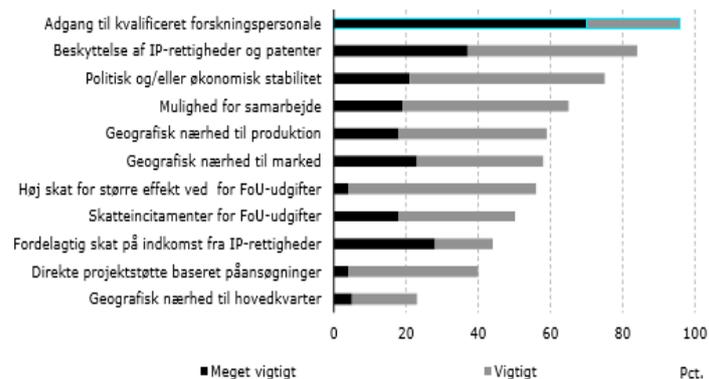


Investigational therapy trials in Denmark

A panel appointed by Danish Health Authorities comprising 5, senior, nationally and internationally well connected specialists to advice patients on investigational therapies

- Panel offer advice and referral to sites with ongoing trials of investigational therapies which could be suitable for the individual patient, in Denmark or to sites outside Denmark.
- Costs for trial participation outside Denmark covered by the patients Amt/Region
- ---
- In 2016 advice given to 372 patients of which 5 were referred to investigational therapy trials outside Denmark

Figur 8 Afgørende faktorer for tiltrækning af FoU-aktiviteter



Note: FoU er en forkortelse for *Forskning og Udvikling*.

Kilde: KPMG (2011) Tax incentives for R&D.

Kønberg report

14 proposals for future Nordic co-operation on health

1. Adopt robust measures against increasing antibiotic resistance
2. Boost co-operation on highly specialized treatments in the Nordic Region
3. Establish a Nordic network for rare diagnoses
4. Establish a Nordic virtual centre for registration-based research
5. Increase co-operation regarding measures to improve public health
6. Establish a Nordic public-health policy platform to reduce inequalities in health
7. Increase patient mobility in the Nordic Region
8. Strengthen co-operation on welfare technology
10. Bolster Nordic co-operation in the field of psychiatry
11. Increase the mandate for co-operation within the field of health preparedness
12. Expand Nordic pharmaceutical co-operation to boost cost-efficiency and improve safety
13. Establish a new Nordic exchange of officials
14. Establish Nordic co-operation between national experts in the European Commission

Not a word about Nordic co-operation on clinical trials !

The screenshot shows the homepage of the Nordic Network for Early Cancer Trials (NORDIC NECT). The website has a blue header with the logo and navigation menu. The main content area features a large image of test tubes and a pipette. Below this, there are sections for 'LATEST NEWS', 'LATEST TRIALS', 'CANCER STUDIES SEARCH', and 'NORDIC COOPERATION'. The 'LATEST TRIALS' section lists a Phase Ib/II study for Melanoma and a study for Solide Tumors. The 'CANCER STUDIES SEARCH' section includes a search form with a dropdown menu for 'Cancer type' and a 'Search' button. The 'NORDIC COOPERATION' section features a map of the Nordic region with markers for Bergen, Oslo, Stockholm, Helsinki, Aarhus, Herlev, and Lund.

NORDIC NECT Nordic Network for Early Cancer Trials www.nordicnect.org

Home About us Contact us Trials News Events Useful links Login LATEST NEWS

Nordic NECT is a cooperation between phase I units in Denmark, Finland, Norway and Sweden, performing early clinical trials in oncology.

LATEST NEWS

- NRI-Conference: Nordic Model for Personalized Medicine [Read more...](#)
- NRI-Conference: Nordic Model for Personalized Medicine [Read more...](#)
- Nordic NECT secretariat [Read more...](#)

LATEST TRIALS

- Melanoma**
A Phase Ib/II Randomised Open Label Study of BGB324 in Combination With Pembrolizumab or Dabrafenib Compared to Pembrolizumab or Dabrafenib Monotherapy, in Patients With Advanced Non-resectable (Stage IIIc) or Metastatic (Stage IV) Melanoma [Read more...](#)
- Solide Tumors**
Safety and pharmacokinetics of ODM-207 in patient with selected advanced tumors; an open-label, non-randomosed, uncontrolled, multicentre, first-in-human study with cohort expansion [Read more...](#)

CANCER STUDIES SEARCH

Cancer type: [Go to Advanced search](#)
All studies open for inclusion

NORDIC COOPERATION

NORWAY FINLAND
Bergen Oslo Stockholm Helsinki
DENMARK Aarhus Herlev Lund Copenhagen
DENMARK • FINLAND • NORWAY • SWEDEN

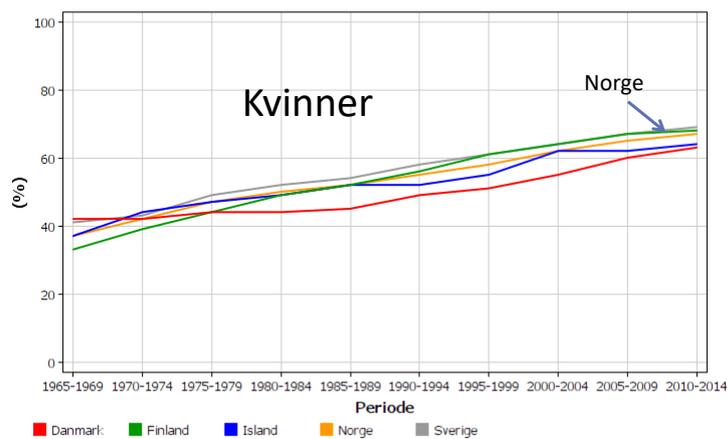
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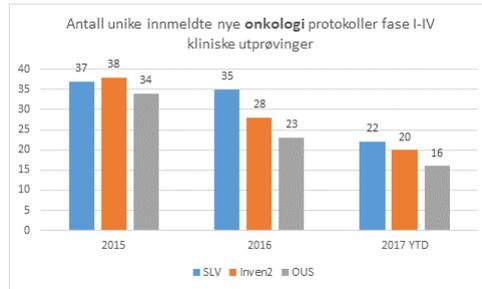


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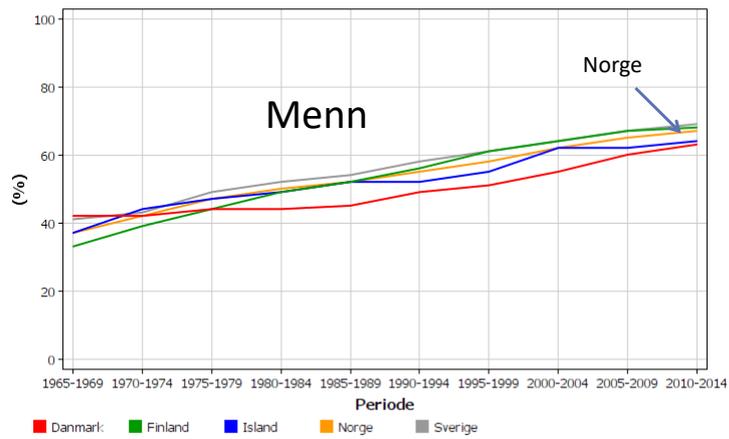


Alle kreftformer
5-års alders-standardisert relativ overlevelse (%), alder 0-89: Kvinner





Alle kreftformer
5-års alders-standardisert relativ overlevelse (%), alder 0-89: Kvinner



The number of CT applications from commercial sponsors to Regulatory Authorities in the Nordics

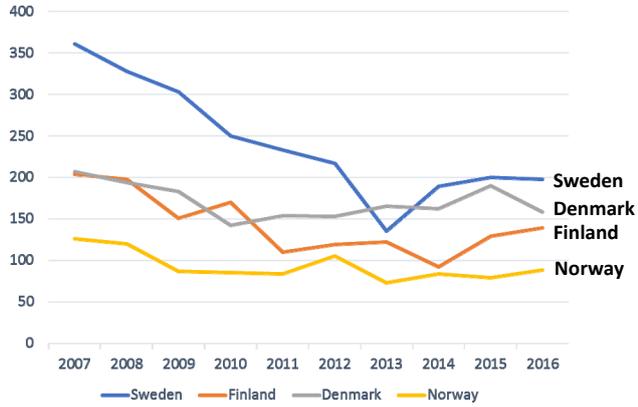


Figure 11. Trends in incidence and mortality rates and 5-year relative survival proportions

Figure 11-A: All sites (ICD10 C00-96, D32-33, D35.2-35.4, D42-43, D44.3-44.5, D45-47)

