REMEDY
CENTER FOR TREATMENT OF RHEUMATIC AND MUSCULOSKELETAL DISEASES

Fra ide til protokoll – hvordan komme i gang?

Siri Lillegraven MD MPH PhD
Nestleder, Center for treatment of Rheumatic and Musculoskeletal Diseases (REMEDY)
Leder, Enhet for klinisk forskning
Diakonhjemmet sykehus

Diakonhjemmet Hospital

Innhold

- Eksempler – fra ide til protokoll
- Problemstilling
  - Klinisk relevans
  - Pasientgrunnlag
  - Nytteverdi
- Praktisk ved prosjektstart
  - Forankring i sykehuset og i klinisk drift
  - Ressurser (personale, tid)
  - Forfatterskap/vitenskapelig samarbeid
- Prosjektskisse

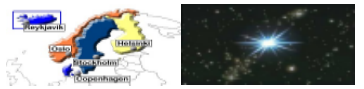
Innhold

- Eksempler – fra ide til protokoll
- Problemstilling
  - Klinisk relevans
  - Pasientgrunnlag
  - Nytteverdi
- Praktisk ved prosjektstart
  - Forankring i sykehuset og i klinisk drift
  - Ressurser (personale, tid)
  - Forfatterskap/vitenskapelig samarbeid
- Prosjektskisse

Forskningsmiljø

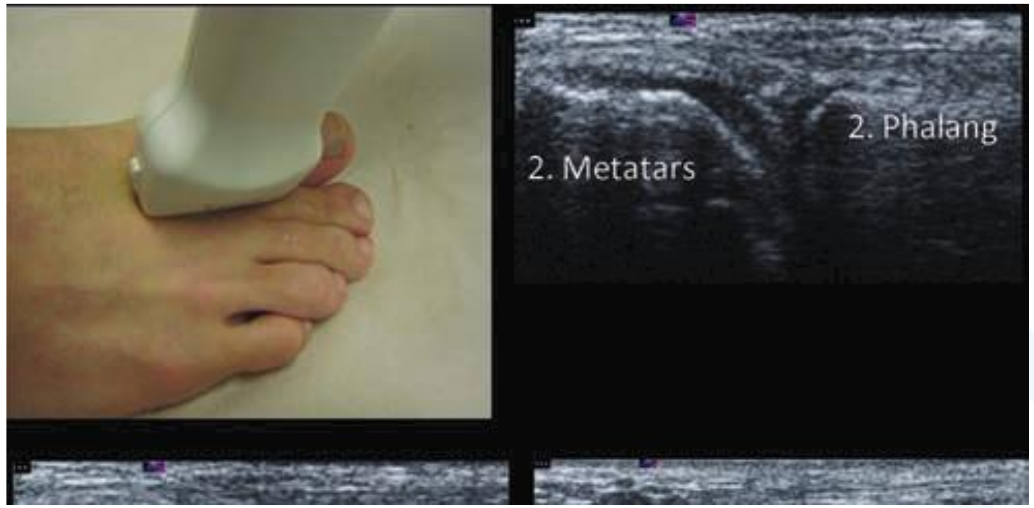
- Diakonhjemmet sykehus
- Klinikk for revmatologi, poliklinikk og forskning
  - Ansvar for artritt-sykdommer i Oslo
  - Regionale og nasjonale funksjoner
- REMEDY senteret
  - Hovedfokus på klinisk forskning

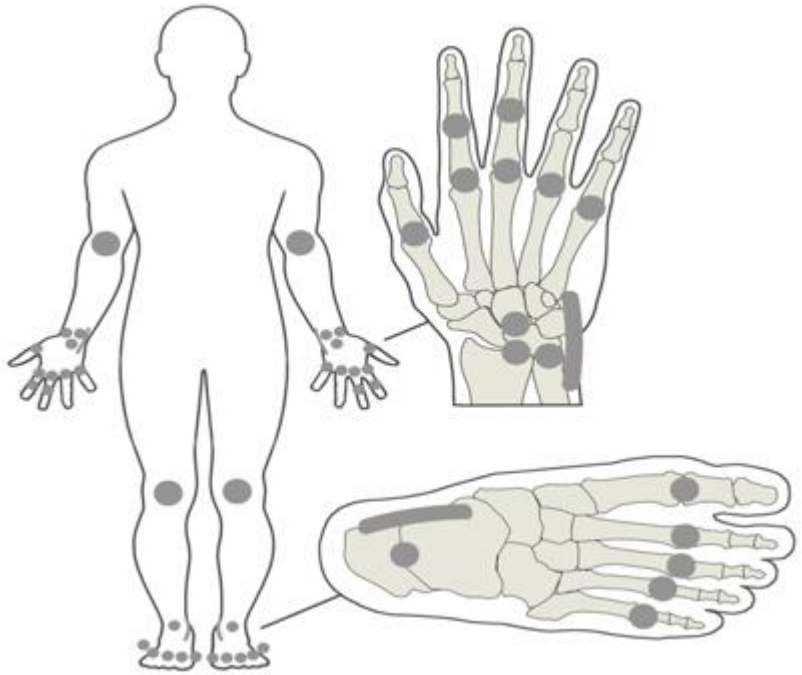
Forskerinitierte studier

ARCTIC – THE ARCTIC TRIAL	Randomized clinical trial in early rheumatoid arthritis assessing management with and without ultrasound	thebmj
NOR SWITCH	Randomized clinical trial of switch from innovator infliximab to biosimilar infliximab	THE LANCET
 NORD-STAR	Nordic randomized clinical trial in early rheumatoid arthritis comparing conventional therapy versus three biologic treatments	thebmj
ARCTIC REWIND	Randomized clinical trial in rheumatoid arthritis assessing withdrawal of disease-modifying drugs	JAMA
NOR DRUM – The Norwegian drug monitoring study	Randomized clinical trial assessing the effectiveness of targeting infliximab treatment by therapeutic drug monitoring versus routine care	JAMA

Eksempel: Ide

- **2000-tallet:** Ultralyd øker i bruk i revmatologisk praksis
- Studier viser sammenheng mellomsubklinisk inflammasjon påvist med ultralyd og leddskade samt sykdomsoppbluss ved RA
- Økt fokus på definerte behandlingsmål





Ref: Hammer HB et al, ARD, 2011

ARCTIC-studien

- Aiming for Remission in rheumatoid arthritis: a randomised trial examining the benefit of ultrasonography in a Clinical TIght Control regimen[1]
  - N=230
  - Inklusjon 2010-2013
- Pasientert randomisert til en av to behandlingsstrategier:
  - Målstyre behandlingen med ultralydinformasjon
  - Målstyre behandling basert på konvensjonelle sykdomsaktivitetsmål
- Strategistudie = sammenligner to behandlingsstrategier, ikke to medikamenter

Ref: Haavardsholm EA et al, The BMJ, 2015

ARCTIC studiegruppe

Local PIs	Study center
Hallvard Fremstad MD	Ålesund Hospital
Tor Magne Madland MD PhD	Haukeland University Hospital
Åse Stavland Lexberg MD	Vestre Viken Hospital Drammen
Hilde Haukeland MD	Martina Hansens Hospital
Erik Rødevand MD	St. Olavs Hospital Trondheim University Hospital
Christian Høili MD	Østfold Hospital Moss
Hilde Stray MD	Haugesund Sanitetsforening Rheumatism Hospital
Anne Noraas Bendvold MD	Specialist practice Bendvold/Dovland Kristiandsand
Inger Johanne Hansen MD	Sørlandet Hospital Kristiansand
Gunnstein Bakland MD PhD	University Hospital of Northern Norway Tromsø
Espen A. Haavardsholm MD PhD	Diakonhjemmet Hospital (coordinating center)

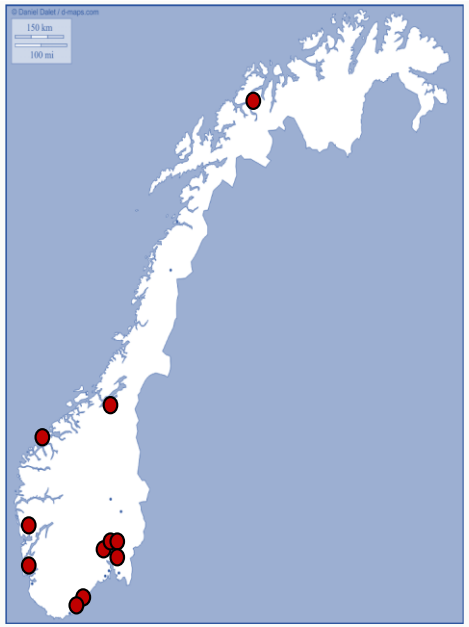
ARCTIC-studien

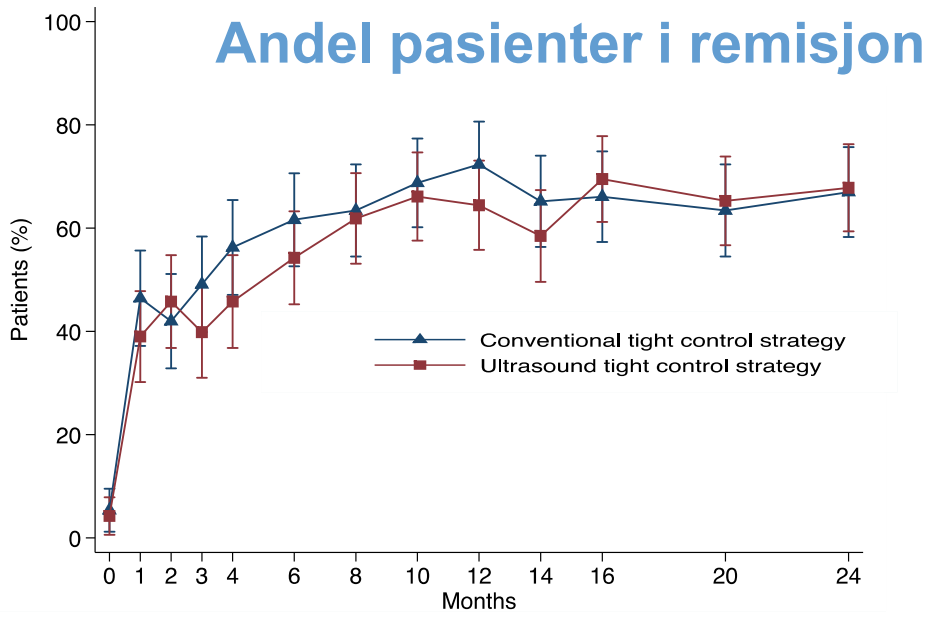
Ultrasound in management of rheumatoid arthritis: ARCTIC randomised controlled strategy trial

Espen A Haavardsholm,[1] Anna-Birgitte Aga,[1] Inge Christoffer Olsen,[1] Siri Lillegraven,[1] Hilde B Hammer,[1] Till Uhlig,[1] Hallvard Fremstad,[2] Tor Magne Madland,[3] Åse Stavland Lexberg,[4] Hilde Haukeland,[5] Erik Rødevand,[6] Christian Høili,[7] Hilde Stray,[8] Anne Noraas,[9] Inger Johanne Widding Hansen,[10] Gunnstein Bakland,[11,12] Lena Bugge Nordberg,[1] Désirée van der Heijde,[1,13] Tore K Kvien[1]

thebmj | *BMJ* 2016;354:i4205 | doi: 10.1136/bmj.i4205

Erfaringer fra gjennomført klinisk studie





– Resultatene er helt oppsiktsvekkende

Aggressiv medisinering endrer behandling av leddgikt.

thebmj Research Education News & Views Campaigns Archive For authors Jobs Hosted Search

RESEARCH

OPEN ACCESS

Ultrasound in management of rheumatoid arthritis: ARCTIC randomised controlled strategy trial

Espen A Haavardsholm,[1] Anna-Birgitte Aga,[1] Inge Christoffer Olsen,[1] Siri Lillegraven,[1] Hilde B Hammer,[1] Till Uhlig,[1] Hallvard Fremstad,[2] Tor Magne Madland,[3] Åse Stavland Lexberg,[4] Hilde Haukeland,[5] Erik Rødevand,[6] Christian Høili,[7] Hilde Stray,[8] Anne Noraas,[9] Inger Johanne Widding Hansen,[10] Gunnstein Bakland,[11,12] Lena Bugge Nordberg,[1] Désirée van der Heijde,[1,13] Tore K Kvien[1]

thebmj | BMJ 2016;354:i4205 | doi: 10.1136/bmj.i4205

Nasjonal veileder i revmatologi

Revmatoid artritt

Forfattere: Anna-Birgitte Aga og Espen A. Haavardsholm Dato publisert: 19.06.2020 Versjon: 0.11

Diakonhjemmet Hospital

REMEDY

Konklusjoner

- Tilsvarende resultater med konvensjonell oppfølging vs. ultralydoppfølging
- Negativ studie – men like viktig
- Illustrerer behovet for studier før innføring av nye behandlingsstrategier og undersøkelsesmetoder, ikke bare medikamenter

Forskerinitierte studier

ARCTIC THE ARCTIC TRIAL	Randomized clinical trial in early rheumatoid arthritis assessing management with and without ultrasound	thebmj
NOR SWITCH	Randomized clinical trial of switch from innovator infliximab to biosimilar infliximab	THE LANCET
NORD-STAR	Nordic randomized clinical trial in early rheumatoid arthritis comparing conventional therapy versus three biologic treatments	thebmj
ARCTIC REWIND	Randomized clinical trial in rheumatoid arthritis assessing withdrawal of disease-modifying drugs	JAMA
NOR DRUM The Norwegian drug monitoring study	Randomized clinical trial assessing the effectiveness of targeting infliximab treatment by therapeutic drug monitoring versus routine care	JAMA

Eksempel Ide 2: Kan vi bytte til biotilsvarende legemidler?

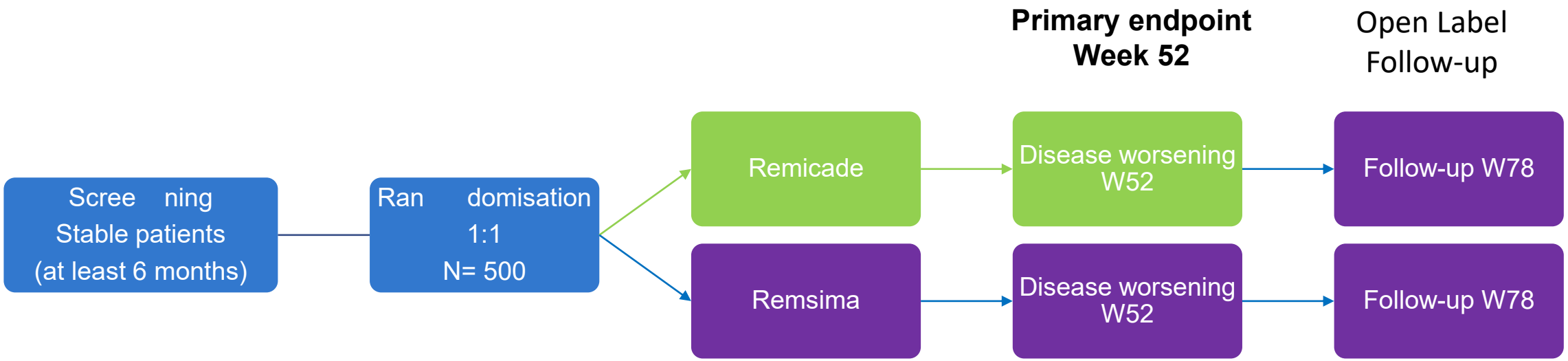
- **2015**
  - Patentet utløper på infliximab
  - Biotilsvarende infliximab blir tilgjengelig
- Hva er biotilsvarende legemidler?
  - Lignende det originale produktet
    - Ikke bedre
    - Ikke verre
  - Billigere
  - Kan gi økt tilgang på effektiv behandling for pasienter med immunmedierte inflammatoriske sykdommer

Hovedmål

- Å undersøke om CT-P13 var **non-inferior (ikke underlegen)** sammenlignet med original infliximab (INX) med tanke på sykdomsforverring hos pasienter som har vært behandlet med stabil infliximab-behandling i minst 6 måneder

- Sekundærmål:
  - Safety
  - Immunogenisitet

NOR- SWITCH Study design



Primary endpoint: Disease worsening
Non-inferiority margin:15%

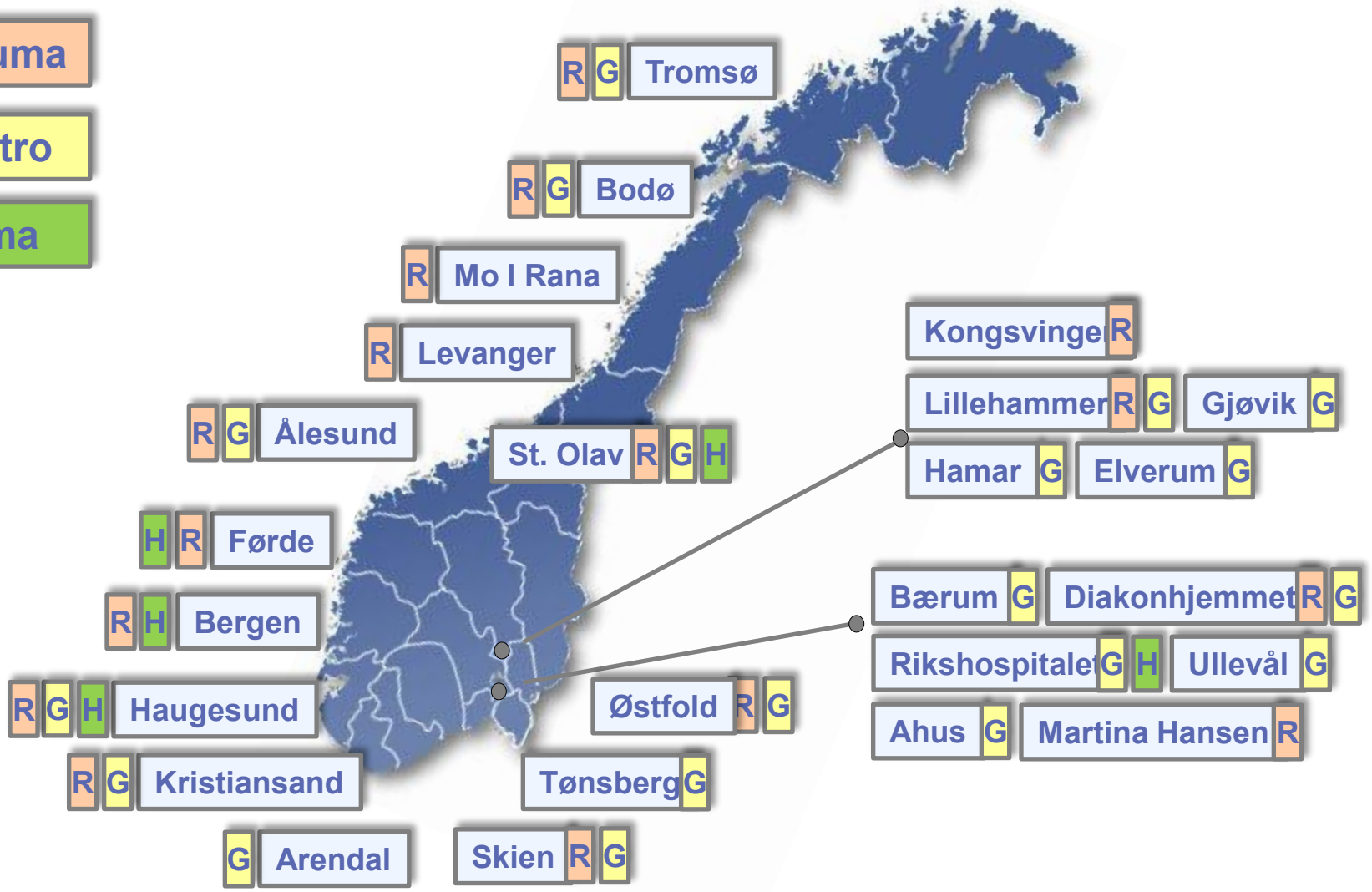
NOR SWITCH

Studiesentre

16 Rheuma

19 Gastro

5 Derma



Resultater: Sykdomsforverring

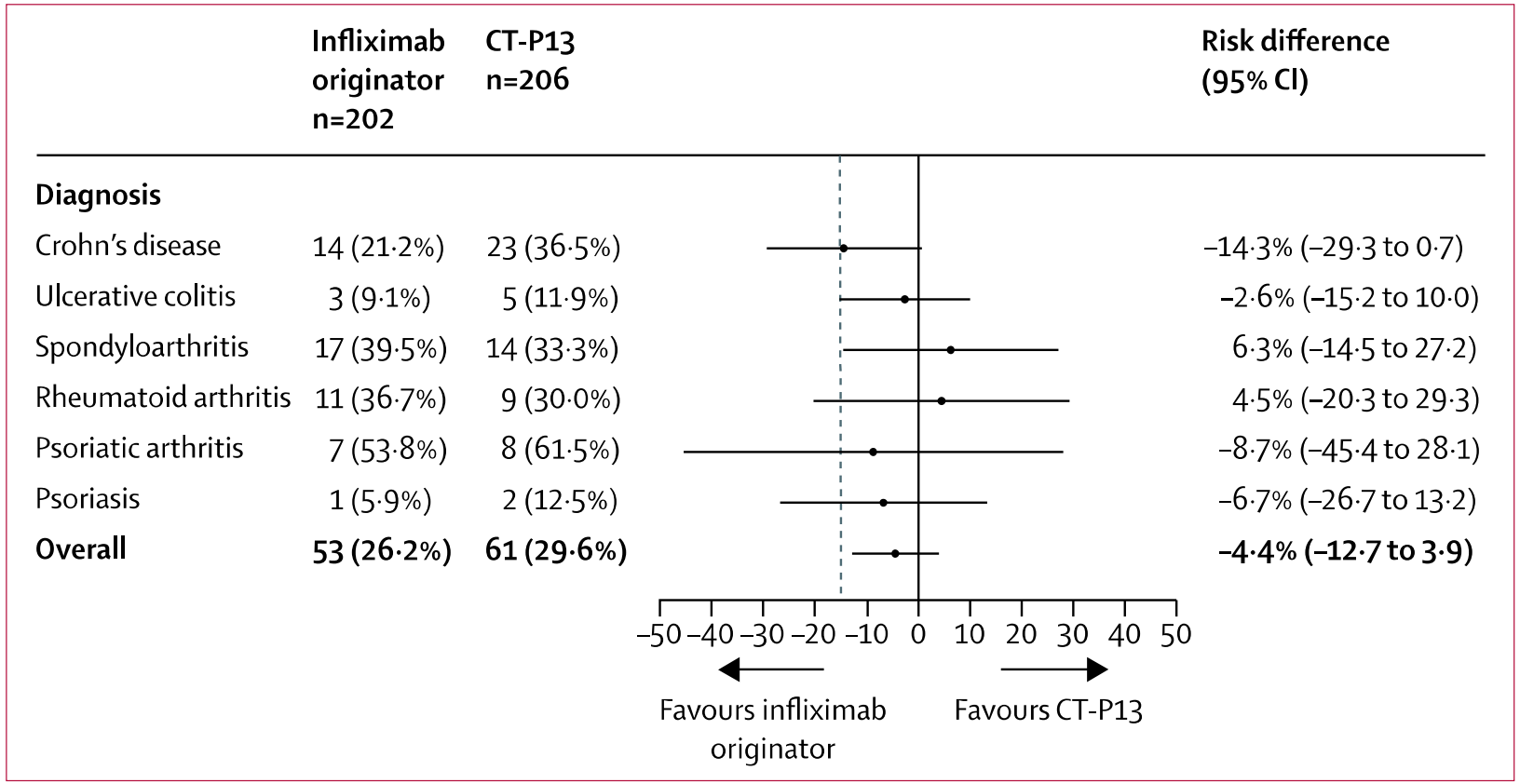
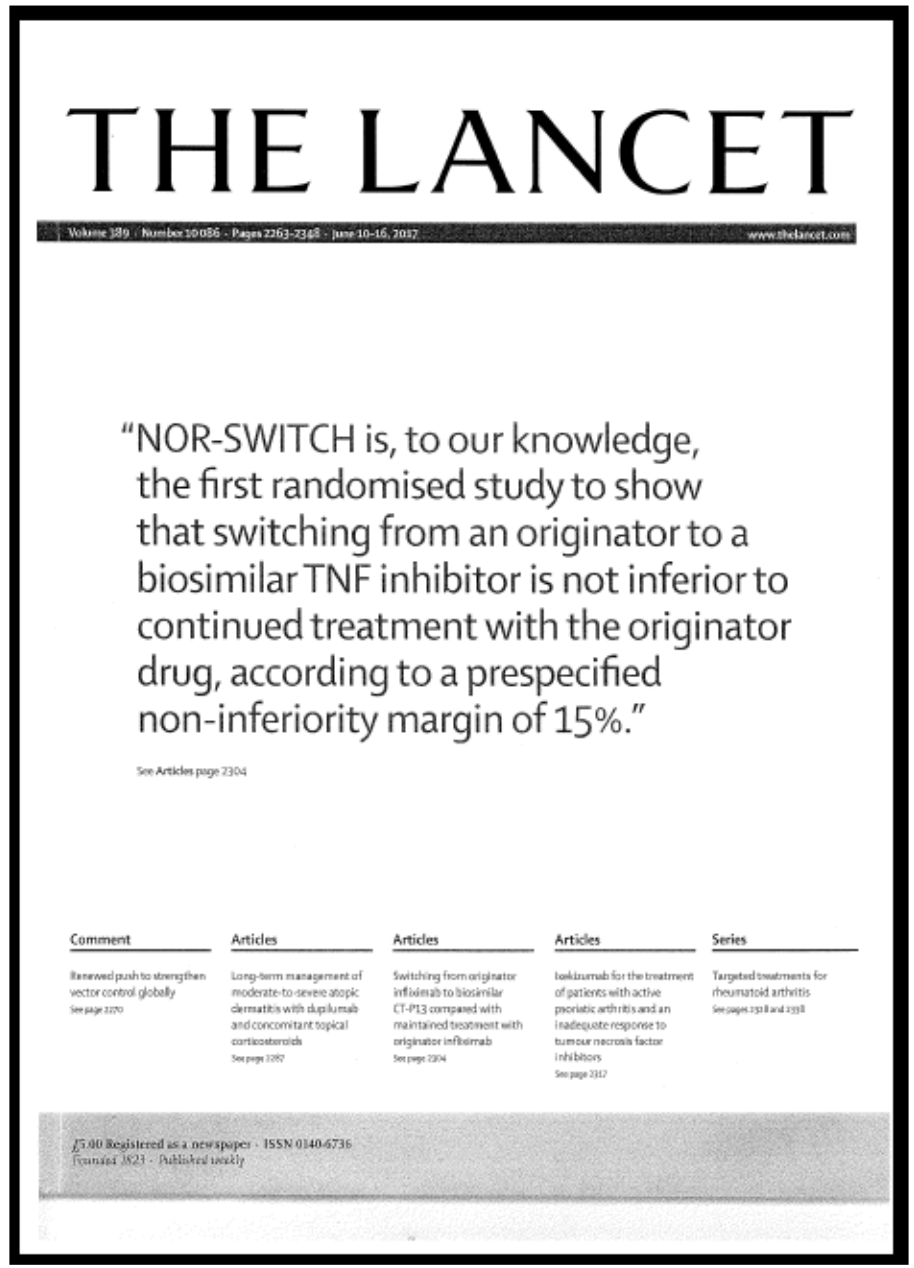


Figure 2: **Forest plot of risk difference according to disease**
Figure shows data for the per-protocol set. Risk difference is adjusted for treatment duration of infliximab originator at baseline.

Diakonhjemmet Hospital

Ref: Jørgensen KK et al, Lancet, 2017

NOR SWITCH DY


THE LANCET
Volume 389 · Number 10086 · Pages 2263–2348 · June 10–16, 2017
www.thelancet.com
"NOR-SWITCH is, to our knowledge, the first randomised study to show that switching from an originator to a biosimilar TNF inhibitor is not inferior to continued treatment with the originator drug, according to a prespecified non-inferiority margin of 15%."
See Articles page 2304
Comment
Renewed push to strengthen vector control globally
See page 2270
Articles
Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids
See page 2287
Articles
Switching from originator infliximab to biosimilar CT-P13 compared with maintained treatment with originator infliximab
See page 2304
Articles
Ixekizumab for the treatment of patients with active psoriatic arthritis and an inadequate response to tumour necrosis factor inhibitors
See page 2317
Series
Targeted treatments for rheumatoid arthritis
See pages 2328 and 2338
£5.00 Registered as a newspaper · ISSN 0140-6736
Founded 1823 · Published weekly

Tolkning NOR-SWITCH

- Bytte fra orginal infliximab til biotilsvarende infliximab var ikke underlegent sammenlignet med fortsatt orginal infliximabbehandling

- Resultatene støtter bytte fra orginal infliximab til biotisvarende infliximab på ikke-medisinsk indikasjon

DAGENS Medisin — Nyheter Debatt DM Arena DMTV

VARSOM MED GENERALISERING – Etter vårt skjønn, må vi være forsiktige med å generalisere bi alle andre biologiske legemidler og deres biotilsvarende, sier Tore K. Kvien ved Diakonhjemmet sykehus. Han presenterer resultatene på gastroenterologisk kongress i Wien tirsdag 18. oktober. Arkivfoto: Vidar Sandnes

RESULTATENE KLARE FRA DEN NORSKE BYTTESTUDIEN

– Trygt å bytte til biotilsvarende

Verden over har ventet i spenning på resultatene fra Nor-Switch, som nå viser at det ikke er forskjell på Remicade og biotilsvarende. – Byttestudien gir tre streker under svaret, sier leder av studien, Tore K. Kvien.

Publisert: 2016-10-17 01:23
Lisbeth Nilsen

DAGENS Medisin — Nyheter Debatt DM Arena DMTV

– Nordmenn har grunn til å være stolte

Den tyske gastroenterologen Stefan Schreiber berømmer de norske forskerne. Han føler seg trygg på å bytte slik det er gjort i Nor-Switch-studien, men vil ha mer data på bytte med andre biotilsvarende.

Publisert: 2016-10-18 11:03 Skrevet av: Lisbeth Nilsen/Lasse Moe

DAGENS Medisin — Nyheter Debatt DM Arena DMTV

Britisk ekspert: – Nor-Switch er et vendepunkt

– Nor-Switch-studien vil øke bruken av biotilsvarende, og gir oss den real world evidence vi trenger, mener den britiske rådgiveren Michael Sobanja.

Publisert: 2016-10-18 09:40 Skrevet av: Lisbeth Nilsen/Lasse Moe
redaksjonen@dagensmedisin.no

DAGENS Medisin — Nyheter Debatt DM Arena DMTV

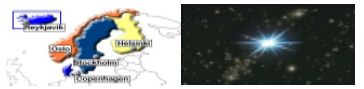
Blogger | Debatt og kronikk | Leder

– Vi trenger mer dokumentasjon enn én studie

Legemiddelindustrien (LMI) er positive til studier som kan føre til store besparelser for samfunnet. De peker på at det må gjøres flere studier som Nor-Switch for å skaffe mer kunnskap om biotilsvarende legemidler.

Publisert: 2016-10-17 12:18 Skrevet av: Lasse Moe

Forskerinitierte studier

ARCTIC – THE ARCTIC TRIAL	Randomized clinical trial in early rheumatoid arthritis assessing management with and without ultrasound	thebmj
NOR SWITCH	Randomized clinical trial of switch from innovator infliximab to biosimilar infliximab	THE LANCET
 NORD-STAR	Nordic randomized clinical trial in early rheumatoid arthritis comparing conventional therapy versus three biologic treatments	thebmj
ARCTIC REWIND	Randomized clinical trial in rheumatoid arthritis assessing withdrawal of disease-modifying drugs	JAMA
NOR DRUM – The Norwegian drug monitoring study	Randomized clinical trial assessing the effectiveness of targeting infliximab treatment by therapeutic drug monitoring versus routine care	JAMA

Eksempel 3

Nedtrappping av medisiner

- Hva gjør vi med pasienter med revmatoid artritt (RA, leddgikt) som er i langvarig remisjon?

- Grunner til å vurdere å trappe ned eller seponere behandling:
  - Pasientene foretrekker å stå på færrest mulig medikamenter
  - Bivirkninger – betydelig immunsuppresjon, ukjente langtidsbivirkninger
  - Helseøkonomi

Studiedesign ARCTIC REWIND

- To randomisert kontrollerte non-inferiority multistudier
  - Fullfinansiert av Helse Sør-Øst og Forskningsrådet
- RA diagnose
  - I henhold til etablerte kriterier
- Remisjon (ingen eller svært få tegn til sykdomsaktivitet)
  - I minst 12 måneder
  - Ved inklusjon ingen artritt i 44 undersøkte ledd
- Stabil behandling i minst 12 måneder

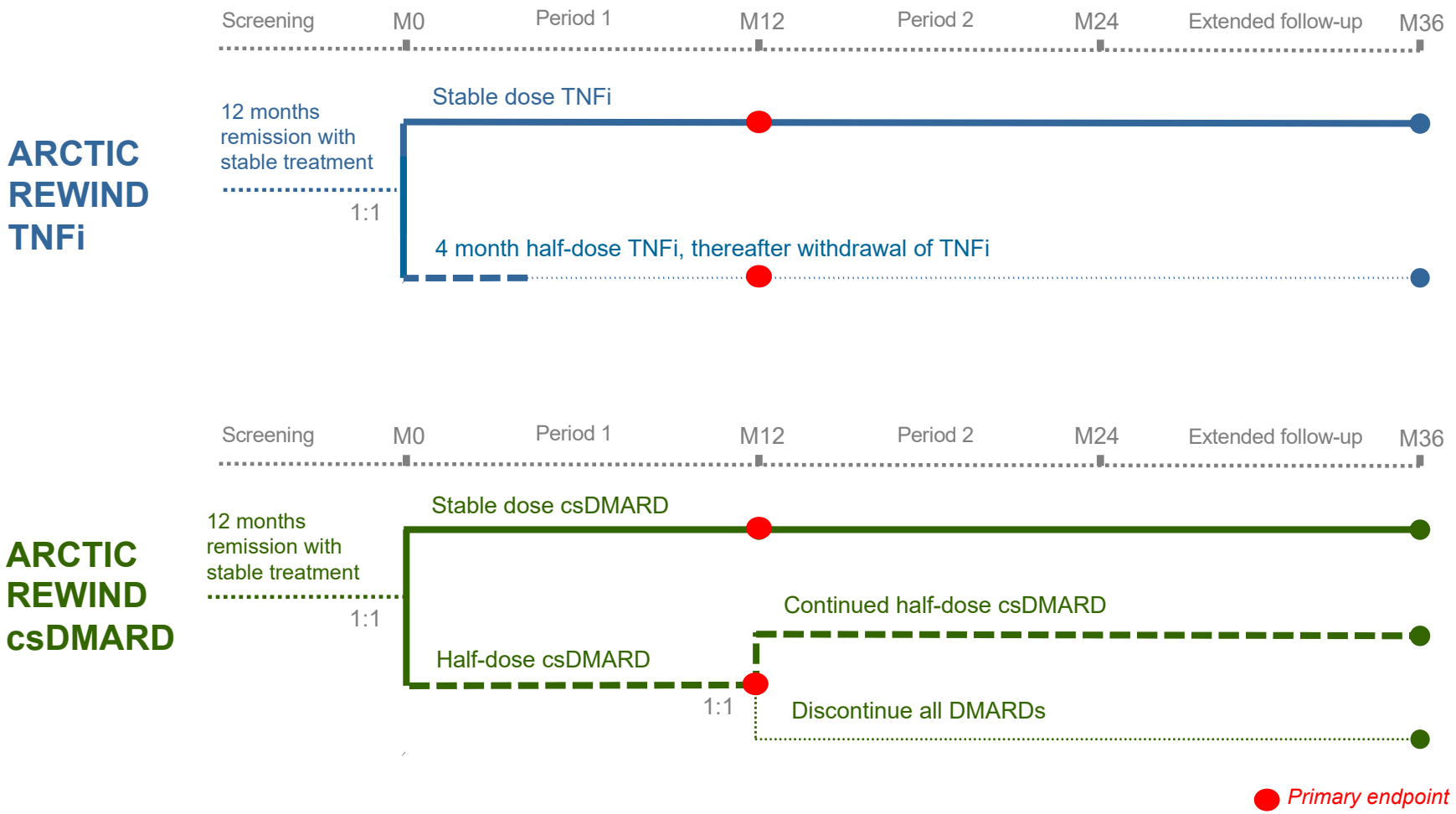
ARCTIC REWIND csDMARD RCT

ARCTIC REWIND TNFi RCT

Diakonhjemmet Hospital

REMEDY

ARCTIC REWIND

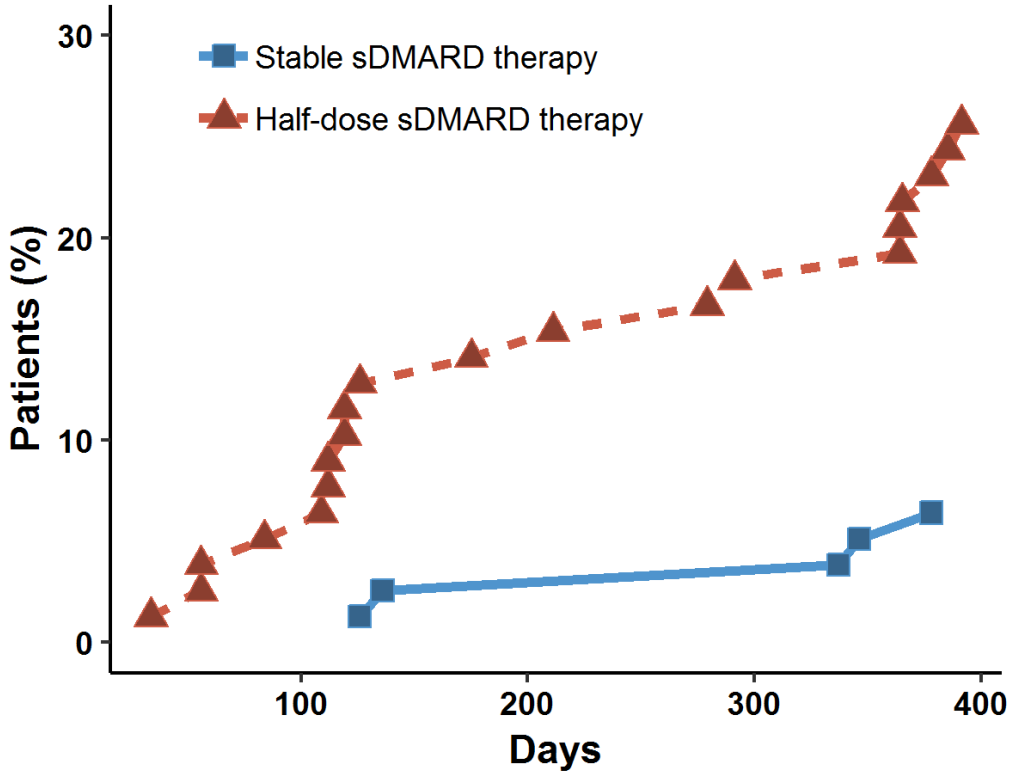


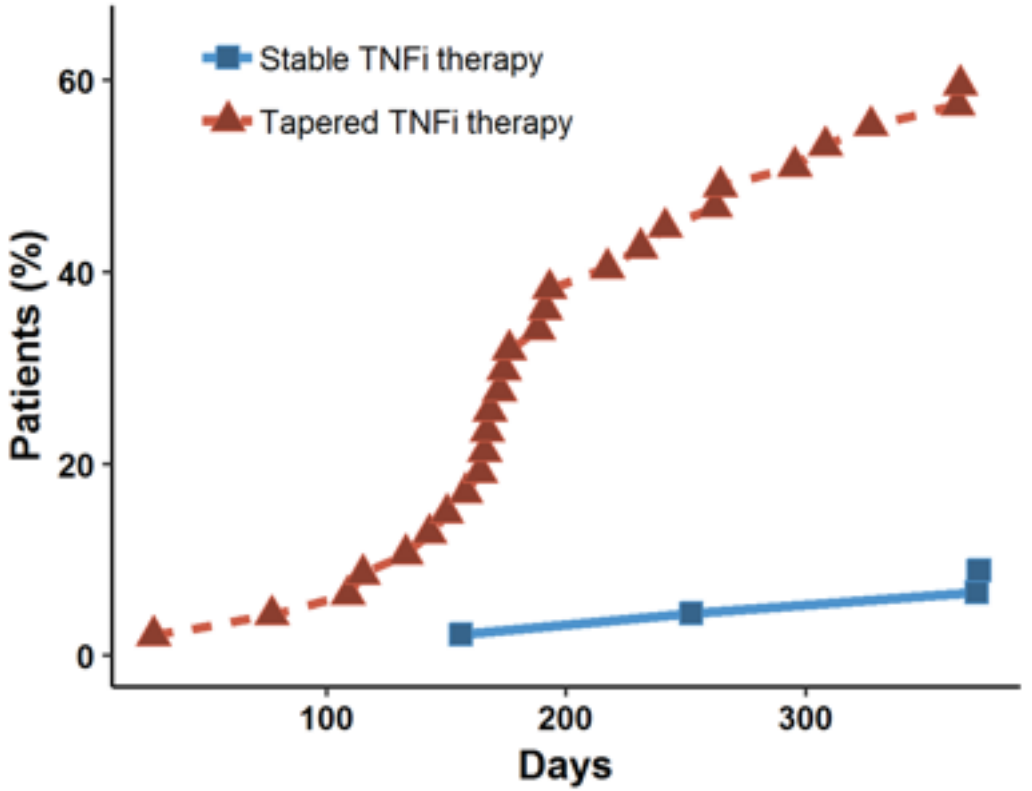
Diakonhjemmet Hospital

REMEDY

Hovedresultater

- Halv dose ikke non-inferior til stabil behandling
- Stabil dose superior – gir mindre oppbluss





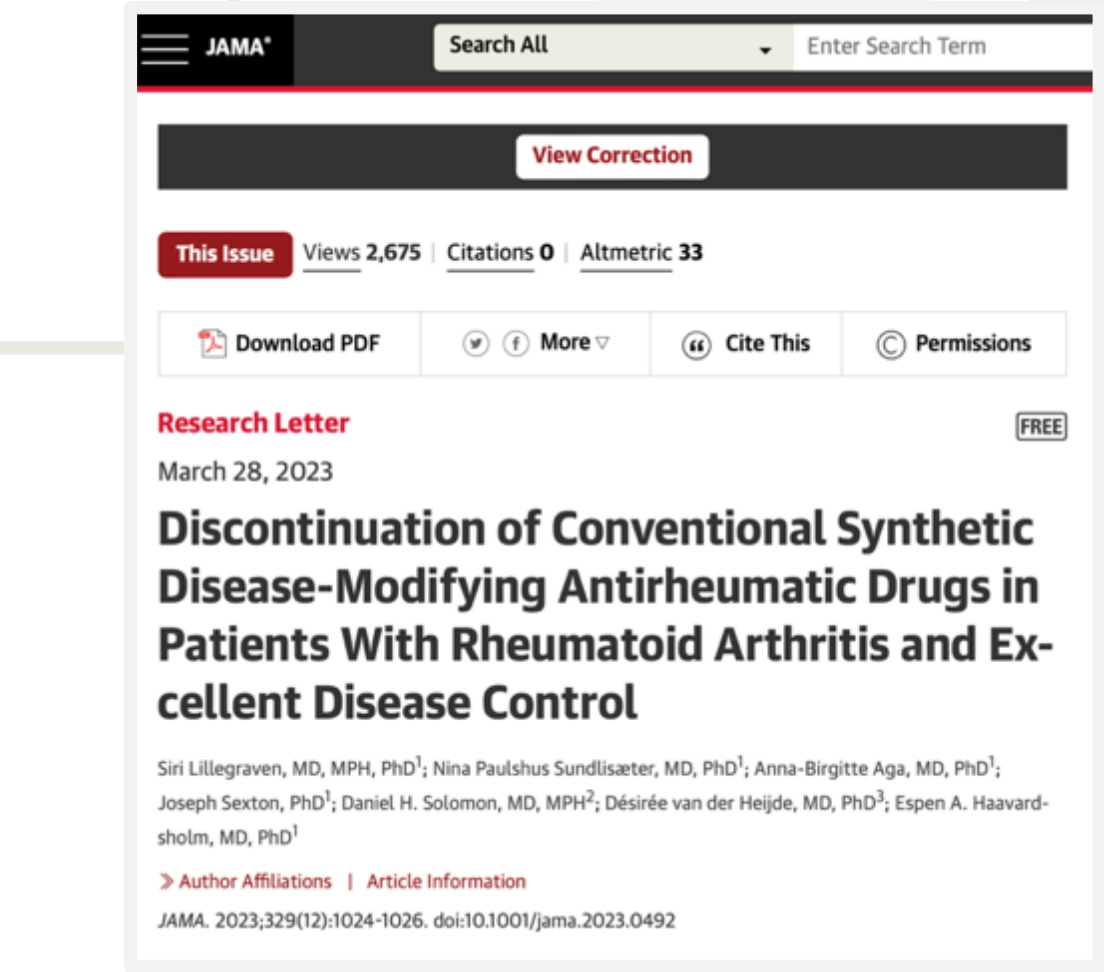
Research

JAMA | Original Investigation

Effect of Half-Dose vs Stable-Dose Conventional Synthetic Disease-Modifying Antirheumatic Drugs on Disease Flares in Patients With Rheumatoid Arthritis in Remission

The ARCTIC REWIND Randomized Clinical Trial

Siri Lillegraven, MD, MPH, PhD; Nina Paulshus Sundlisæter, MD, PhD; Anna-Birgitte Aga, MD, PhD; Joseph Sexton, PhD; Inge C. Olsen, PhD; Hallvard Fremstad, MD; Cristina Spada, MD; Tor Magne Madland, MD, PhD; Christian A. Høili, MD; Gunnstein Bakland, MD, PhD; Åse Lexberg, MD; Inger Johanne Widding Hansen, MD; Inger Myrnes Hansen, MD; Hilde Haukeland, MD; Maud-Kristine Aga Ljoså, MD; Ellen Moholt, RN, Msc; Till Uhlig, MD, PhD; Daniel H. Solomon, MD, MPH; Désirée van der Heijde, MD, PhD; Tore K. Kvien, MD, PhD; Espen A. Haavardsholm, MD, PhD



OPEN ACCESS

CLINICAL SCIENCE

Annals of the Rheumatic Diseases

Effect of tapered versus stable treatment with tumour necrosis factor inhibitors on disease flares in patients with rheumatoid arthritis in remission: a randomised, open label, non-inferiority trial

Siri Lillegraven ,[1] Nina Paulshus Sundlisæter ,[1] Anna-Birgitte Aga ,[1] Joseph Sexton,[1] Inge Christoffer Olsen,[2] Åse Stavland Lexberg,[3] Tor Magne Madland,[4] Hallvard Fremstad,[5] Christian A. Høili,[6] Gunnstein Bakland,[7] Cristina Spada,[8] Hilde Haukeland,[9] Inger Myrnes Hansen,[10] Ellen Moholt,[1] Till Uhlig ,[1,11] Daniel H Solomon,[12,13] Désirée van der Heijde ,[1,14] Tore K Kvien ,[1,11] Espen A Haavardsholm[1,11]

Oppsummering - eksempler

- Viktig at begge utfall av studien er av interesse
- Studier som svarer på kliniske spørsmål → innvirkning på klinisk praksis
- Gjennomføring av studier er krevende, krever årelang innsats og betydelig finansiering
  - Men er mulig på ikke-universitetssykehus!

Innhold

- Eksempler – fra ide til protokoll
- Problemstilling
  - Klinisk relevans
  - Pasientgrunnlag
  - Nytteverdi
- Praktisk ved prosjektstart
  - Forankring i sykehuset og i klinisk drift
  - Ressurser (personale, tid)
  - Forfatterskap/vitenskapelig samarbeid
- Prosjektskisse

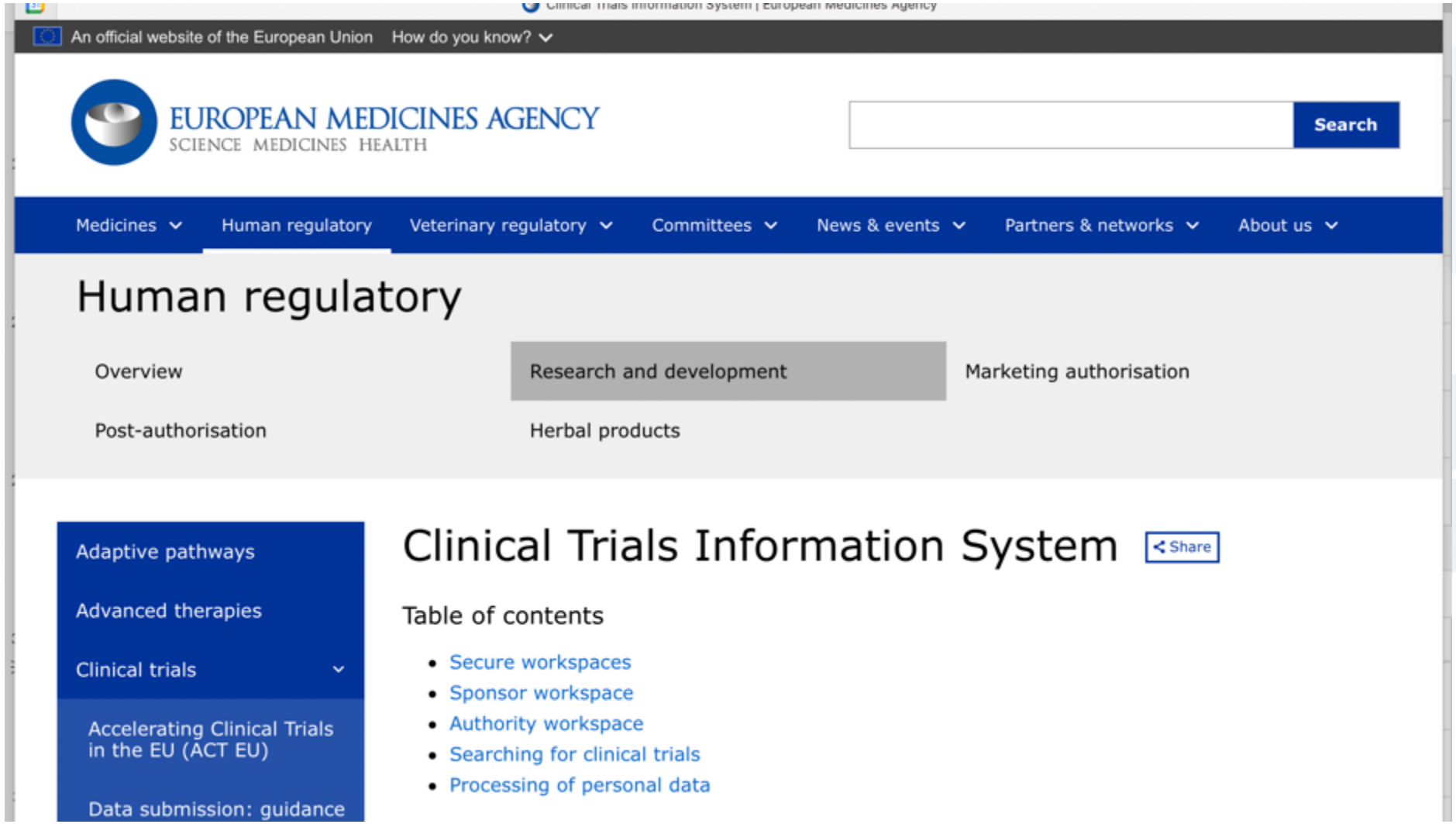
Forskningsspørsmål

- Forskningsspørsmålet bør/skal besvare en viktig problemstilling og påvirke klinisk praksis

- Forskningsspørsmålet bør være så viktig at du ikke er i tvil om:
  - At du bør få innvilget støtte
  - At du vil bruke mange av dine (beste?) år i arbeidslivet på studien

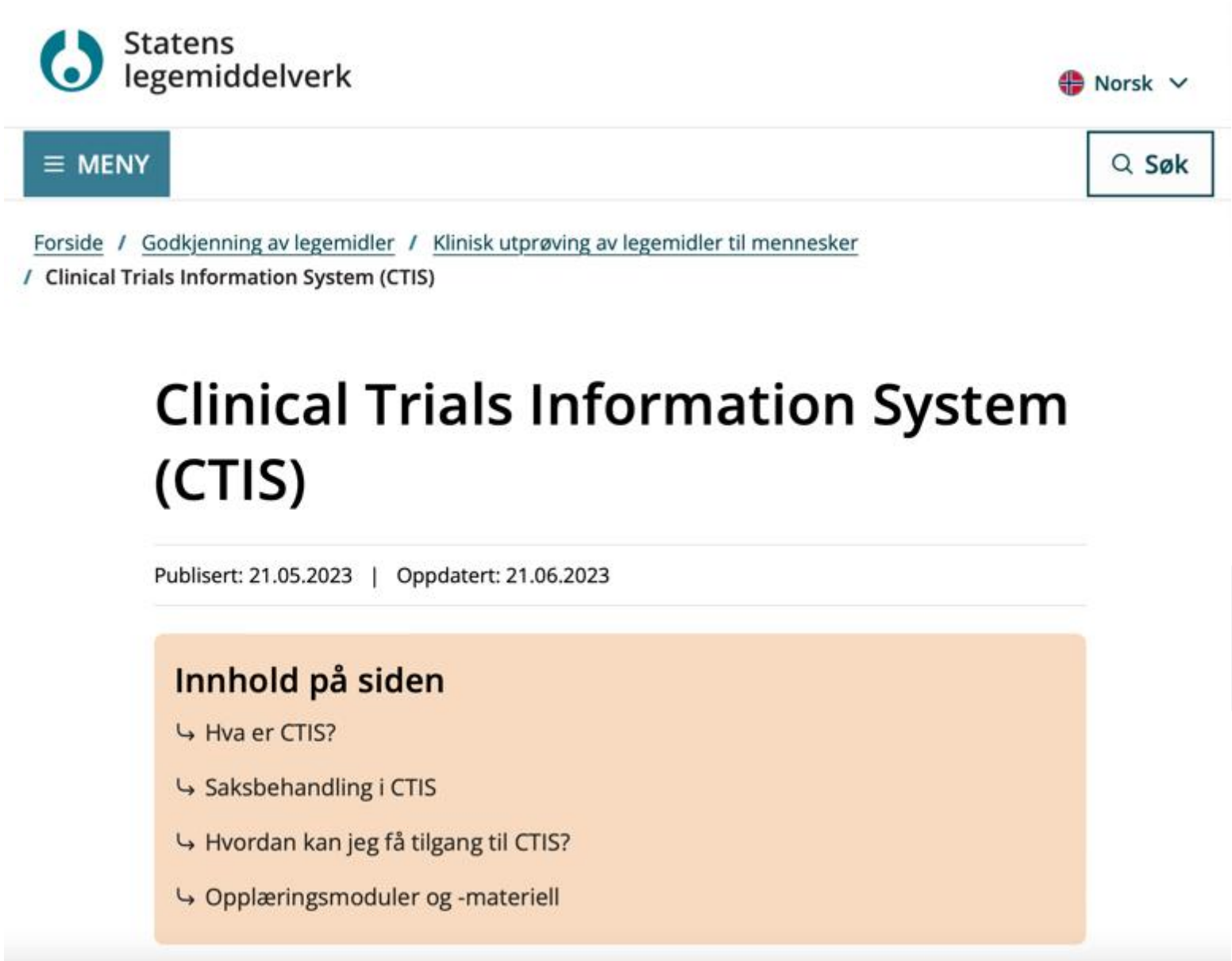
- Hvis du er i tvil, vanskeligere å overbevise andre

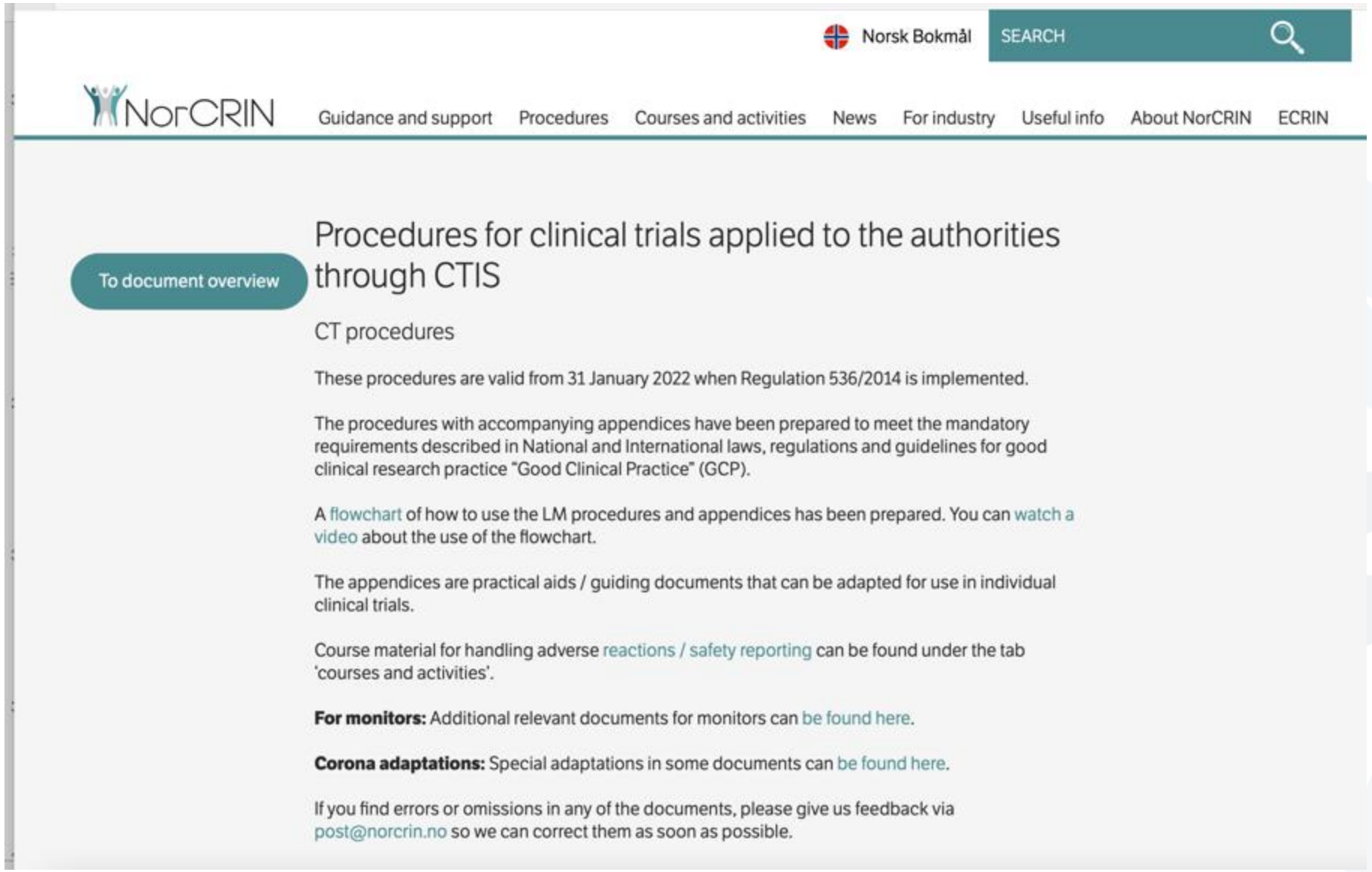
VIKTIG AVKLARING!! Søknadspliktig CTIS?



Diakonhjemmet Hospital

REMEDY


Statens legemiddelverk
Norsk
MENY
Søk
Forside / Godkjenning av legemidler / Klinisk utprøving av legemidler til mennesker / Clinical Trials Information System (CTIS)
Clinical Trials Information System (CTIS)
Publisert: 21.05.2023 | Oppdatert: 21.06.2023
Innhold på siden
Hva er CTIS?
Saksbehandling i CTIS
Hvordan kan jeg få tilgang til CTIS?
Opplæringsmoduler og -materiell


Norsk Bokmål
SEARCH
NorCRIN
Guidance and support
Procedures
Courses and activities
News
For industry
Useful info
About NorCRIN
ECRIN
To document overview
Procedures for clinical trials applied to the authorities through CTIS
CT procedures
These procedures are valid from 31 January 2022 when Regulation 536/2014 is implemented.
The procedures with accompanying appendices have been prepared to meet the mandatory requirements described in National and International laws, regulations and guidelines for good clinical research practice "Good Clinical Practice" (GCP).
A flowchart of how to use the LM procedures and appendices has been prepared. You can watch a video about the use of the flowchart.
The appendices are practical aids / guiding documents that can be adapted for use in individual clinical trials.
Course material for handling adverse reactions / safety reporting can be found under the tab 'courses and activities'.
For monitors: Additional relevant documents for monitors can be found here.
Corona adaptations: Special adaptations in some documents can be found here.
If you find errors or omissions in any of the documents, please give us feedback via post@norcrin.no so we can correct them as soon as possible.

Pasientgrunnlag

- Inklusjons- og eksklusjonskriterier
- Eksisterer disse pasientene?
- VIKTIG! Avgjørende del av studieplanleggingen

Tidslinje

- **Tidlig fase**
  - Definere forskningsspørsmål/hypotese
  - Synopsis
  - Finansiering
- **Studie besluttet igangsatt**
  - Utvikle protokoll
  - Regional etisk komite / Statens legemiddelverk

1-2 år

- **Aktiv fase**
  - Pasientinklusjon
  - Datainnsamling
  - Datasjekker

1-5 år

- **Resultater**
  - Koding
  - Analyser inkl. analyseplan
  - Publisering

6-12 mnd.

- **Forlengelse, publisering sekundære mål**

REMEDY

- **Tidlig fase**
  - Definere forskningsspørsmål/hypotese
  - Synopsis
  - Finansiering
- **Studie besluttet igangsatt**
  - Utvikle protokoll
  - Regional etisk komite / Statens legemiddelverk

1-2 år

- **Aktiv fase**
  - Pasientinklusjon
  - Datainnsamling
  - Datasjekker

1-5 år

- **Resultater**
  - Koding
  - Analyser inkl. analyseplan
  - Publisering

6-12 mnd.

- **Forlengelse, publisering sekundære mål**

Inklusjon 1. pasient

KLINBEFORSK

Nasjonal oppstart

Siste pasient inkludert A

Siste pasient fullført A

Siste pasient inkludert B

Siste pasient fullført B

Publikasjon NOR-DRUM A

Publikasjon NOR-DRUM B

2016 **2017** **2018** **2019** **2020** **2021**

JAMA JAMA JIM

Diakonhjemmet Hospital

REMEDY

Dedikasjon

- Kliniske studier er kompliserte!
- Krever betydelig dedikasjon og utholdenhet, særlig av hovedutprøver/prosjektleder
- Krever støtte fra koordinerende senter

Innhold

- Eksempler – fra ide til protokoll
- Problemstilling
  - Klinisk relevans
  - Pasientgrunnlag
  - Nytteverdi
- Praktisk ved prosjektstart
  - Forankring i sykehuset og i klinisk drift
  - Ressurser (personale, tid)
  - Forfatterskap/vitenskapelig samarbeid
- Prosjektskisse

Synopsis

PROTOCOL SYNOPSIS

TITLE	
Phase of development	
Investigational treatment strategy	
Study Centres	
Study organisation	
Study Period	
Duration	
Primary objective	
Secondary objectives	
Endpoints	
Study Design	
Main Inclusion Criteria	
Main exclusion criteria	
Sample size	
Hypothesis and statistical model	

Diakonhjemmet Hospital

REMEDY

Prosjektbeskrivelse

Modern treatment of rheumatoid arthritis

Applicant Siri Lillegraven, MD MPH PhD
Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo

2) INTRODUCTION

This application for a career fellowship outlines five work packages (WPs) to improve modern treatment of rheumatoid arthritis (RA) (**figure 1**). The proposed work aims to increase the knowledge of how early RA and RA remission should be treated, considering both patients and society. The project uses data from three studies and includes the main analyses of the Norwegian multi-center randomized clinical trial ARCTIC REWIND, which assesses the effects of tapering and withdrawal of disease-modifying antirheumatic drugs (DMARDs) in sustained RA remission.

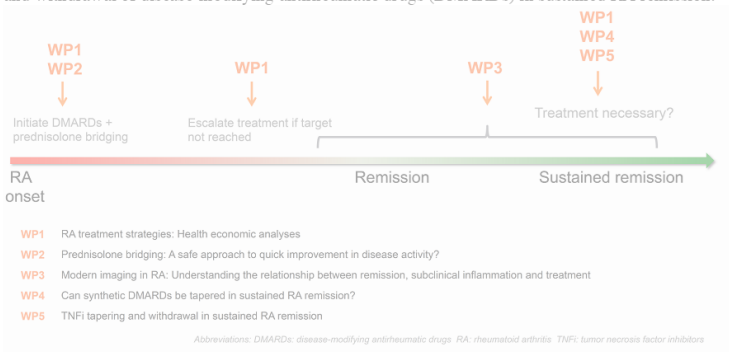


Figure 1: Conceptual illustration of the project

An introduction to RA

RA is a chronic inflammatory disease predominantly affecting women [3]. The main feature is joint inflammation with subsequent joint destruction, but the disease can also have extra-articular manifestations and be associated with increased risk of cardiovascular disease and reduced life-expectancy [4]. In early disease, disability is driven by disease activity, and thus reversible with successful medical treatment (**figure 2**). RA is treated with DMARDs, which are classified as synthetic (e.g. methotrexate, sulfasalazine), biologic (e.g. tumor necrosis factor inhibitors (TNFi), rituximab) [3, 5, 6] or targeted synthetic (e.g. janus kinase inhibitors) [3].

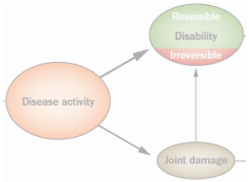


Figure 2: Disease activity, disability and joint damage in early RA [2]

Modern RA treatment and remission

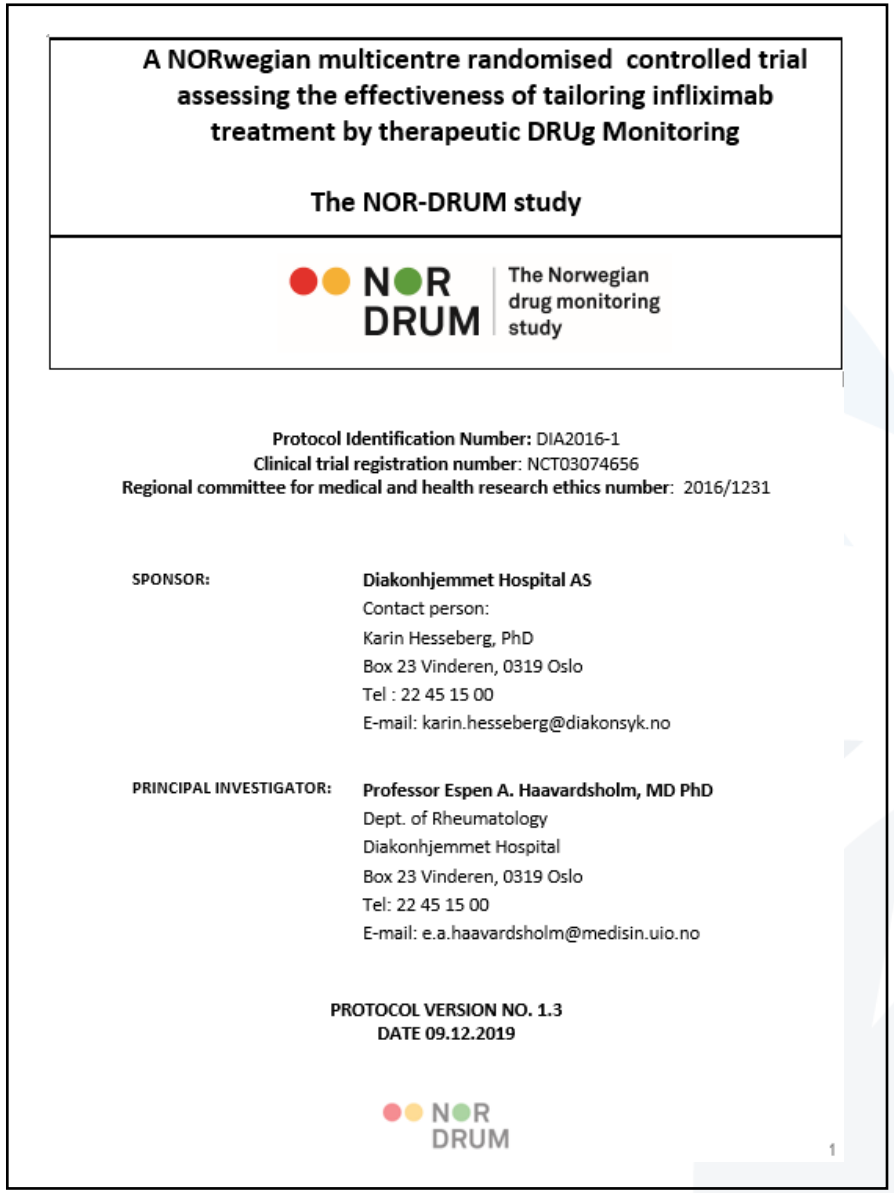
The introduction of biologic DMARDs has changed the outcome of RA, and the goal in modern RA treatment has become to reach and sustain remission, with prevention of structural joint damage and disability [5, 6]. Synthetic DMARD treatment is started when a patient is diagnosed, with initial corticosteroid bridging according to current treatment recommendations [3, 5]. Although the use of corticosteroids when initiating synthetic DMARDs is supported by considerable evidence, the dosing, administration route and duration is debated and experts struggle to agree on a definite recommendation [5]. RA treatment strategies now implement tight control of RA care, with a

Diakonhjemmet Hospital

REMEDY

Protokoll – et lagarbeid

- Dedikert hovedutprøver/prosjektleder
- Styringsgruppe
  - Nasjonale meningsbærere, forskere med erfaring fra kliniske studier, hovedutprøvere, statistikere, klinikere
  - Internasjonalt advisory board
  - Internasjonalt ledende forskere
- Brukerrepresentanter
- Studieleger og studiesykepleiere
- Forankring klinikk



A NORwegian multicentre randomised controlled trial assessing the effectiveness of tailoring infliximab treatment by therapeutic DRUg Monitoring

The NOR-DRUM study

NOR DRUM The Norwegian drug monitoring study

Protocol Identification Number: DIA2016-1
Clinical trial registration number: NCT03074656
Regional committee for medical and health research ethics number: 2016/1231

SPONSOR: **Diakonhjemmet Hospital AS**
Contact person:
Karin Hesseberg, PhD
Box 23 Vinderen, 0319 Oslo
Tel : 22 45 15 00
E-mail: karin.hesseberg@diakonsyk.no

PRINCIPAL INVESTIGATOR: **Professor Espen A. Haavardsholm, MD PhD**
Dept. of Rheumatology
Diakonhjemmet Hospital
Box 23 Vinderen, 0319 Oslo
Tel: 22 45 15 00
E-mail: e.a.haavardsholm@medisin.uio.no

PROTOCOL VERSION NO. 1.3
DATE 09.12.2019

NOR DRUM

1

Diakonhjemmet Hospital

REMEDY

TABLE OF CONTENTS

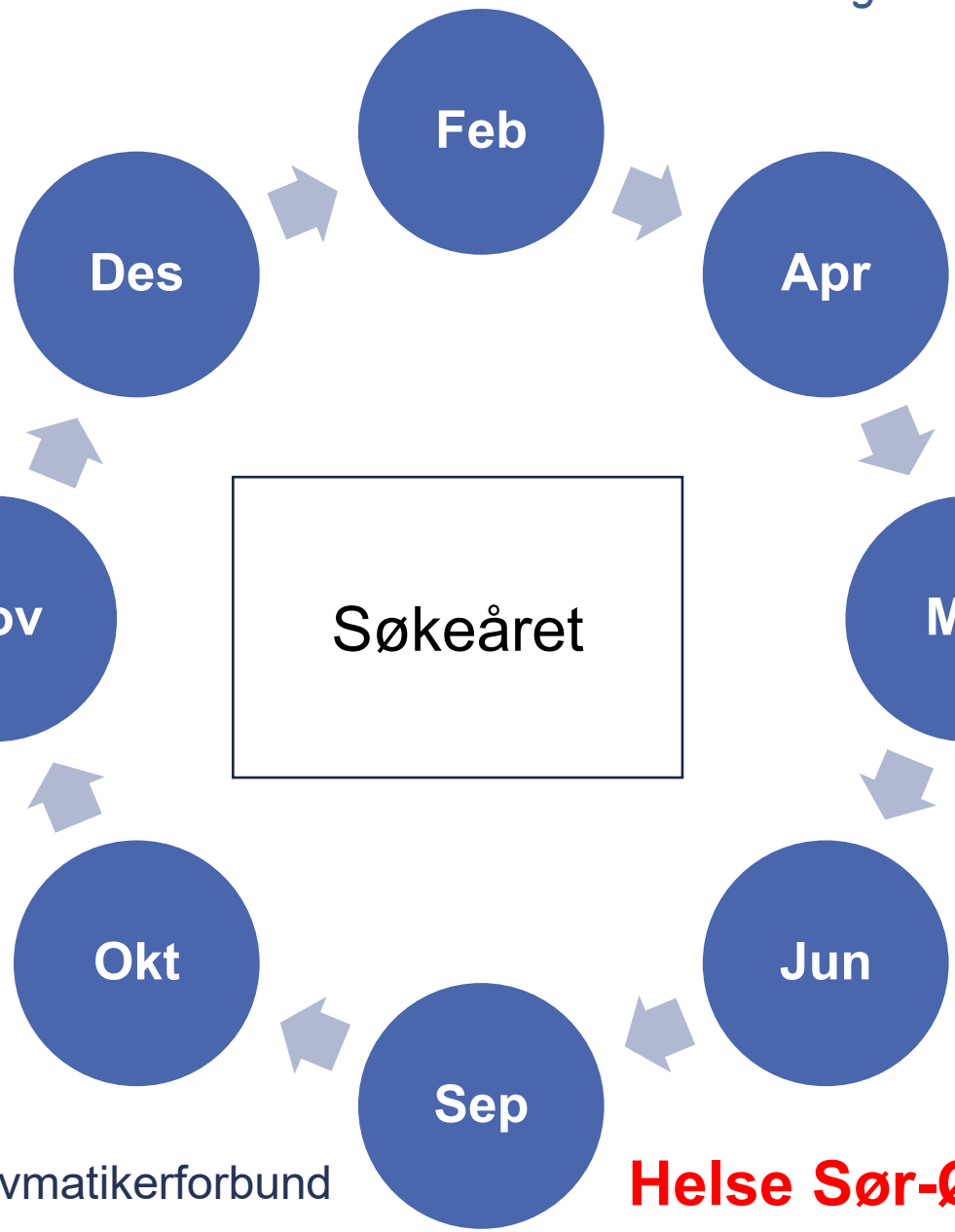
Diakonhjemmet Hospital

REMEDY

Ressurser

- Kliniske studier er kostbart!
- Adekvat finansiering avgjørende
- Nødvendig for å rekruttere studiesentra
  - Studiepersonell
  - Legemiddel
  - Prosedyrer (radiologi, biobanking)
  - Forsikring
  - Monitorering

Forskningsrådet - året rundt



Prekvalifisering Stiftelsen Dam

Tildeling Helse Sør-Øst
Tildeling Forskningsrådet

KLINBEFORSK

Tildeling KLINBEFORSK
Tildeling Stiftelsen Dam

Utvalgte søknader Stiftelsen Dam

Sykehusets fond

Sanitetskvinnene

Norsk revmatikerforbund

Helse Sør-Øst

Diakonhjemmet Hospital

REMEDY

Helse Sør-Øst 2024

Tabell 3. Antall søknader innstilt til støtte per søknadskategori – åpen tematisk utlysning, prioriterte områder og midler til ikke-universitetssykehus.

Søknadskategori	Antall vurderte søknader	Antall innstilte søknader	Beløp - tusen kroner	
Doktorgradsstipend	205	31	34 081	15,1%
Postdoktorstipend	101	18	20 109	17,8%
Åpen prosjektstøtte	159	37	94 986	23,3%
Totalt	**465**	**86**	**149 176**	

KLINBEFORSK

Antall pågående studier koordinert i hver helseregion og totalt antall vurderte søknader per helseregion i perioden 2016–2023

Helseregion	Antall regionalt koordinerte studier	Totalt antall vurderte søknader etter åpen utlysning	Tildelingsandel
Sør-Øst	40 (57%)	180 (62%)	22%
Vest	19 (27%)	63 (22%)	30%
Midt-Norge	9 (13%)	38 (13%)	24%
Nord	2 (3%)	10 (3%)	20%
Totalt	**70 (100%)**	**291 (100%)**	**24%**

Prosjektbeskrivelse: Metodeavsnitt

- **Hvordan besvares forskningsspørsmålet best?**
  - RCT? Mulig bruke allerede innsamlede data?

- **Hva er realistisk å gjennomføre innenfor gitte rammer?**
  - Styrkeberegning
  - NB! Viktigheten av riktig utfallsmål for å optimalisere hvor mange pasienter man må inkludere
  - Multisenter? Fordel og ulemper

- **Hvordan planlegge for god datakvalitet?**
  - Vise forståelse for krav om søknad til REK, CTIS
  - Plan for monitorering dersom legemiddelstudie
  - Ta stilling til CRF-løsning?

Evalueringskriterier

	Project quality	Impact
1	**Originality:** • Scientific novelty /originality relative to the research front of the subject area • Degree of innovation; does the project challenge current practices (clinical and research), e.g. through innovative use of theory/methods?	**Needs justification:** • Target group(s), i.e. patient group(s), carers, other identified users • Needs in the specialist health services • Filling knowledge gaps • Meeting other needs of society
2	**Design of the application:** • Scientific background of the project • Overview of the research front, state-of-the-art, relevant references / literature • Description of hypotheses, objectives and milestones • Description of positions (particularly important for PhD grants) and roles	**Importance of generating new knowledge:** • Realistic importance for the health services, possible improvements of existing offers/practices • Importance of new knowledge / filling knowledge gaps, academic impact • Impact on society, potential for generalisation / broad use of new knowledge
3	**Feasibility:** • Realistic, well-reasoned and appropriate project plans (data collection, methods, analyses, statistics etc.) • Identified risks, alternative strategies for conducting the project • Data available from pilot projects or other preliminary data where relevant • Realistic budgets	**Potential for implementation:** • Realistic plans for implementation / translation of research into improved practice • Realistic time line for implementation (short/long term) • Identified dependencies on development in other areas
4	**Quality of the applicant (relative to career stage):** • Expertise and qualifications • Productivity • Skills related to project management and supervision • Independency relative to career stage (particularly important for career fellowship proposals)	**Competence building:** • Gain of knowledge/skills required in the health services • Development of methods, techniques • Strengthening of the research area
5	**Research environment:** • Infrastructure, access to equipment and resources, necessary/relevant scientific networks • Relevant collaborators • Educational environment, capacity and ability to supervise • Cross-disciplinarity if relevant	**Dissemination and visibility:** • Plan for dissemination; publications, articles, web sites etc. • Plan for user involvement when relevant • Other relevant plans for disseminating new knowledge, nationally and internationally

Helse Sør-Øst

Scientific quality
Project design and originality: ☐ Scientific background of the project, overview of the research front, state-of-the-art, relevant references / literature ☐ Description of hypotheses, objectives and milestones ☐ Description of positions (particularly important if including PhD grants) and roles ☐ Scientific novelty /originality relative to the research front of the subject area ☐ Degree of innovation. Does the project challenge current practices (clinical and research), e.g. through innovative use of theory/methods?
Feasibility: ☐ Realistic, well-reasoned and appropriate project plans (data collection, methods, analyses, statistic strength etc.) ☐ Identified risks, alternative strategies for conducting the project ☐ Data available from pilot projects or other preliminary data where relevant ☐ Realistic budgets
Quality of the applicant and the research environment: ☐ Expertise, productivity and qualifications ☐ Skills related to project management and supervision ☐ Infrastructure, access to equipment and resources, necessary/relevant scientific networks ☐ Relevant collaborators creating a research environment of capacity ☐ Cross-disciplinarity if relevant
Impact
Needs justification: ☐ Needs in the specialist health services ☐ Target group(s), i.e. patient group(s), carers, other identified users ☐ Filling knowledge gaps
Potential for implementation: ☐ Realistic plans for implementation / translation of research into improved practice ☐ Realistic time line for implementation (short/long term) ☐ Identified dependencies on development in other areas, alternative strategies
Importance of generating new knowledge and competence building: ☐ Realistic importance for the health services, possible improvements of existing offers/practices ☐ Importance of new knowledge / filling knowledge gaps, academic impact ☐ Impact on society, potential for generalisation / broad use of new knowledge/methods/procedures
Mandatory items of the application
Dissemination and visibility: ☐ Plan for dissemination; publications, articles, web sites etc. ☐ Other relevant plans for disseminating new knowledge, nationally and internationally
Plan for user involvement

KLINBEFORSK

Excellence
The extent to which the proposed work is ambitious, novel, and goes beyond the state of the art
- Scientific creativity and originality.
- Novelty and boldness of hypotheses or research questions.
- Potential for development of new knowledge beyond the current state-of-the-art, including significant theoretical, methodological, experimental or empirical advancement.

The quality of the proposed R&D activities
- Quality of the research questions, hypotheses and project objectives, and the extent to which they are clearly and adequately specified.
- Credibility and appropriateness of the theoretical approach, research design and use of scientific methods. Appropriate consideration of interdisciplinary approaches.
- Where relevant, the extent to which appropriate consideration has been given to ethical issues, safety issues, gender dimension in research content, and appropriate use of stakeholder/user knowledge.

Impact
Potential impact of the proposed research
- The extent to which the planned outputs of the project address important present and/or future scientific challenges.
- If relevant with respect to the project objectives, the extent to which the planned outputs will address UN Sustainable Development Goals or other important present and/or future societal challenges.
- The extent to which the potential impacts are clearly formulated and plausible.

Communication and exploitation
Quality and scope of communication and engagement activities with different target audiences, including relevant stakeholders/users.

Implementation
The quality of the project manager and project group
- The extent to which the project manager has relevant expertise and experience, and has demonstrated the ability to perform high-quality research (as appropriate to the career stage).
- The degree of complementarity of the participants and the extent to which the project group as a whole encompasses the expertise needed to undertake the research effectively, and provides added value.

The quality of the project organisation and management
- Effectiveness of the work plan, including the extent to which resources assigned to work packages are aligned with project objectives and deliverables.
- Appropriateness of the allocation of tasks, ensuring that all participants have a valid role and adequate resources in the project to fulfil that role.
- Appropriateness of the proposed management structures and governance.

Forskningsrådet

Diakonhjemmet Hospital

REMEDY

Evalueringskriterier

Originalitet/novelty

	Project quality	
1	**Originality:** • Scientific novelty /originality relative to the research front of the subject area • Degree of innovation; does the project challenge current practices (clinical and research), e.g. through innovative use of theory/methods?	**Needs justification:** • Target group(s), i.e. patient group(s), carers, other identified users • Needs in the specialist health services • Filling knowledge gaps • Meeting other needs of society
2	**Design of the application:** • Scientific background of the project • Overview of the research front, state-of-the-art, relevant references / literature • Description of hypotheses, objectives and milestones • Description of positions (particularly important for PhD grants) and roles	**Importance of generating new knowledge:** • Realistic importance for the health services, possible improvements of existing offers/practices • Importance of new knowledge / filling knowledge gaps, academic impact • Impact on society, potential for generalisation / broad use of new knowledge
3	**Feasibility:** • Realistic, well-reasoned and appropriate project plans (data collection, methods, analyses, statistics etc.) • Identified risks, alternative strategies for conducting the project • Data available from pilot projects or other preliminary data where relevant • Realistic budgets	**Potential for implementation:** • Realistic plans for implementation / translation of research into improved practice • Realistic time line for implementation (short/long term) • Identified dependencies on development in other areas
4	**Quality of the applicant (relative to career stage):** • Expertise and qualifications • Productivity • Skills related to project management and supervision • Independency relative to career stage (particularly important for career fellowship proposals)	**Competence building:** • Gain of knowledge/skills required in the health services • Development of methods, techniques • Strengthening of the research area
5	**Research environment:** • Infrastructure, access to equipment and resources, necessary/relevant scientific networks • Relevant collaborators • Educational environment, capacity and ability to supervise • Cross-disciplinarity if relevant	**Dissemination and visibility:** • Plan for dissemination; publications, articles, web sites etc. • Plan for user involvement when relevant • Other relevant plans for disseminating new knowledge, nationally and internationally

Scientific quality
Project design and original
☐ Scientific background of the project, overview of the research front, state-of-the-art, relevant references / literature ☐ Description of hypotheses, objectives and milestones ☐ Description of positions (particularly important if including PhD grants) and roles ☐ Scientific novelty /originality relative to the research front of the subject area ☐ Degree of innovation. Does the project challenge current practices (clinical and research), e.g. through innovative use of theory/methods?
Feasibility:
☐ Realistic, well-reasoned and appropriate project plans (data collection, methods, analyses, statistic strength etc.) ☐ Identified risks, alternative strategies for conducting the project ☐ Data available from pilot projects or other preliminary data where relevant ☐ Realistic budgets
Quality of the applicant and the research environment:
☐ Expertise, productivity and qualifications ☐ Skills related to project management and supervision ☐ Infrastructure, access to equipment and resources, necessary/relevant scientific networks ☐ Relevant collaborators creating a research environment of capacity ☐ Cross-disciplinarity if relevant
Impact
Needs justification:
☐ Needs in the specialist health services ☐ Target group(s), i.e. patient group(s), carers, other identified users ☐ Filling knowledge gaps
Potential for implementation:
☐ Realistic plans for implementation / translation of research into improved practice ☐ Realistic time line for implementation (short/long term) ☐ Identified dependencies on development in other areas, alternative strategies
Importance of generating new knowledge and competence building:
☐ Realistic importance for the health services, possible improvements of existing offers/practices ☐ Importance of new knowledge / filling knowledge gaps, academic impact ☐ Impact on society, potential for generalisation / broad use of new knowledge/methods/procedures
Mandatory items of the application
Dissemination and visibility:
☐ Plan for dissemination; publications, articles, web sites etc. ☐ Other relevant plans for disseminating new knowledge, nationally and internationally
Plan for user involvement

Excellence
The extent to which the proposed work is ambitious, novel, and goes beyond the state of the art
- Scientific creativity and originality.
- Novelty and boldness of hypotheses or research questions.
- Potential for development of new knowledge beyond the current state-of-the-art, including significant theoretical, methodological, experimental or empirical advancement.

The quality of the proposed R&D activities
- Quality of the research questions, hypotheses and project objectives, and the extent to which they are clearly and adequately specified.
- Credibility and appropriateness of the theoretical approach, research design and use of scientific methods. Appropriate consideration of interdisciplinary approaches.
- Where relevant, the extent to which appropriate consideration has been given to ethical issues, safety issues, gender dimension in research content, and appropriate use of stakeholder/user knowledge.

Impact
Potential impact of the proposed research
- The extent to which the planned outputs of the project address important present and/or future scientific challenges.
- If relevant with respect to the project objectives, the extent to which the planned outputs will address UN Sustainable Development Goals or other important present and/or future societal challenges.
- The extent to which the potential impacts are clearly formulated and plausible.

Communication and exploitation
Quality and scope of communication and engagement activities with different target audiences, including relevant stakeholders/users.

Implementation
The quality of the project manager and project group
- The extent to which the project manager has relevant expertise and experience, and has demonstrated the ability to perform high-quality research (as appropriate to the career stage).
- The degree of complementarity of the participants and the extent to which the project group as a whole encompasses the expertise needed to undertake the research effectively, and provides added value.

The quality of the project organisation and management
- Effectiveness of the work plan, including the extent to which resources assigned to work packages are aligned with project objectives and deliverables.
- Appropriateness of the allocation of tasks, ensuring that all participants have a valid role and adequate resources in the project to fulfil that role.
- Appropriateness of the proposed management structures and governance.

Helse Sør-Øst

Diakonhjemmet Hospital

KLINBEFORSK

Forskningsrådet

REMEDY

Evalueringskriterier

	Project quality	Impact
1	**Originality:** • Scientific novelty /originality relative to the research front of the subject area • Degree of innovation; does the project challenge current practices (clinical and research), e.g. through innovative use of theory/methods?	**Needs justification:** • Target group(s), i.e. patient group(s), carers, other identified users • Needs in the specialist health services • Filling knowledge gaps • Meeting other needs of society
2	**Design of the application:** • Scientific background of the project • Overview of the research front, state-of-the-art, relevant references / literature • Description of hypotheses, objectives and milestones • Description of positions (particularly important for PhD grants) and roles	**Importance of generating new knowledge** • Realistic importance for the health servic possible improvements of e offers/practices • Importance of new kno edge / fi knowledge gaps, acad mic imp • Impact on society, otential f generalisation / oad use new knowledge
3	**Feasibility:** • Realistic, well-reasoned and appropriate project plans (data collection, methods, analyses, statistics etc.) • Identified risks, alternative strategies for conducting the project • Data available from pilot projects or other preliminary data where relevant • Realistic budgets	**Potential for im ementat n:** • Realis c plans f implementation / tra slation o research into improved ractice • Realisti ime line for implementation (short long term) • Ide ified dependencies on development in r areas
4	**Quality of the applicant (relative to career stage):** • Expertise and qualifications • Productivity • Skills related to project manag ent and supervision • Independency relative to reer stage (particularly important r career fellowship proposals)	**Competence building:** • Gain of knowledge/skills required in the health services • Development of methods, techniques • Strengthening of the research area
5	**Research environment:** • Infrastructure, access to equipment and resources, necessary/relevant scientific networks • Relevant collaborators • Educational environment, capacity and ability to supervise • Cross-disciplinarity if relevant	**Dissemination and visibility:** • Plan for dissemination; publications, articles, web sites etc. • Plan for user involvement when relevant • Other relevant plans for disseminating new knowledge, nationally and internationally

Quality of project manager / project group

Scientific quality
Project design and originality: ☐ Scientific background of the project, overview of the research front, state-of-the-art, relevant references / literature ☐ Description of hypotheses, objectives and milestones ☐ Description of positions (particularly important if including PhD grants) and roles ☐ Scientific novelty /originality relative to the research front of the subject area ☐ Degree of innovation. Does the project challenge current practices (clinical and research), e.g. through innovative use of theory/method
Feasibility: ☐ Realistic, well-reasoned and appropriate project plans (data collection, methods, analyses, statistic strength etc.) ☐ Identified risks, alternative strategies for conducting the project ☐ Data available from pilot projects or other preliminary data where relevant ☐ Realistic budgets
Quality of the applicant and the research environment: ☐ Expertise, productivity and qualifications ☐ Skills related to project management and supervision ☐ Infrastructure, access to equipment and resources, necessary/relevant scientific networks ☐ Relevant collaborators creating a research environment of capacity ☐ Cross-disciplinarity if relevant
Impact
Needs justification: ☐ Needs in the specialist health services ☐ Target group(s), i.e. patient group(s), carers, other identified users ☐ Filling knowledge gaps
Potential for implementation: ☐ Realistic plans for implementation / translation of research into improved practice ☐ Realistic time line for implementation (short/long term) ☐ Identified dependencies on development in other areas, alternative strategies
Importance of generating new knowledge and competence building: ☐ Realistic importance for the health services, possible improvements of existing offers/practices ☐ Importance of new knowledge / filling knowledge gaps, academic impact ☐ Impact on society, potential for generalisation / broad use of new knowledge/methods/procedures
Mandatory items of the application
Dissemination and visibility: ☐ Plan for dissemination; publications, articles, web sites etc. ☐ Other relevant plans for disseminating new knowledge, nationally and internationally
Plan for user involvement

Excellence

The extent to which the proposed work is ambitious, novel, and goes beyond the state of the art

- Scientific creativity and originality.
- Novelty and boldness of hypotheses or research questions.
- Potential for development of new knowledge beyond the current state-of-the-art, including significant theoretical, methodological, experimental or empirical advancement.

The quality of the proposed R&D activities

- Quality of the research questions, hypotheses and project objectives, and the extent to which they are clearly and adequately specified.
- Credibility and appropriateness of the theoretical approach, research design and use of scientific methods. Appropriate consideration of interdisciplinary approaches.
- Where relevant, the extent to which appropriate consideration has been given to ethical issues, safety issues, gender dimension in research content, and appropriate use of stakeholder/user knowledge.

Impact

Potential impact of the proposed research

- The extent to which the planned outputs of the project address important present and/or future scientific challenges.
- If relevant with respect to the project objectives, the extent to which the planned outputs will address UN Sustainable Development Goals or other important present and/or future societal challenges.
- The extent to which the potential impacts are clearly formulated and plausible.

Communication and exploitation

Quality and scope of communication and engagement activities with different target audiences, including relevant stakeholders/users.

Implementation

The quality of the project manager and project group

- The extent to which the project manager has relevant expertise and experience, and has demonstrated the ability to perform high-quality research (as appropriate to the career stage).
- The degree of complementarity of the participants and the extent to which the project group as a whole encompasses the expertise needed to undertake the research effectively, and provides added value.

The quality of the project organisation and management

- Effectiveness of the work plan, including the extent to which resources assigned to work packages are aligned with project objectives and deliverables.
- Appropriateness of the allocation of tasks, ensuring that all participants have a valid role and adequate resources in the project to fulfil that role.
- Appropriateness of the proposed management structures and governance.

Helse Sør-Øst

Diakonhjemmet Hospital

KLINBEFORSK

Forskningsrådet

REMEDY

Evalueringskriterier

Quality of research questions, methodology

	Project quality	Impact
1	**Originality:** • Scientific novelty /originality relative to the research front of the subject area • Degree of innovation; does the project challenge current practices (clinical and research), e.g. through innovative use of theory/methods?	**Needs justification:** • Target group(s), i.e. patient group(s), carers, other identified users • Needs in the specialist health servi • Filling knowledge gaps • Meeting other needs society
2	**Design of the application:** • Scientific background of the project • Overview of the research front, state-of-the-art, relevant references / literature • Description of hypotheses, objectives and milestones • Description of positions (particularly important for PhD grants) and roles	**portance of generating new knowledge:** • Realistic importance for the health services, possible improvements of existing offers/practices • Importance of new knowledge / filling knowledge gaps, academic impact • Impact on society, potential for generalisation / broad use of new knowledge
3	**Feasibility:** • Realistic, well-reasoned and appropriate project plans (data collection, methods, analyses, statistics etc.) • Identified risks, alternative strategies for conducting the project • Data available from pilot projects or other preliminary data where relevant • Realistic budgets	**Potential for implementation:** • Realistic plans for implementation / translation of research into improved practice • Realistic time line for implementation (short/long term) • Identified dependencies on development in other areas
4	**Quality of the applicant (relative to career stage):** • Expertise and qualifications • Productivity • Skills related to project management and supervision • Independency relative to career stage (particularly important for career fellowship proposals)	**Competence building:** • Gain of knowledge/skills required in the health services • Development of methods, techniques • Strengthening of the research area
5	**Research environment:** • Infrastructure, access to equipment and resources, necessary/relevant scientific networks • Relevant collaborators • Educational environment, capacity and ability to supervise • Cross-disciplinarity if relevant	**Dissemination and visibility:** • Plan for dissemination; publications, articles, web sites etc. • Plan for user involvement when relevant • Other relevant plans for disseminating new knowledge, nationally and internationally

Scientific quality
Project design and originality: ☐ Scientific background of the project / overview of the research front, state-of-the-art, relevant references / literature ☐ Description of hypotheses, ob es and milestones ☐ Description of positions (parti y important if including PhD grants) and roles ☐ Scientific novelty /originality relative to the research front of the subject area ☐ Degree of innovation. Does the project challenge current practices (clinical and research), e.g. through innovative use of theory/methods?
Feasibility: ☐ Realistic, well-reasoned and appropriate project plans (data collection, methods, analyses, statistic strength etc.) ☐ Identified risks, alternative strategies for conducting the project ☐ Data available from pilot projects or other preliminary data where relevant ☐ Realistic budgets
Quality of the applicant and the research environment: ☐ Expertise, productivity and qualifications ☐ Skills related to project management and supervision ☐ Infrastructure, access to equipment and resources, necessary/relevant scientific networks ☐ Relevant collaborators creating a research environment of capacity ☐ Cross-disciplinarity if relevant
Impact
Needs justification: ☐ Needs in the specialist health services ☐ Target group(s), i.e. patient group(s), carers, other identified users ☐ Filling knowledge gaps
Potential for implementation: ☐ Realistic plans for implementation / translation of research into improved practice ☐ Realistic time line for implementation (short/long term) ☐ Identified dependencies on development in other areas, alternative strategies
Importance of generating new knowledge and competence building: ☐ Realistic importance for the health services, possible improvements of existing offers/practices ☐ Importance of new knowledge / filling knowledge gaps, academic impact ☐ Impact on society, potential for generalisation / broad use of new knowledge/methods/procedures
Mandatory items of the application
Dissemination and visibility: ☐ Plan for dissemination; publications, articles, web sites etc. ☐ Other relevant plans for disseminating new knowledge, nationally and internationally
Plan for user involvement

Excellence

The extent to which the proposed work is ambitious, novel, and goes beyond the state of the art

- Scientific creativity and originality.
- Novelty and boldness of hypotheses or research questions.
- Potential for development of new knowledge beyond the current state-of-the-art, including significant theoretical, methodological, experimental or empirical advancement.

The quality of the proposed R&D activities

- Quality of the research questions, hypotheses and project objectives, and the extent to which they are clearly and adequately specified.
- Credibility and appropriateness of the theoretical approach, research design and use of scientific methods. Appropriate consideration of interdisciplinary approaches.
- Where relevant, the extent to which appropriate consideration has been given to ethical issues, safety issues, gender dimension in research content, and appropriate use of stakeholder/user knowledge.

Impact

Potential impact of the proposed research

- The extent to which the planned outputs of the project address important present and/or future scientific challenges.
- If relevant with respect to the project objectives, the extent to which the planned outputs will address UN Sustainable Development Goals or other important present and/or future societal challenges.
- The extent to which the potential impacts are clearly formulated and plausible.

Communication and exploitation

Quality and scope of communication and engagement activities with different target audiences, including relevant stakeholders/users.

Implementation

The quality of the project manager and project group

- The extent to which the project manager has relevant expertise and experience, and has demonstrated the ability to perform high-quality research (as appropriate to the career stage).
- The degree of complementarity of the participants and the extent to which the project group as a whole encompasses the expertise needed to undertake the research effectively, and provides added value.

The quality of the project organisation and management

- Effectiveness of the work plan, including the extent to which resources assigned to work packages are aligned with project objectives and deliverables.
- Appropriateness of the allocation of tasks, ensuring that all participants have a valid role and adequate resources in the project to fulfil that role.
- Appropriateness of the proposed management structures and governance.

Helse Sør-Øst

Diakonhjemmet Hospital

KLINBEFORSK

Forskningsrådet

REMEDY

Nytte

- Pasient
- Samfunn

Sørg for å beskrive begge deler i søknaden!

Formelle godkjenninger

- Clinical Trials Information System (CTIS)
- Regional Etisk Komite, REK
- Personvernombud
- Lokale forskningsutvalg
- Registrering
  - Eks: clinicaltrials.gov

Lokale forskningsutvalg

Diakonhjemmet Sykehus Administrerende Direktør - Forskningsutvalget - Forskning, kvalitet og registre			Dok.id.: EK.13.6.1.3
Forskningsprosjekter - planlegging og gjennomføring			Versjon:5.00
Dokumenttype: Rutine	Fagansvarlig: Forskningsutvalg	Godkjent av: Administrerende direktør Anders Mohn Frafjord	Gyldig fra: 27.02.2019

Utskrift kun gyldig på utskriftstidspunktet: 26.11.2019

Endringer siden forrige versjon

Flere endringer - bl.a. i tråd med registreringssystem for kvalitet og forskningsprosjekter, innføring av personvernombud på sykehuset og trinnvis fremstilling av fremgangsmåte.

1. HENSIKT

Sikre at planlegging, godkjenning og gjennomføring av medisinsk og helsefaglig forskning ved sykehuset skjer i samsvar med krav i lov og forskrifter.

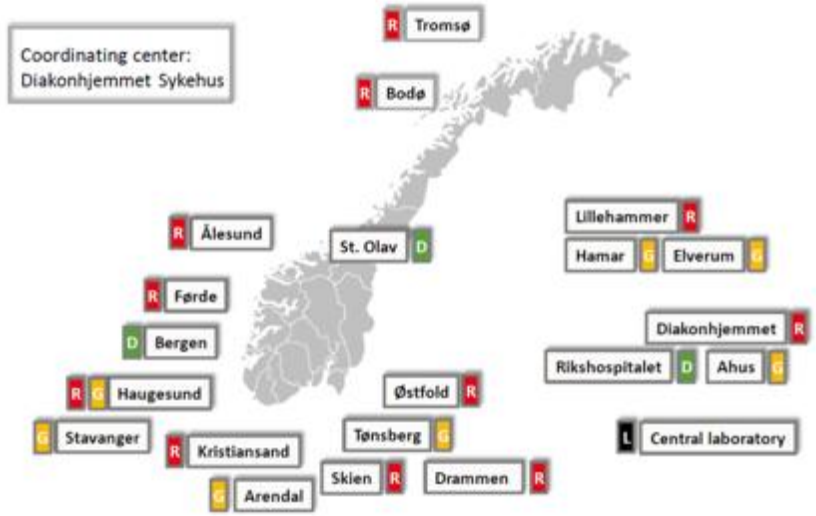
- På koordinerende senter
- På andre studiesentra

Rekruttering av studiesentre

- **Viktige personer**
  - Avdelingsleder – må være positiv!
  - **Lokal hovedutprøver**
  - Studiesykepleier(e) og studieleger

- **Ressurser og forskningsinfrastruktur**
  - Bildediagnostikk, lab, biobank, apotek, CTU-enhet, monitorer etc

- **Lokale møter for rekruttering av studiesentra**
  - Informasjon
  - Vurdere senteret (motivasjon, personell, ressurser)
  - Mulighet for vitenskapelig samarbeid



Diakonhjemmet Hospital

REMEDY

Rekruttering av studiesentre

- Bidra til økt kunnskap
- Meritterende
- Nettverk
- Krydre hverdagen
- Dugnadsånd
- Pasientene
- Penger

- Kapasitet
- Egen forskning på feltet
- Prosjektets relevans

Diakonhjemmet Hospital

REMEDY

Vellykket rekruttering av studiesentra

- Vær innstilt på reising. Besøk alle studiesentra
- Sørg for finansiering
- Vitenskapelig samarbeid – medforfatterskap, tilgang til data

Studiedrift

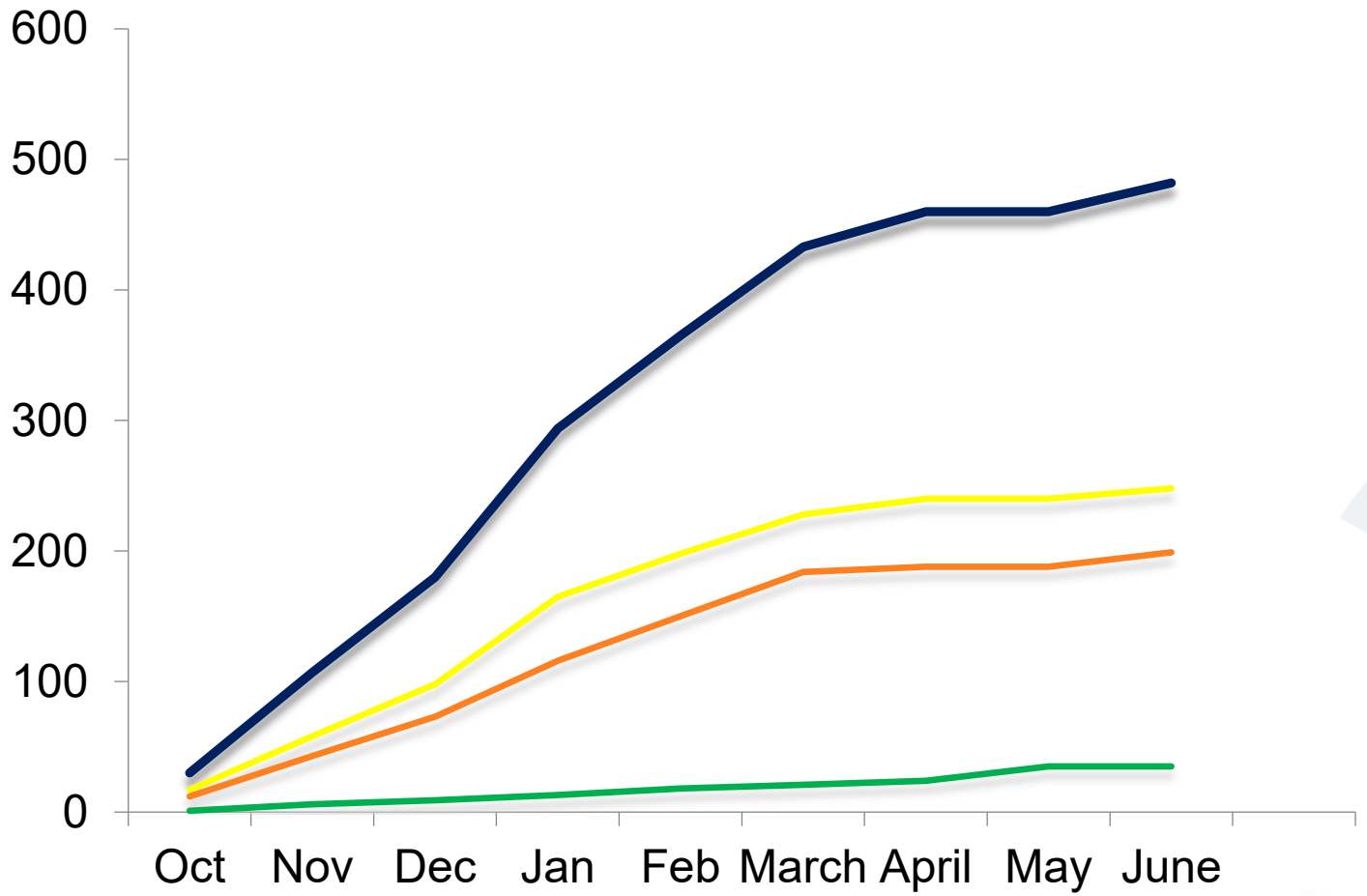
- Motivasjon
- Senterkontakt
  - Tilgjengelighet
- Nyhetsbrev
- Utprøvermøter
- Datasjekker/regelmessige kontroller av datainnsamlingen
- Samarbeid med monitor/forskningsstøtte
  - Egne monitor-møter

Rekruttering av deltakere

- Inklusjons- og eksklusjonskriterier
  - Eksisterer disse pasientene ved studiesenteret?

- Skriftlig og muntlig informasjon om studien
  - Muntlig viktigst – avgjørende å informere, motivere og inkludere pasienter, få frem positive sider ved studien, informere om potensiell risiko og skade
  - Finansiering
  - Ingen egenandel for studiespesifikke prosedyrer
  - Kompensasjon for reisekostnader/tid?

NOR-SWITCH : 2014-2015



482 in total

248 Gastro

199 Rheuma

35 Derma

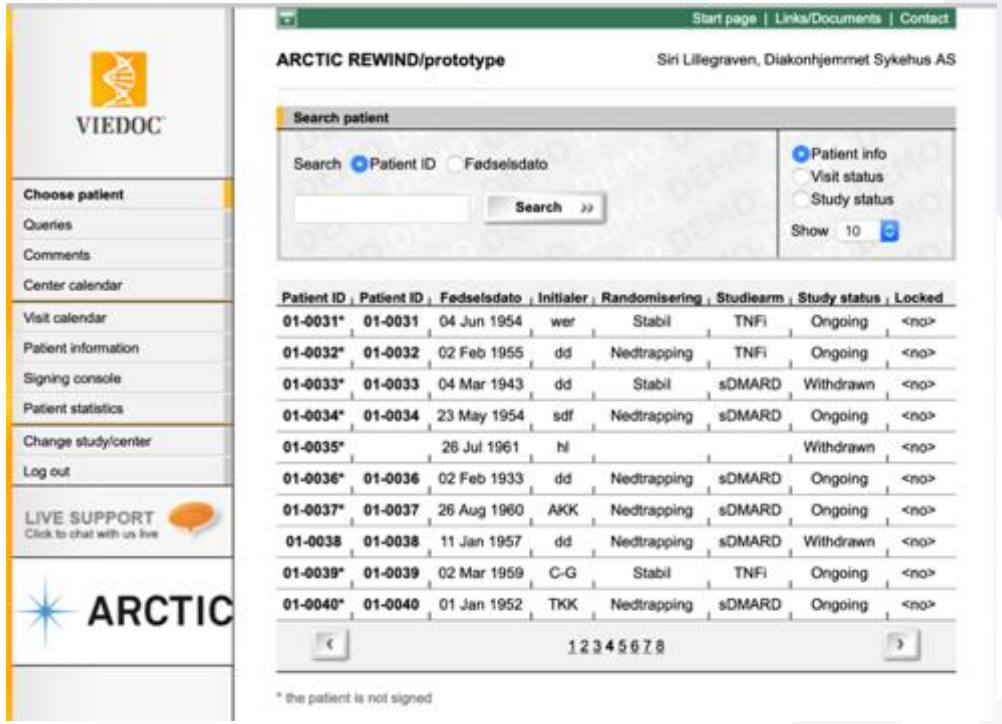
Diakonhjemmet Hospital

NOR SWITCH

REMEDY

Elektronisk datainnsamling

- Avgjørende for vellykket studie
- God erfaring med Viedoc



Diakonhjemmet Hospital

REMEDY

Good Clinical Practice (GCP)

- «Internasjonal, etisk, vitenskapelig kvalitetsstandard for design, utførelse, innsamling, dokumentasjon, lagring og rapportering av data i kliniske studier på mennesker»

- Bruk sertifisert elektronisk datainnsamlingsverktøy som legger til rette for GCP
  - Monitorering (pragmatisk)

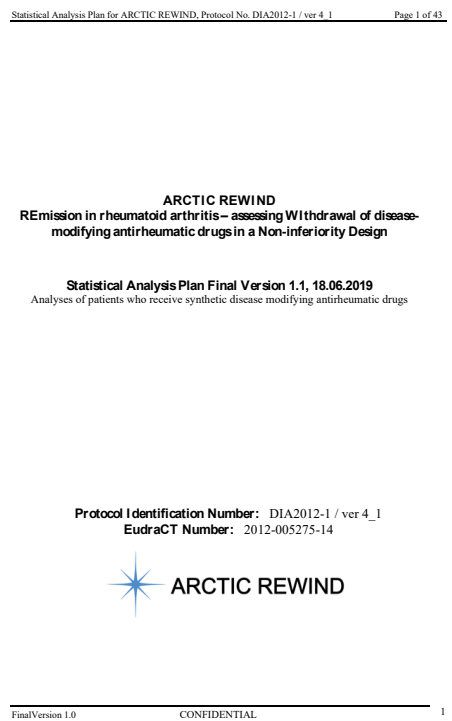
- GCP-kursing for alt studiepersonell
  - Oppstartsmøte, NorCRIN, onlinekurs

Analyser

- Flink biostatistiker

- Statistisk analyseplan (SAP)
  - Utvikle og signere før databasen «låses»
  - **Predefiner** alle analyser
  - SAP og protokoll submitteres med studiens hovedresultater
  - Prespesifiserte sekundæranalyser

- Oppdater underveis
  - SAP, protokoll og studieregistrering – med samme opplysninger


Statistical Analysis Plan for ARCTIC REWIND, Protocol No. DIA2012-1 / ver 4_1 Page 1 of 43

ARCTIC REWIND
REmission in rheumatoid arthritis – assessing WIthdrawal of disease-modifying antirheumatic drugs in a Non-inferiority Design

Statistical Analysis Plan Final Version 1.1, 18.06.2019
Analyses of patients who receive synthetic disease modifying antirheumatic drugs

Protocol Identification Number: DIA2012-1 / ver 4_1
EudraCT Number: 2012-005275-14

ARCTIC REWIND

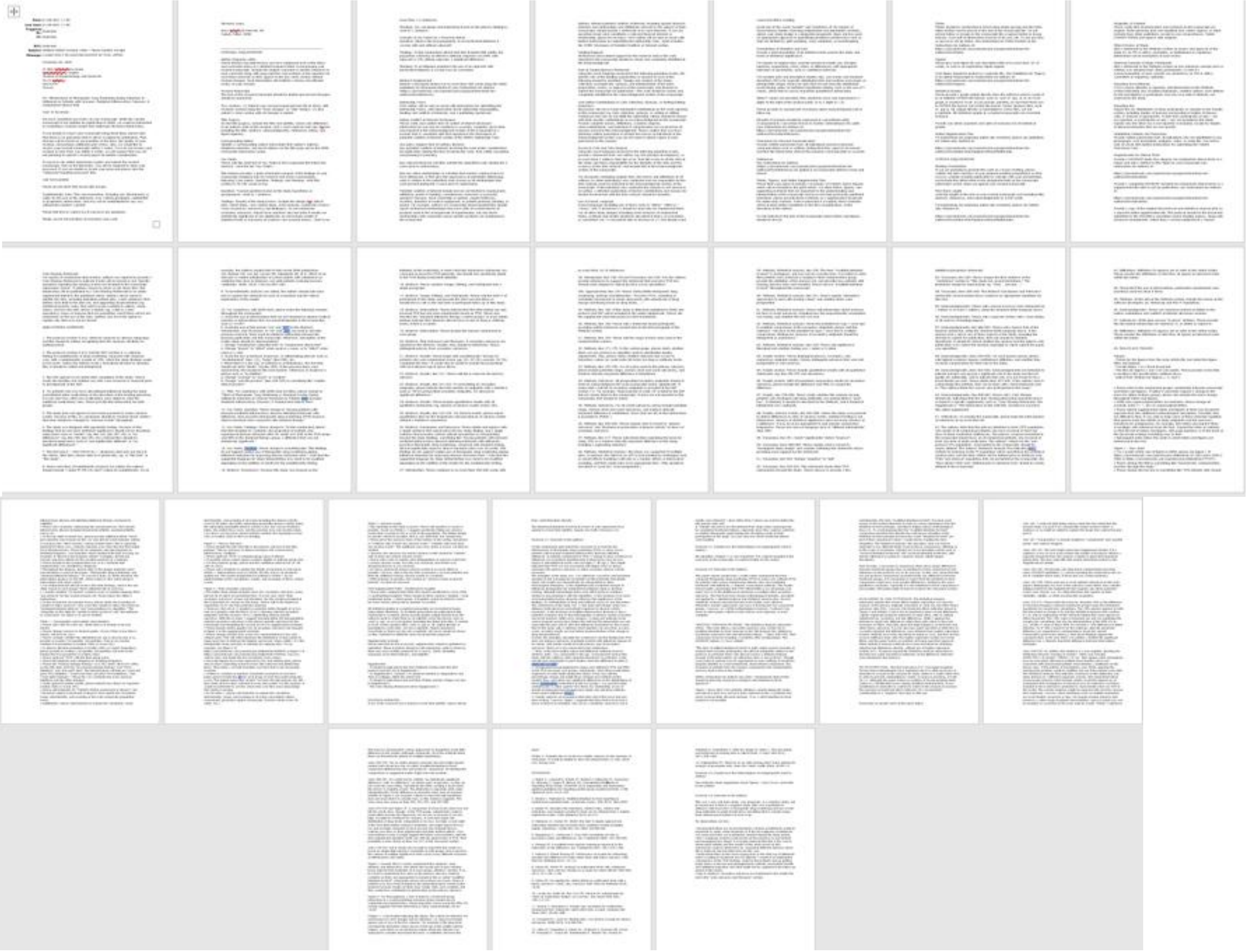
FinalVersion 1.0 CONFIDENTIAL 1

Diakonhjemmet Hospital

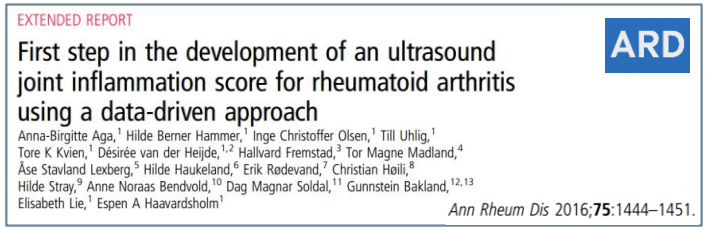
REMEDY

Publisering: Hovedresultater

- NEJM:
  - Ultrasound in the management of Rheumatoid Arthritis
- Lancet:
  - Ultrasound in the management of rheumatoid arthritis: results from the randomized controlled ARCTIC trial
- BMJ:
  - Ultrasound in management of rheumatoid arthritis: ARCTIC randomised controlled strategy trial



Viktig å tenke på: Sekundære analyser



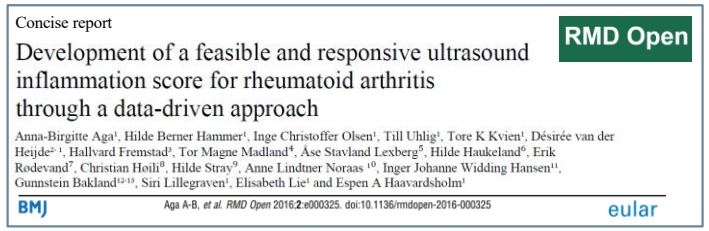
EXTENDED REPORT

ARD

First step in the development of an ultrasound joint inflammation score for rheumatoid arthritis using a data-driven approach

Anna-Birgitte Aga,[1] Hilde Berner Hammer,[1] Inge Christoffer Olsen,[1] Till Uhlig,[1] Tore K Kvien,[1] Désirée van der Heijde,[1,2] Hallvard Fremstad,[3] Tor Magne Madland,[4] Åse Stavland Lexberg,[5] Hilde Haukeland,[6] Erik Rødevand,[7] Christian Høili,[8] Hilde Stray,[9] Anne Noraas Bendvold,[10] Dag Magnar Soldal,[11] Gunnstein Bakland,[12,13] Elisabeth Lie,[1] Espen A Haavardsholm[1]

Ann Rheum Dis 2016;**75**:1444–1451.



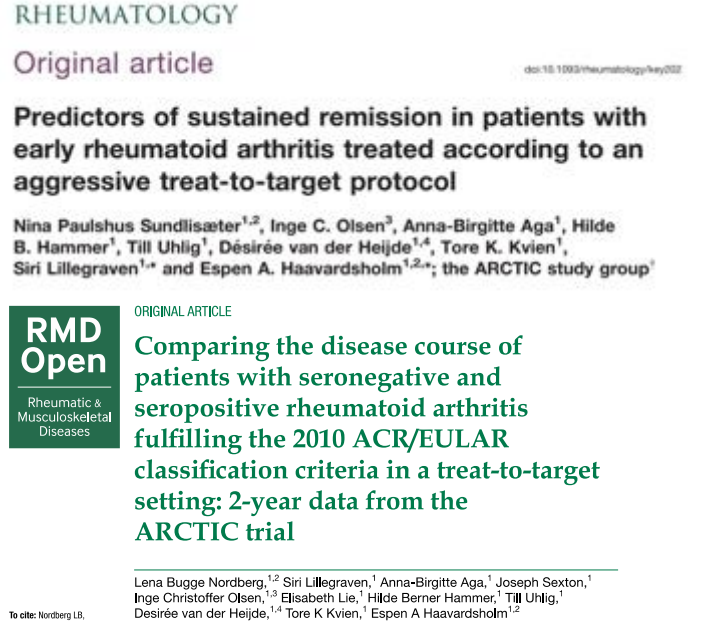
Concise report

RMD Open

Development of a feasible and responsive ultrasound inflammation score for rheumatoid arthritis through a data-driven approach

Anna-Birgitte Aga[1], Hilde Berner Hammer[1], Inge Christoffer Olsen[1], Till Uhlig[1], Tore K Kvien[1], Désirée van der Heijde[2-1], Hallvard Fremstad[3], Tor Magne Madland[4], Åse Stavland Lexberg[5], Hilde Haukeland[6], Erik Rødevand[7], Christian Høili[8], Hilde Stray[9], Anne Lindtner Noraas [10], Inger Johanne Widding Hansen[11], Gunnstein Bakland[12-13], Siri Lillegraven[1], Elisabeth Lie[1] and Espen A Haavardsholm[1]

BMJ Aga A-B, *et al. RMD Open* 2016;**2**:e000325. doi:10.1136/rmdopen-2016-000325 eular



RHEUMATOLOGY

Original article

doi:10.1093/rheumatology/key032

Predictors of sustained remission in patients with early rheumatoid arthritis treated according to an aggressive treat-to-target protocol

Nina Paulshus Sundlisæter[1,2], Inge C. Olsen[3], Anna-Birgitte Aga[1], Hilde B. Hammer[1], Till Uhlig[1], Désirée van der Heijde[1,4], Tore K. Kvien[1], Siri Lillegraven[1,*] and Espen A. Haavardsholm[1,2,*]; the ARCTIC study group[†]

RMD Open

Rheumatic & Musculoskeletal Diseases

ORIGINAL ARTICLE

Comparing the disease course of patients with seronegative and seropositive rheumatoid arthritis fulfilling the 2010 ACR/EULAR classification criteria in a treat-to-target setting: 2-year data from the ARCTIC trial

Lena Bugge Nordberg,[1,2] Siri Lillegraven,[1] Anna-Birgitte Aga,[1] Joseph Sexton,[1] Inge Christoffer Olsen,[1,3] Elisabeth Lie,[1] Hilde Berner Hammer,[1] Till Uhlig,[1] Désirée van der Heijde,[1,4] Tore K Kvien,[1] Espen A Haavardsholm[1,2]

To cite: Nordberg LB,

CONCISE REPORT

Clinical and ultrasound remission after 6 months of treat-to-target therapy in early rheumatoid arthritis: associations to future good radiographic and physical outcomes

Nina Paulshus Sundlisæter,[1,2] Anna-Birgitte Aga,[1] Inge Christoffer Olsen,[3] Hilde Berner Hammer,[1] Till Uhlig,[1] Désirée van der Heijde,[1,4] Tore K Kvien,[1] Siri Lillegraven,[1] Espen A Haavardsholm,[1,2] the ARCTIC study group

Arthritis & Rheumatology

Full Length | Full Access

The impact of ultrasound on the use and efficacy of intra-articular glucocorticoid injections in early rheumatoid arthritis: Secondary analyses from the randomised ARCTIC trial

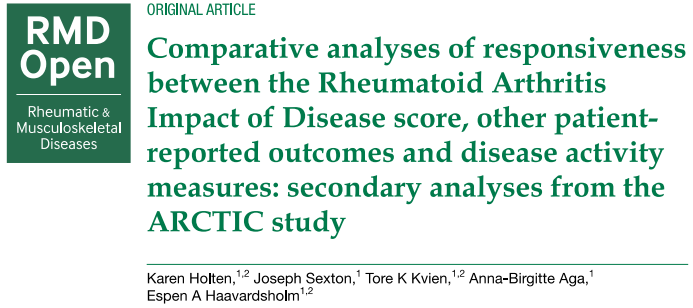
Lena B. Nordberg, Siri Lillegraven, Anna-Birgitte Aga, Joe Sexton, Elisabeth Lie, Hilde B. Hammer, Inge C. Olsen, Till Uhlig, Désirée van der Heijde, Tore K. Kvien, Espen A. Haavardsholm

First published: 25 March 2018 | https://doi.org/10.1002/art.40494

CONCISE REPORT

Patients with seronegative RA have more inflammatory activity compared with patients with seropositive RA in an inception cohort of DMARD-naïve patients classified according to the 2010 ACR/EULAR criteria

Lena Bugge Nordberg,[1] Siri Lillegraven,[1] Elisabeth Lie,[1] Anna-Birgitte Aga,[1] Inge Christoffer Olsen,[1] Hilde Berner Hammer,[1] Till Uhlig,[1] Maria Karolina Jonsson,[1,2] Désirée van der Heijde,[1,3] Tore K Kvien,[1] Espen Andre Haavardsholm,[1] and the ARCTIC working group



RMD Open

Rheumatic & Musculoskeletal Diseases

ORIGINAL ARTICLE

Comparative analyses of responsiveness between the Rheumatoid Arthritis Impact of Disease score, other patient-reported outcomes and disease activity measures: secondary analyses from the ARCTIC study

Karen Holten,[1,2] Joseph Sexton,[1] Tore K Kvien,[1,2] Anna-Birgitte Aga,[1] Espen A Haavardsholm[1,2]

Conventional versus ultrasound treat to target: no difference in magnetic resonance imaging inflammation or joint damage over 2 years in early rheumatoid arthritis

Ulf Sundin ✉, Anna-Birgitte Aga, Øivind Skare, Lena B Nordberg, Till Uhlig, Hilde B Hammer, Désirée van der Heijde, Tore K Kvien, Siri Lillegraven, Espen A Haavardsholm ... Show more

Rheumatology, kez674, https://doi.org/10.1093/rheumatology/kez674

Published: 30 January 2020 **Article history** ▾

Research Article | OMERACT 2018: International Consensus Conference on Outcome Measures in Rheumatology, Terrigal, Australia, May 2018 Special Interest Groups, Part 1

Validity and Responsiveness of Combined Inflammation and Combined Joint Damage Scores Based on the OMERACT Rheumatoid Arthritis MRI Scoring System (RAMRIS)

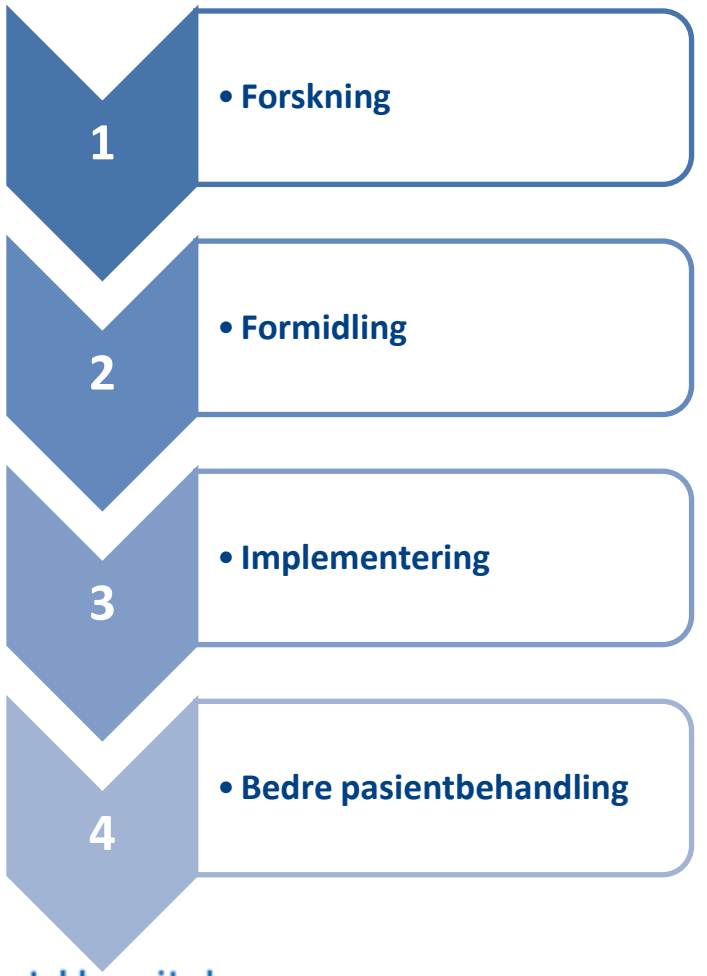
Ulf Sundin, Mikkel Østergaard, Daniel Glinatsi, Anna-Birgitte Aga, Kim Hørslev-Petersen, Merete L. Hetland, Kristian Stengard-Pedersen, Peter Junker, Bo J. Ejbjerg, Paul Bird, Philip G. Conaghan, Siri Lillegraven and Espen A. Haavardsholm

The Journal of Rheumatology September 2019, 46 (9) 1222-1227; DOI: https://doi.org/10.3899/jrheum.181064

Forfatterskap/vitenskapelig samarbeid

- Hovedpublikasjon vs sekundære publikasjoner
  - Legge til rette for at lokale hovedutprøvere har naturlig rolle som medforfattere
- Studiegruppe med PubMed-kreditering
- Nytten av internasjonale medforfattere
  - Både i tidlig og sen fase av studien
  - Fortolkning resultater
  - Implementering

Vellykket klinisk studie



- Egenfinansiering (EU/NORDFORSK/NFR etc)
- Forskerutdanning (PhD/Post.doc)
- Internasjonal forskningsfront - flaggskip
- Mobilitet av forskere/nettverk
- Innovasjon/patenter

- Publikasjoner på høyt nivå/riktig målgruppe
- Delta i samfunnsdebatt
- Kunnskapsgrunnlag for politiske beslutninger
- Formidling på internasjonale kongresser
- Pasienttidsskrifter/møter/web/sosiale medier

- Samhandling med pasienter/brukere
- Prosedyrer (lokale/nasjonale)
- Retningslinjer (nasjonale/internasjonale)
- Kommersialisering/verdiskapning

- Burden-of-disease
- Mortalitet/morbiditet
- Livskvalitet
- Fysisk funksjon
- Arbeidslivsdeltakelse
- Sosial fungering

Er kliniske studier verdt innsatsen?

Kliniske studier skal besvare spørsmål som:

- Virker en behandling?
- Virker behandlingen bedre enn andre behandlinger?
- Har den bivirkninger?
- Er behandlingen kostnadseffektiv?

Resultatene fra en vellykket klinisk studie
bør endre klinisk praksis –
da er det verdt innsatsen å gjennomføre studien!

Oppsummering

- Problemstilling
  - Må være klart definert
- Klinisk relevans/pasientgrunnlag/nytteverdi
  - Endre klinisk praksis
- Forankring i sykehuset
  - Følge lokale prosedyrer
- Ressurser (personale, tid)
  - Planlegg nøye
- Forankring i klinikken
  - Involver klinikere, sykepleiere, sekretærer, lab, rtg etc.
- Forfatterskap/vitenskapelig samarbeid
  - Avklare tidlig vs. sent
  - Krav fra finansieringskilde?
- Prosjektskisse
  - Synopsis – fint utgangspunkt
  - Skille mellom prosjektsøknad og full protokoll

Takk for oppmerksomheten!