

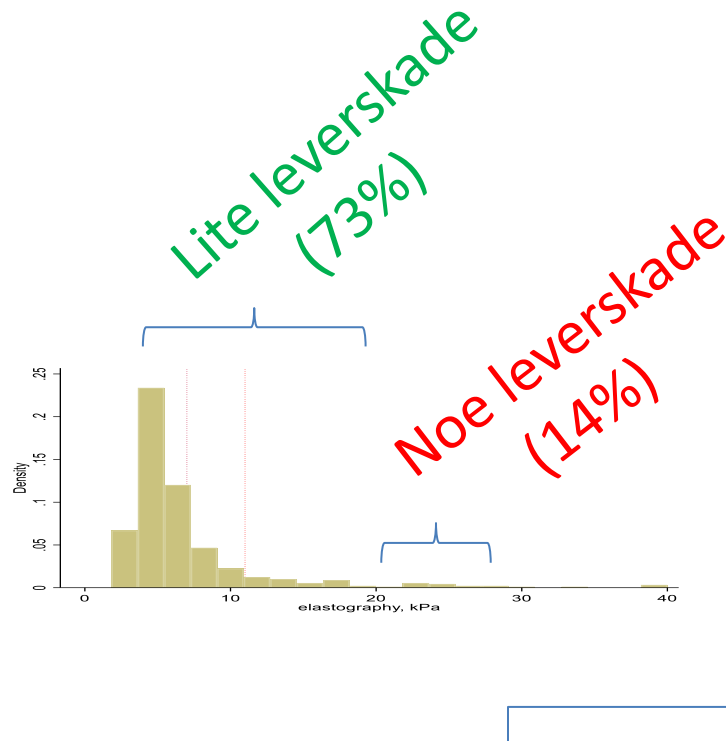


*Hva er effekten  
av integrert behandling?*

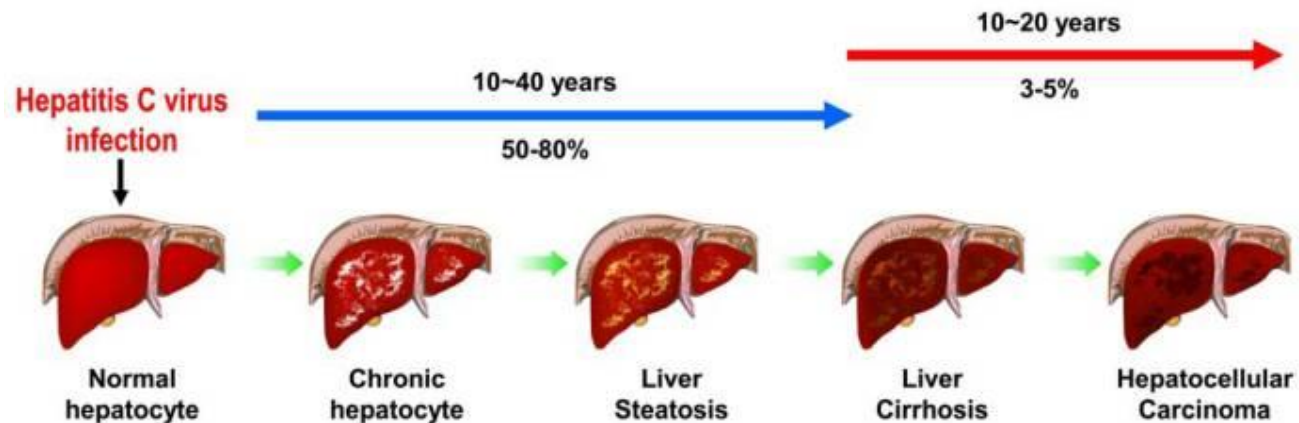
Lars T. Fadnes

Haukeland University hospital (research group leader of BAR) and University of Bergen (professor)

# Bakgrunn



- 54% påvist HCV (2017/8)
- 84% har hatt eller har HCV
- <1 % syfilis eller HIV
- 2-3% aktiv hepatitt B (HBsAg)



# Kartlegging

Årlig helseundersøkelse (800 kartlagt)

Intervju og undersøkelse av sykepleier/lege

Blodprøver

Elastografi (ultralydbasert)



**HELSE BERGEN**  
Haukeland universitetssjukehus









BERGEN KOMMUNE



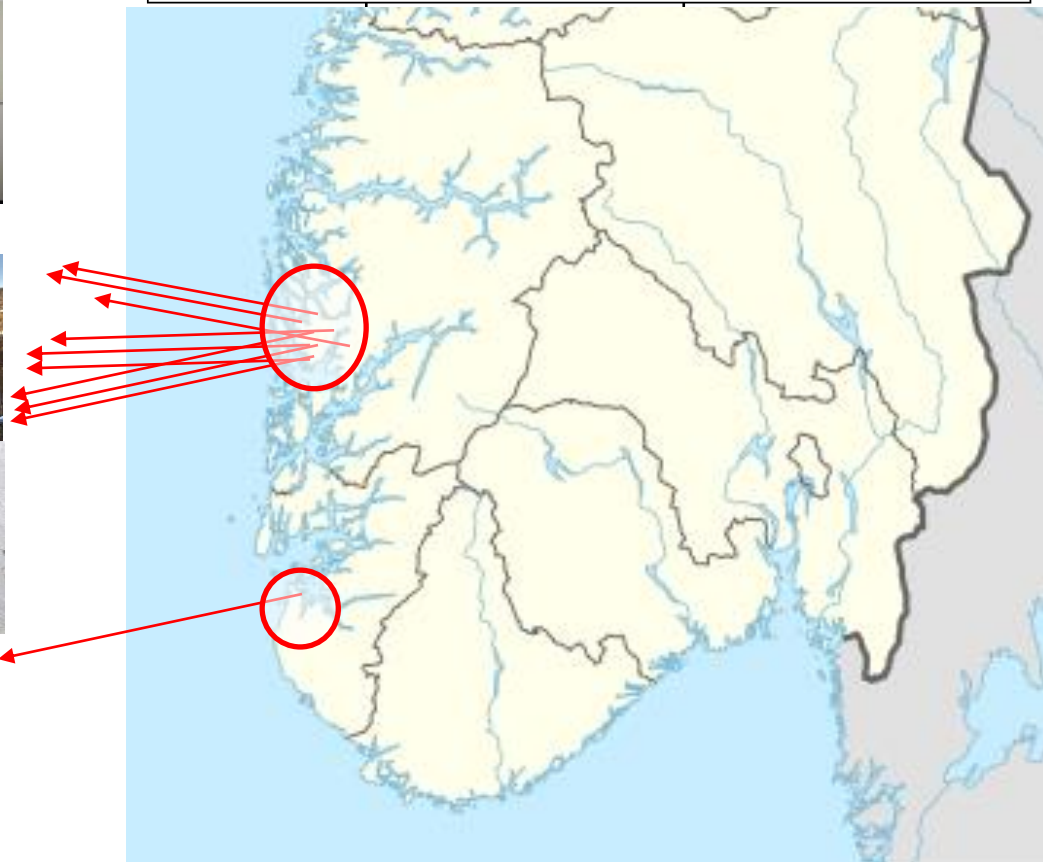
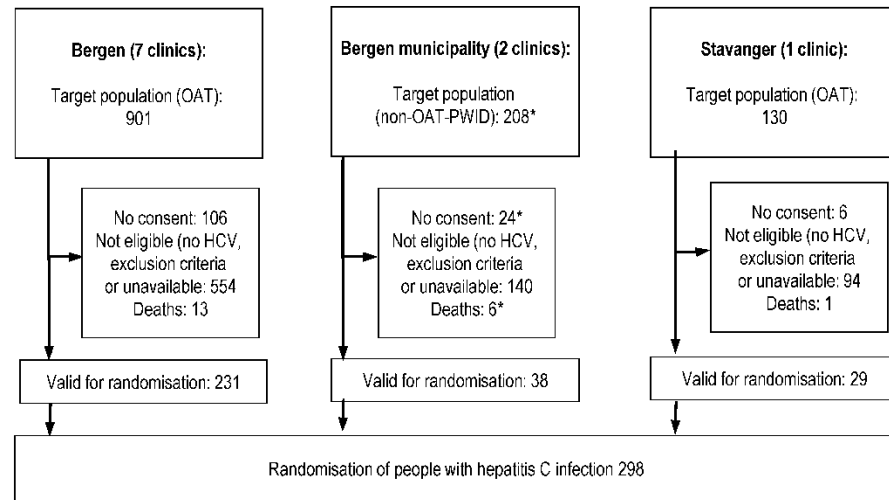
**HELSE STAVANGER**  
Stavanger universitetssjukehus



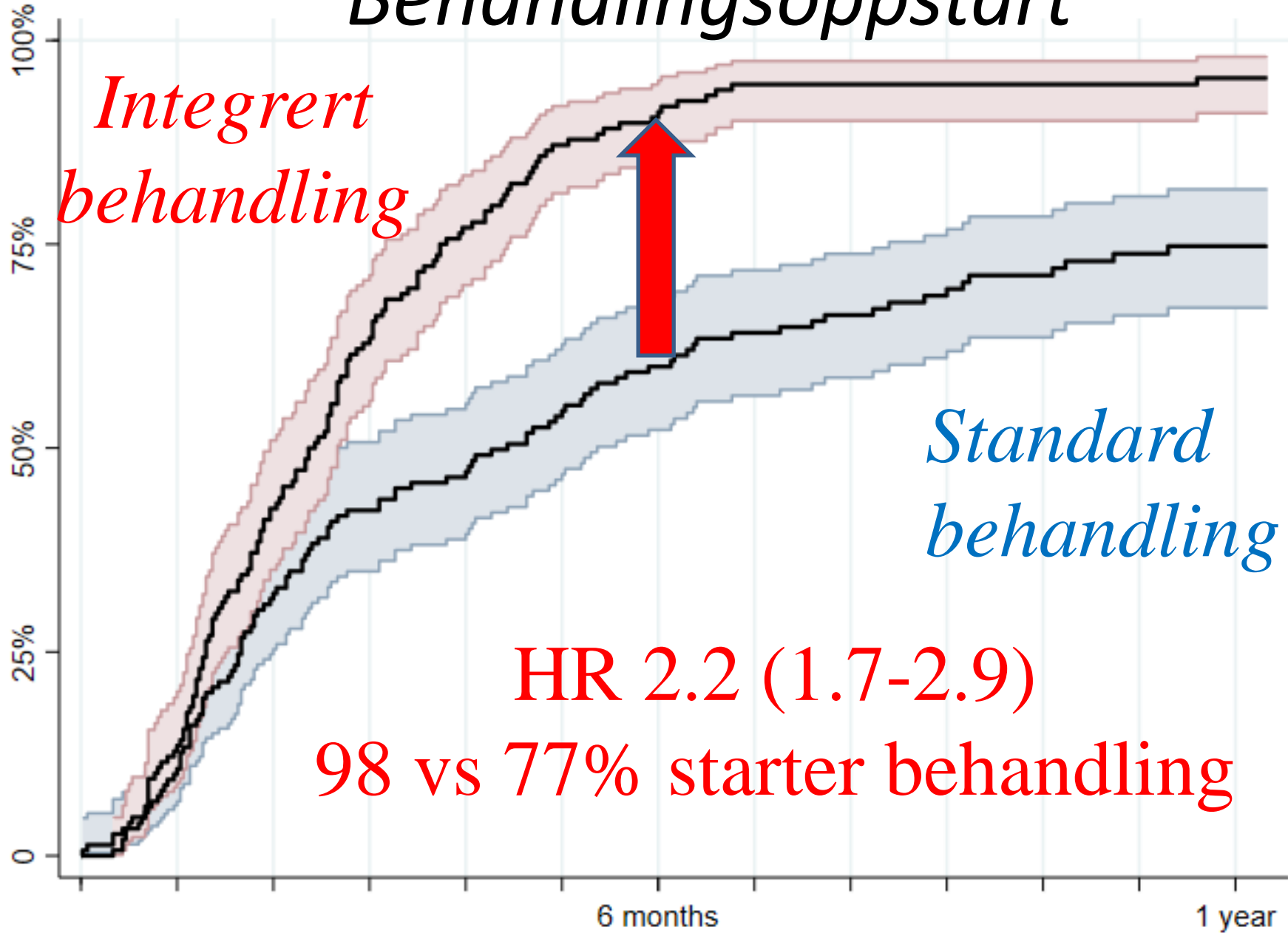
UNIVERSITETET I BERGEN







# Behandlingsoppstart



*Integrert  
behandling*

*Standard  
behandling*

**HR 2.2 (1.7-2.9)**

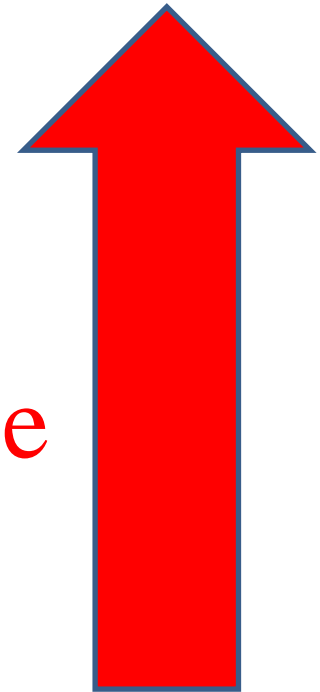
**98 vs 77% starter behandling**

# *HCV virusfrihet*

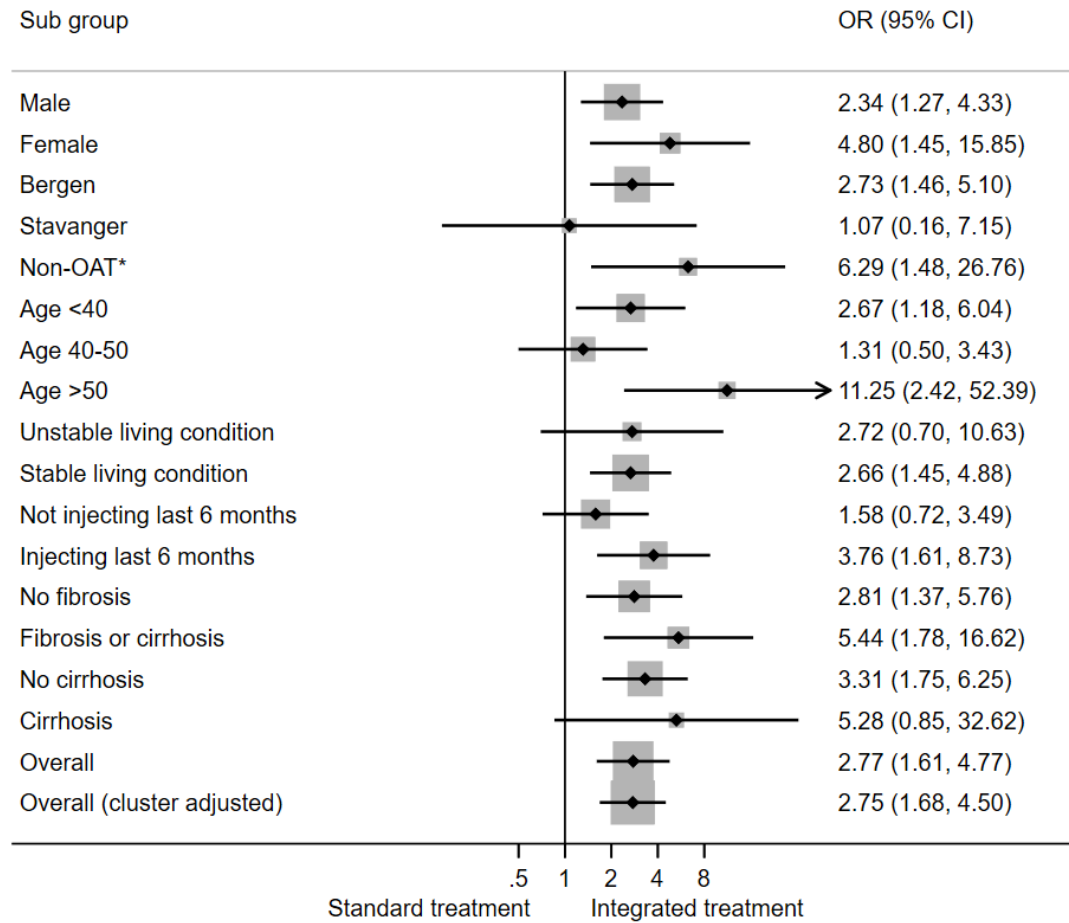
*Integrert vs. standard behandling*

20% økning i virusfrihet

93 vs 73% som testede virusfrie  
(OR 5.0, 2.3-11)

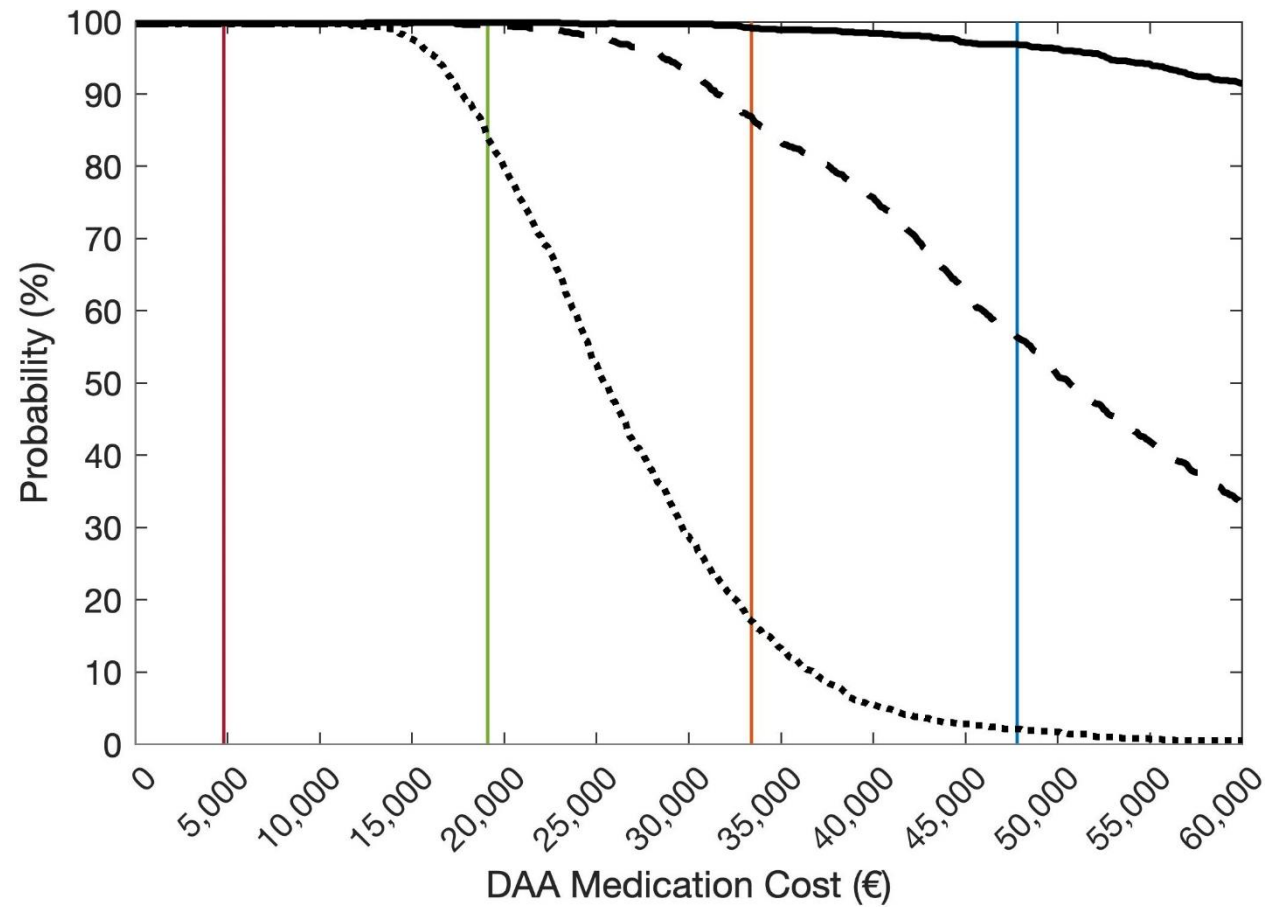






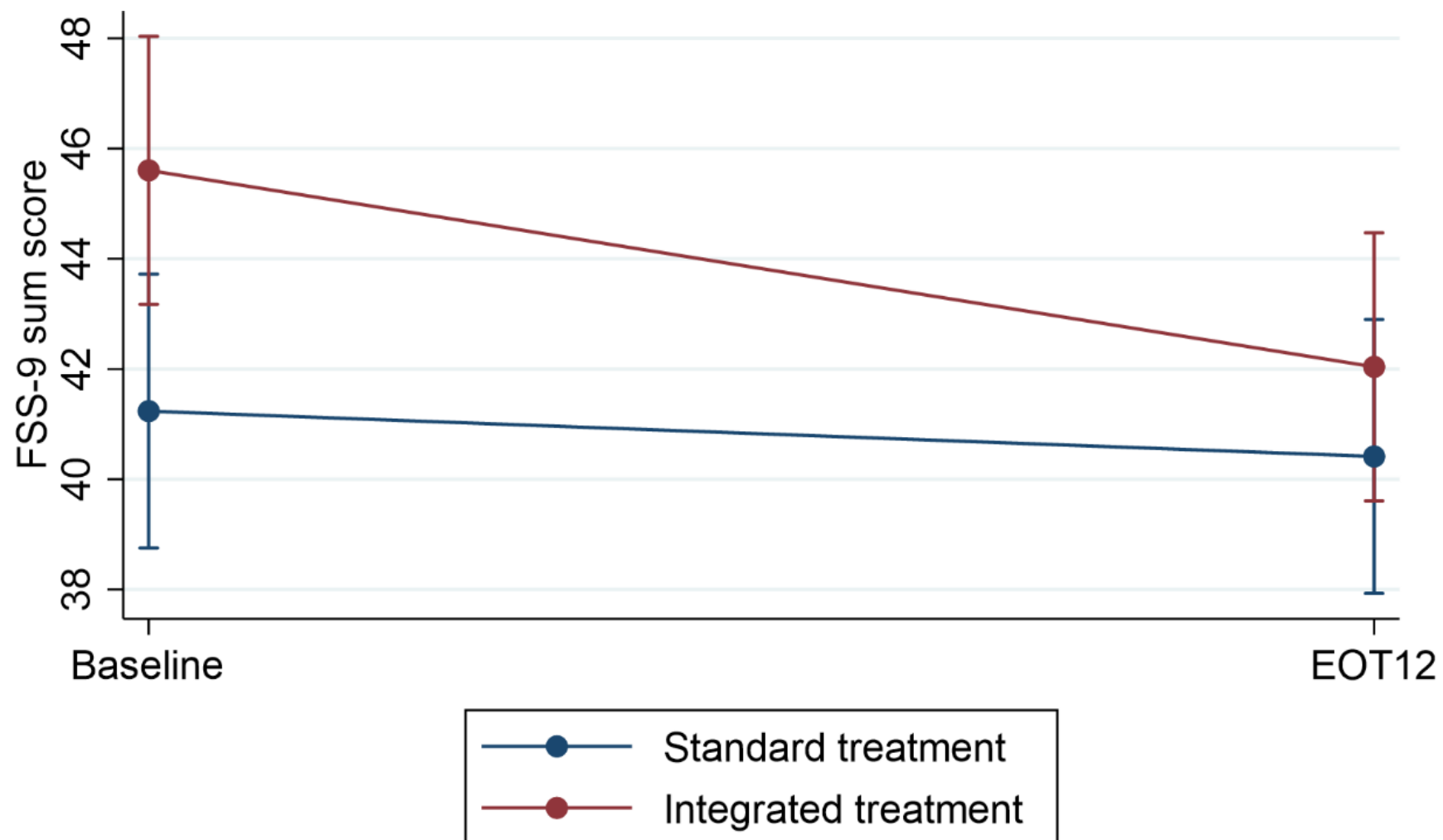
*Hvilke grupper*

# *Kostnadseffektivitet av integrert HCV behandling*

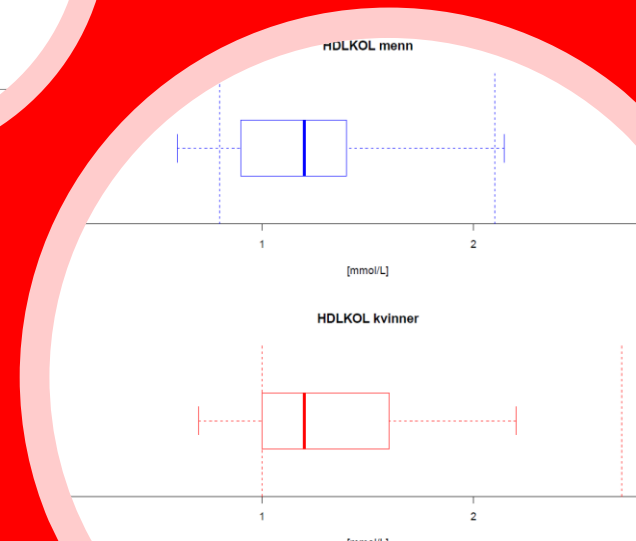
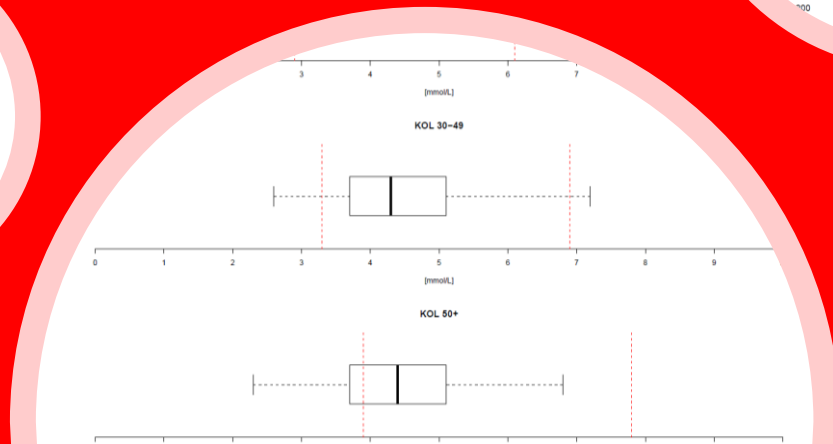
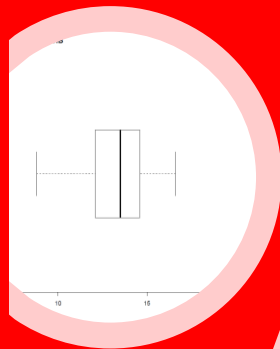
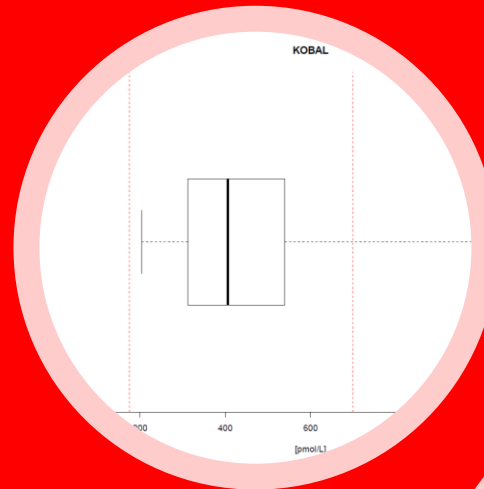
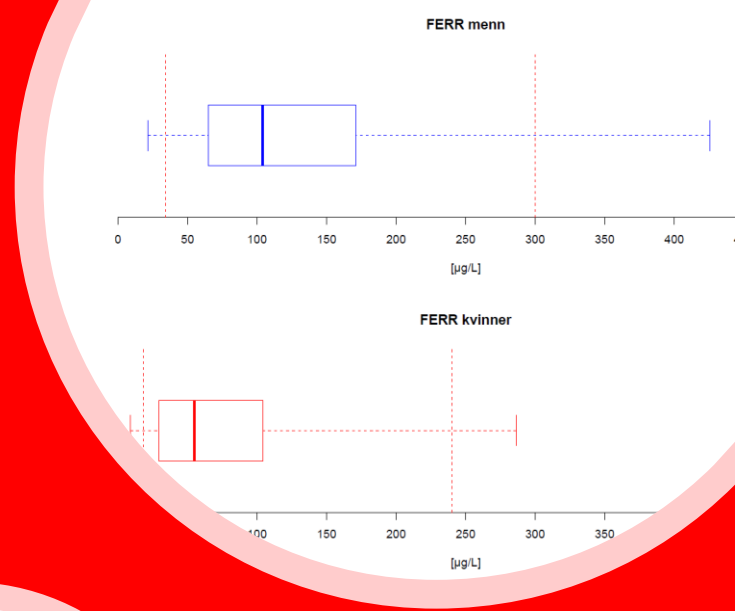
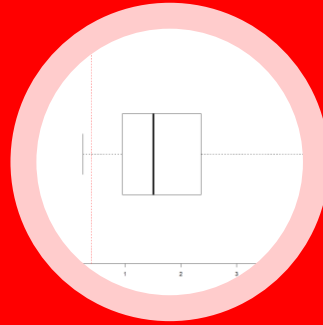


- Probability Cost-Effective At Conventional WTP Threshold (€70,000/QALY)
- - Probability Cost-Effective At Lower WTP Threshold (€20,000/QALY)
- ..... Probability Cost-Saving
- Current DAA Costs (List Price: €47,800)
- Cheaper DAA Drug Costs (30% Less: €33,400)
- Cheaper DAA Drug Costs (60% Less: €19,100)
- Cheaper DAA Drug Costs (90% Less: €4,800)

# Integrert HCV behandling og fatigue



# Prøver i LAR helseundersøkelse





Integrated care of severe infectious diseases to people with substance use disorders; a systematic review

Jam Henrik Vold<sup>1,2\*</sup>, Christer Aas<sup>1,2</sup>, Ralfat Alexander Lera<sup>1</sup>, Peter Vikström<sup>3,4</sup>, Fatemeh Chahabianloo<sup>1,2</sup>, Eide Marie Leberg<sup>1,2</sup>, Kjell Arne Johansson<sup>1,2</sup> and Lars Thore Fadnes<sup>1,2</sup>

**Abstract** Various integrated care models have been used to improve treatment completion of medications for chronic hepatitis B virus (HBV), chronic hepatitis C virus (HCV), Mycobacterium tuberculosis (MTB), and human immunodeficiency virus (HIV) among people with substance use disorders (SUD). We have conducted a systematic review to evaluate whether integrated models have impacts on the treatment of infectious diseases among incarcerated people with SUD. The included studies were assessed qualitatively. **Methods:** We searched MEDLINE/PubMed (1946 to 2018), on July 26, 2018 and Embase from 1914 to 2018, on July 26, 2018 for randomised controlled trials (RCTs) and other studies evaluating diverse integrated models effects on sustained virological response (SVR), HIV suppression, HBV cessation or suppression, completion of TB treatment regimen among people with SUD. The included studies were assessed qualitatively. **Results:** Altogether, 1960 studies, and references to 1113 related reviews, and RCTs were considered and only seven RCTs and three cohort studies fulfilled the inclusion criteria. We identified nine integrated care models. Two studies, one RCT and one cohort study, showed a significant effect of their integrated models. The RCT evaluated psychosocial treatment, opioid agonist treatment (OAT) and directly observed TB treatment, and found a significant increase in TB treatment completion among intervention group compared to control group (60% versus 19%, p < 0.01). The cohort study including OAT and TB treatment had an effect on TB treatment completion in hospitalized patients (20% versus 7%, p < 0.01). Eight out of ten studies showed no significant effects of their integrated care models on defined outcomes. One of which having included for HCV showed no effect on SVR compared to the control group when the results adjusted for active substance use and alcohol dependence in a per-protocol analysis (17% versus 7%, p = 0.48). **Conclusions:** The findings indicate uncertainty on the effects of integrated care models on treatment for severe infectious diseases among people with SUD. Some studies point toward that integrated models could improve care of people with SUD yet high-quality studies and preferably, preferably sized clinical trials are needed to conclude on the degree of impact. **Keywords:** Hepatitis C, human immunodeficiency virus, Mycobacterium tuberculosis, integrated care, Collaborative L.A. Substance use disorder, Epidemiology, Systematic review

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Dental health care workers' attitude towards patients with substance use disorders in medically assisted rehabilitation (MAR)

Anne Nordrehaug Aatrem, Ferda Ozkaya, Jorma Virtanen & Lars Thore Fadnes

Aas et al. Substance Abuse Treatment, Prevention, and Policy (2018) 13:48  
https://doi.org/10.1186/s12927-018-0140-7

Health-related quality of life of long-term patients receiving opioid agonist therapy: a nested prospective cohort study in Norway

Christer Aas<sup>1,2\*</sup>, Jam Henrik Vold<sup>1,2</sup>, Svetlana Skurtveit<sup>3,4</sup>, Arsen G. Levit<sup>5</sup>, Sabine Barthel<sup>6,7</sup>, Harald Malm<sup>8,9</sup>, Jan Erik Aalviksøyr<sup>10</sup>, Eide Marie Leberg<sup>1,11,12</sup>, Lars Thore Fadnes<sup>1,2</sup>, Kjell Arne Johansson<sup>1,2</sup> and for the INTRIO-HCV Study Group

**Abstract** Opioid dependence carries the highest disease burden of all illicit drugs. Opioid agonist therapy (OAT) is an evidence-based medical intervention that reduces morbidity and mortality. There is limited knowledge of the health-related quality of life (HRQL) of long-term patients in OAT. This study measures HRQL and self-perceived health of long-term patients on OAT, compares the scores to a Norwegian reference population, and

BMC Infectious Diseases

Integrated treatment of hepatitis C virus infection among people who inject drugs: study protocol for a randomised controlled trial (INTRIO-HCV)

Lars T. Fadnes<sup>1,2\*</sup>, Christer Aas<sup>1,2</sup>, Jam Henrik Vold<sup>1,2</sup>, Christer Ochiaick<sup>1</sup>, Ralfat Alexander Lera<sup>1</sup>, Fatemeh Chahabianloo<sup>1,2</sup>, Svetlana Skurtveit<sup>3,4</sup>, Ole Jørgen Ljøvnes<sup>5</sup>, Olav Dalgjard<sup>6</sup>, Peter Vikström<sup>3,4</sup>, Harald Malm<sup>8,9</sup>, Eide Marie Leberg<sup>1,11,12</sup>, Kjell Arne Johansson<sup>1,2</sup> and for the INTRIO-HCV Study Group

**Background:** A large proportion of people who inject drugs (PWID) living with hepatitis C virus (HCV) infection have not been treated. It is unknown whether inclusion of HCV diagnosis and treatment into integrated substance use disorder treatment and care clinics will improve uptake and outcome of HCV treatment in PWID. The aim is to assess the efficacy of integrating HCV treatment to PWID and this paper will present the protocol for an ongoing trial. **Methods:** INTRIO-HCV is a multicentre, randomised controlled clinical trial that will compare the efficacy of integrated treatment of HCV in PWID with the current standard treatment. Integrated treatment include testing for HCV, assessing blood fibrosis with transient elastography, counselling, treatment delivery, follow-up and evaluation provided by integrated substance use disorder treatment and care clinics. Most of these clinics for PWID provide opioid agonist therapy while some clinics provide methadone therapy without opioid agonist therapy. Standard care includes referral to further diagnosis, treatment and treatment follow-up given in a hospital outpatient clinic with equivalent medications. The difference between the delivery platform in the two trial arms include use of a drop-in approach rather than specific appointment times, no need for additional travelling, less blood sample taken during treatment, and treatment given from directly involved clinicians. The trial will recruit approximately 200 HCV infected individuals in Bergen and Stavanger, Norway. The primary outcome, as time to treatment initiation and sustained virologic response, defined as undetectable HCV RNA 12 weeks after end of treatment. Secondary outcomes are cost-effectiveness, treatment adherence, changes in quality of life, fatigue and psychological well-being, changes in drug use, injection related risk behaviour, and risk of reinfection. The target group is PWID with HCV diagnosed receiving treatment and care within clinics for PWID. **Discussion:** This study will inform on the effects of an integrated treatment program for HCV in clinics for PWID compared to standard care aiming to increase uptake and improving treatment adherence. If the integrated treatment model is found to be safe and efficacious, it can be considered for further roll-out. **Trial registration:** ClinicalTrials.gov, NCT03159506

**Keywords:** Chronic hepatitis C, Opioid substitution treatment, Integrated health care, Substance abuse treatment centres

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Too much or too little opioids to patients receiving opioid agonist therapy in Norway (2013–2017): a prospective cohort study

Jam Henrik Vold<sup>1,2\*</sup>, Svetlana Skurtveit<sup>3,4</sup>, Christer Aas<sup>1,2</sup>, Kjell Arne Johansson<sup>1,2</sup> and Lars Thore Fadnes<sup>1,2</sup>

Vold et al. BMC Health Services Research (2018) 18:262  
https://doi.org/10.1186/s12916-018-0226-y

Too much or too little opioids to patients receiving opioid agonist therapy in Norway (2013–2017): a prospective cohort study

**Abstract** Dispensations of opioid agonists to patients on opioid agonist therapy (OAT) may increase the risk of overdose. The current study objectives are to investigate the dispensation rates and mean daily dose of dispensed opioid agonists among patients who received OAT agonists in Norway during 2013–2017 and evaluate whether discontinuing OAT agonists affects the dispensation dose of opioid agonists. **Methods:** Information on opioids was collected from the Norwegian Prescription Database. Dispensation rates were calculated by dividing the number of patients who were dispensed at least one opioid agonist by the total number of patients on OAT agonist. We also calculated the mean daily dose of dispensed agonists in and morphine equivalents. The OAT agonist dose was defined as a ratio between the dispensation of an opioid agonist, a dose of OAT agonist, having chronic pain, and being on palliative care. **Results:** A total of 1037 patients were dispensed OAT agonists during the study period. In 2013–196 were dispensed an opioid agonist, with a mean daily dose of 20 mg of oral morphine equivalents. Being dispensed an opioid agonist was associated with being chronic pain (adjusted odds ratio (aOR) 1.2, 95% confidence interval (CI) 1.2–1.3), being on palliative care (aOR 4.4, 95% CI 3.8–5.0), and receiving an OAT agonist dose below half of the recommended OAT agonist dose (aOR 0.5, 95% CI 0.4–0.6). Strongly results were seen in 2013–2014. The discontinuation of OAT agonist could increase the dose of dispensed opioid agonists.

BMC Health Services Research

Dispensations of benzodiazepines, z-hypnotics, and gabapentinoids to pain-receiving opioid agonist therapy; a prospective cohort study in Norway 2013 to 2017

Jam Henrik Vold<sup>1,2\*</sup>, Svetlana Skurtveit<sup>3,4</sup>, Christer Aas<sup>1,2</sup>, Fatemeh Chahabianloo<sup>1,2</sup>, Kjell Arne Johansson<sup>1,2</sup> and Lars Thore Fadnes<sup>1,2</sup>

**Abstract** Dispensations of benzodiazepines, z-hypnotics, and gabapentinoids to therapy (OAT) are common and have pros and cons. The objectives of the current study are to investigate the dispensation rates of these potentially addictive drugs, and whether the number and dispensed OAT agonists and discontinuation OAT, are associated with being dispensed z and gabapentinoids among patients on OAT in Norway in the period 2013 to 2017. **Methods:** Information about all dispensed opioids, benzodiazepines, z-hypnotics and gabapentinoids among patients on OAT in Norway in the period 2013 to 2017. **Results:** Information about all dispensed opioids, benzodiazepines, z-hypnotics and gabapentinoids among patients on OAT in Norway in the period 2013 to 2017. The dispensation rates were defined as the number of patients who were dispensed a potentially addictive drug divided among the number of patients who have dispensed an OAT agonist. Mean daily doses were calculated, and for benzodiazepines and z-hypnotics equivalents. The association between dispensed potentially addictive drugs, and the dispensed OAT agonist were calculated by using logistic regression models. (Continued on next page)

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Dispensation of attention deficit hyperactivity disorder (ADHD) medication in patients receiving opioid agonist therapy; a national prospective study in Norway from 2015 to 2017

Jam Henrik Vold<sup>1,2\*</sup>, Christer Aas<sup>1,2</sup>, Svetlana Skurtveit<sup>3,4</sup>, Ingvild Odaick<sup>5</sup>, Kjell Arne Johansson<sup>1,2</sup> and Lars Thore Fadnes<sup>1,2</sup>

Vold et al. BMC Psychiatry (2018) 20:119  
https://doi.org/10.1186/s12916-018-0226-y

Dispensation of attention deficit hyperactivity disorder (ADHD) medication in patients receiving opioid agonist therapy; a national prospective study in Norway from 2015 to 2017

**Abstract** It is estimated that up to a third of patients on opioid agonist therapy (OAT) receive attention deficit hyperactivity disorder (ADHD) medication, including atomoxetine as one of the essential approaches. This study evaluated the dispensation of attention deficit hyperactivity disorder (ADHD) medication in patients receiving opioid agonist therapy in Norway from 2015 to 2017. Types of dispensed ADHD medication were estimated by summing the number of dispensed ADHD medications. Logistic regression analyses were employed to assess the association of ADHD medication with chronic pain, and dispensation of other potentially addictive drugs and OAT agonist. (Continued on next page)

Substance Abuse Treatment, Prevention, and Policy

Peer involvement and cross-sector efforts in establishing integrated treatment of hepatitis C virus infection for people with substance use disorders: experiences from Norway

Ole Jørgen Ljøvnes<sup>1\*</sup>, Rasmus Børnøsen<sup>2,3</sup>, Eide Marie Leberg<sup>1,2</sup>, Martin Løyen Børnøsen<sup>4</sup>, Vidar Eldredh Subject<sup>5</sup>, Kjell Arne Johansson<sup>1,2</sup>, Lars T. Fadnes<sup>1,2</sup> and for the INTRIO-HCV Study Group

**Abstract** For people with opioid dependence in Norway, chronic hepatitis C virus (HCV) infection contributes to high morbidity and high mortality. Around 80% of patients in medically assisted rehabilitation (MAR) have been shown to have HCV, and the current prevention and control efforts have been mostly unsuccessful. Thus, there is a need for new strategies to prevent onward virus delivery and increase uptake of integrated health care services. **Methods:** Over the last ten years the city of Bergen, Norway, has developed a cross-sector collaboration with the aim of peer involvement in research and health promotion related to substance use. One approach is to engage individuals with addiction through the health promotion. This study reports on the municipality, low-threshold health care services for people with substance use disorders in Bergen. Municipality and members of the INTRIO-HCV patient have conducted efforts to support the development and implementation of the INTRIO-HCV study. **Results:** We have established an integrated HCV treatment platform for people who inject drugs in one of the largest municipalities. More than 800 persons have been tested for HCV within three months, and more than 200 persons have been treated for HCV within the project. The integrated treatment of HCV is offered both in MAR outpatient clinics, municipal low-threshold health care services, and local and regional prisons. The primary aim is to increase the uptake of HCV treatment among those seeking integrated treatment. Secondary objectives were to assess the engagement of people with substance use disorders in research, health promotion and policy planning, support networks and policy changes (see text). (Continued on next page)

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Integrated treatment of hepatitis C virus infection among people who inject drugs: A multicenter randomized controlled trial (INTRIO-HCV)

Lars T. Fadnes<sup>1,2\*</sup>, Christer Aas<sup>1,2</sup>, Jam Henrik Vold<sup>1,2</sup>, Christer Ochiaick<sup>1</sup>, Ralfat Alexander Lera<sup>1</sup>, Fatemeh Chahabianloo<sup>1,2</sup>, Svetlana Skurtveit<sup>3,4</sup>, Ole Jørgen Ljøvnes<sup>5</sup>, Olav Dalgjard<sup>6</sup>, Peter Vikström<sup>3,4</sup>, Harald Malm<sup>8,9</sup>, Eide Marie Leberg<sup>1,11,12</sup>, Kjell Arne Johansson<sup>1,2</sup> and for the INTRIO-HCV Study Group

**Background:** A large proportion of people who inject drugs (PWID) living with hepatitis C virus (HCV) infection have not been treated. It is unknown whether inclusion of HCV diagnosis and treatment into integrated substance use disorder treatment and care clinics will improve uptake and outcome of HCV treatment in PWID. The aim is to assess the efficacy of integrating HCV treatment to PWID and this paper will present the protocol for an ongoing trial. **Methods:** INTRIO-HCV is a multicentre, randomised controlled clinical trial that will compare the efficacy of integrated treatment of HCV in PWID with the current standard treatment. Integrated treatment include testing for HCV, assessing blood fibrosis with transient elastography, counselling, treatment delivery, follow-up and evaluation provided by integrated substance use disorder treatment and care clinics. Most of these clinics for PWID provide opioid agonist therapy while some clinics provide methadone therapy without opioid agonist therapy. Standard care includes referral to further diagnosis, treatment and treatment follow-up given in a hospital outpatient clinic with equivalent medications. The difference between the delivery platform in the two trial arms include use of a drop-in approach rather than specific appointment times, no need for additional travelling, less blood sample taken during treatment, and treatment given from directly involved clinicians. The trial will recruit approximately 200 HCV infected individuals in Bergen and Stavanger, Norway. The primary outcome, as time to treatment initiation and sustained virologic response, defined as undetectable HCV RNA 12 weeks after end of treatment. Secondary outcomes are cost-effectiveness, treatment adherence, changes in quality of life, fatigue and psychological well-being, changes in drug use, injection related risk behaviour, and risk of reinfection. The target group is PWID with HCV diagnosed receiving treatment and care within clinics for PWID. **Discussion:** This study will inform on the effects of an integrated treatment program for HCV in clinics for PWID compared to standard care aiming to increase uptake and improving treatment adherence. If the integrated treatment model is found to be safe and efficacious, it can be considered for further roll-out. **Trial registration:** ClinicalTrials.gov, NCT03159506

**Keywords:** Chronic hepatitis C, Opioid substitution treatment, Integrated health care, Substance abuse treatment centres

**Background:** The current study objectives are to investigate the dispensation rates and mean daily dose of dispensed opioid agonists among patients who received OAT agonists in Norway during 2013–2017 and evaluate whether discontinuing OAT agonists affects the dispensation dose of opioid agonists. **Methods:** Information on opioids was collected from the Norwegian Prescription Database. Dispensation rates were calculated by dividing the number of patients who were dispensed at least one opioid agonist by the total number of patients on OAT agonist. We also calculated the mean daily dose of dispensed agonists in and morphine equivalents. The OAT agonist dose was defined as a ratio between the dispensation of an opioid agonist, a dose of OAT agonist, having chronic pain, and being on palliative care. **Results:** A total of 1037 patients were dispensed OAT agonists during the study period. In 2013–196 were dispensed an opioid agonist, with a mean daily dose of 20 mg of oral morphine equivalents. Being dispensed an opioid agonist was associated with being chronic pain (adjusted odds ratio (aOR) 1.2, 95% confidence interval (CI) 1.2–1.3), being on palliative care (aOR 4.4, 95% CI 3.8–5.0), and receiving an OAT agonist dose below half of the recommended OAT agonist dose (aOR 0.5, 95% CI 0.4–0.6). Strongly results were seen in 2013–2014. The discontinuation of OAT agonist could increase the dose of dispensed opioid agonists.

Evaluere nå nye intervensjoner i samme gruppe for å teste en bredere behandlingstilnærming

- Nikotinsubstitusjon
- Aktivitetsgrupper
- Fruktsmoothie

Først pilotert, oppskaleres nå i multimodal intervensjonsstudie



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