Rigshospitalet
Centre for Cancer and Organ Diseases

UNIVERSITY OF COPENHAGEN
FACULTY OF HEALTH AND MEDICAL SCIENCES

A research protocol on opioid addiction

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Background

- A cornerstone in palliative medicine
- Denmark, one of the highest legal opioid consumptions worldwide
- The evidence regarding the possible consequences of long-term opioid treatment (L-TOT)
- Prevalence of opioid addiction: >20% in chronic non-cancer pain (CNCP) and around 20% in patients with cancer-related pain

World Health Organization, 1996
Sundhedsstyrelsen, 2018
Birke et al., 2017
Elsesser and Cegla, 2017
Højsted et al., 2013
Yennurajalingam et al., 2018

Why is this study protocol important?

Longer life expectance and higher survivor rates among patients with cancer

The high consumption of opioids in CNCP

The abuse liability of opioids and the possible consequences

Research plan

- Three protocols based on former research experience in pain and opioids
- Studies of not only national interest
- The studies will provide information on the risk factors and consequences of L-TOT to develop more targeted therapies for patients suffering from cancer and CNCP

Hypotheses for research program

1. L-TOT for CNCP is associated with ↑mortality, ↑morbidity, adverse life-style behavior, and ↑use of health care services

2. Postoperative pain management may substantially contribute to L-TOT

3. The prevalence of iatrogenic opioid addiction in patients in L-TOT for cancer-related pain is of similar extent as the prevalence in patients with CNCP

4. The immune and endocrine systems are suppressed by L-TOT, which may affect cognitive function, pain, sleep, and quality of life

5. A program consisting of specialized pain treatment, systematic opioid reduction/substitution, and additional cognitive-behavioral intervention can be effective in tapering off opioids, benzodiazepines/benzodiazepine-like hypnotics and/or cannabinoids

Study 1
Epidemiologic study

Study 2
Iatrogenic opioid addiction
(clinical study)

Study 3
The immune and endocrine systems
(clinical study)

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- Mortality
- Lifestyle behaviors
- Morbidity
- Use of health care services

- Selected surgical procedures and the initiation of L-TOT

Danish National Health Surveys in 2010 (N=298,550), 2013 (N=300,450), and 2017 (N=312,349) (≥16 years)

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- Prevalence study
- Genetic study
- Pilot study

Study 1
Epidemiologic study

Study 2
Iatrogenic opioid addiction
(clinical study)

Study 3
The immune and endocrine systems
(clinical study)

- Endocrine consequences
- Immune consequences
- Cognition, pain, sleep, mood and quality of life

Study 1
Epidemiologic study

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- Prevalence study
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Aims for study 2

- To identify and compare the prevalence of medication misuse risk among patients in L-TOT with CNCP and cancer-related pain
- To examine the prevalence of medication misuse risk assessed by Pain Medication Questionnaire (PMQ) and Portenoy's criteria
- To analyze risk factors for opioid misuse, including genetic variation
- To test an opioid taper off program in a pilot study of patients with CNCP

Methods

Prevalence studies
prospective, cross-sectional

L-TOT (≥ 60 mg morphine equivalents/day for ≥3 months)

Multidisciplinary Pain centre
n=245

Department of Oncology
n=245

Pilot Study
pre/post intervention
n=20

Independent variables:

-Sociodemographics

ependent variables (medication addiction):

f opioid misuse (PMQ)

d addiction classification (ICD-11, Portnoy's criteria)

Withdrawal symptoms (Subjective and Objective Opiate Withdrawal Scales)

-Aberrant behaviors (tobacco, alcohol, illicit drugs, benzodiazepines/like, cannabinoids)

- Genetic variations (biobank, Genome Analysis Toolkit)

Inclusion and exclusion criteria

Prevalence study - Inclusion criteria

1. Patients ≥ 18 years with cancer-related pain or CNCP
2. Patients should be on opioid therapy for at least 3 months at their respective treatment centers
3. They should be treated with at least 60 mg morphine equivalents /day at the inclusion time

Genetic study - Inclusion criteria

1. Blood sample

Prevalence study - Exclusion criteria

1. Patients who do not master the Danish language in speech and writing
2. Patients with a diagnosis of cognitive dysfunction
3. Patients in poor general condition, where it is estimated that the questionnaire would be a strain on the patient
4. Participation in other studies interfering with the present study

Inclusion and exclusion criteria

Pilot study - Inclusion criteria

1. No improvement in function or pain after at least 3 months of opioid treatment
2. Opioid treatment produces significant adverse effects or patient has experienced a severe adverse outcome or overdose event
3. Risk from continued treatment outweighs the benefit
4. Substance use disorder
5. Use of opioids is not in compliance with pain guidelines stablished by the Danish Health Authority
6. High risk for opioid addiction according PMQ
7. Patient wishes to discontinue the opioid treatment

Manchikanti et al 2012,
Højsted et al., 2018

Washington State Agency Medical Directors' Group 2015

Opioid taper off program

Pharmacological strategy

- Sequential tapering of ≤10% of the original dose per week for 4 months
- Tapering order: 1) opioids, 2) benzodiazepines, and 3) cannabinoids
- Withdrawal symptoms/opioid abstinence
- Rate, intensity, and duration of the tapering off

Kurita et al., 2018
Washington State Agency Medical Directors' Group 2015

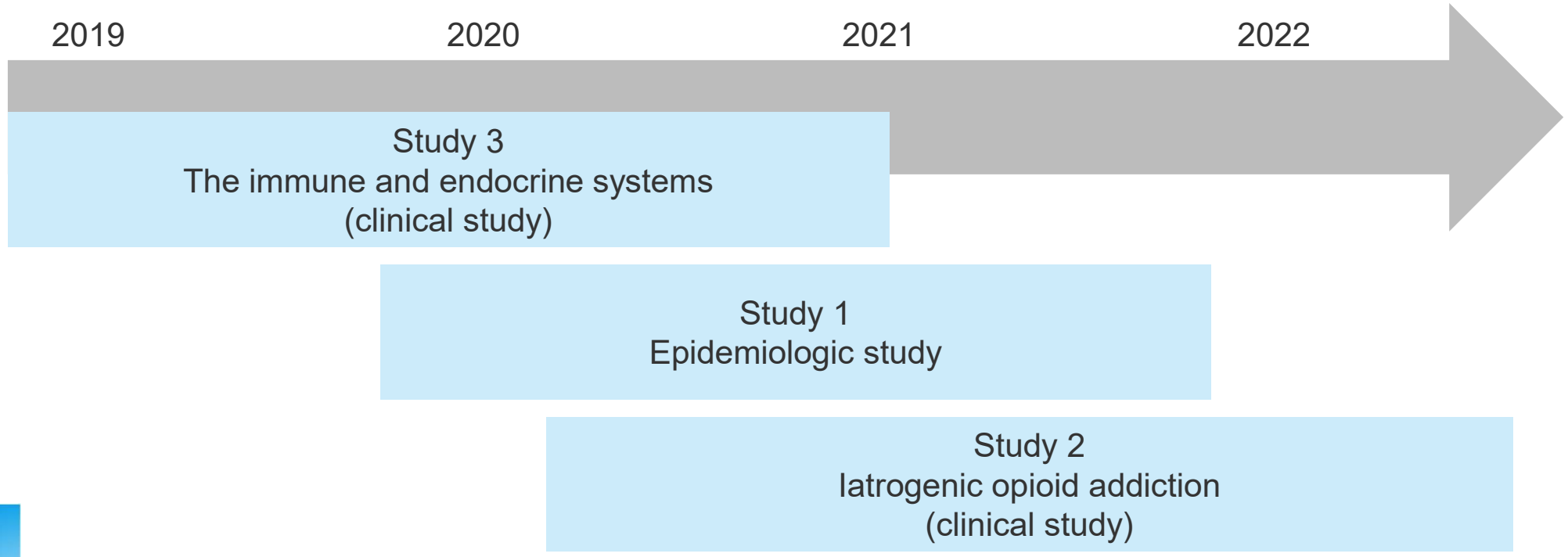
Opioid taper off program

Cognitive-behavioral/mindfulness strategy

- Nine sessions in two months (duration 2-3 hours)
- Session 1: Education in causes of pain, principles and aims of pain treatment, desired and undesired effects of analgesic medication
- Session 2-8: Integrative therapy with aspects of mindfulness training, cognitive-behavioral therapy, and principles from positive psychology administered by a psychologist

Garland et al., 2014

Timeframe


2019
2020
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2022
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