



# Ultra Low Dose Methadone as Coadjuvant Opioid Therapy for Cancer Pain: A Double Blind Randomized Controlled Trial

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## BACKGROUND

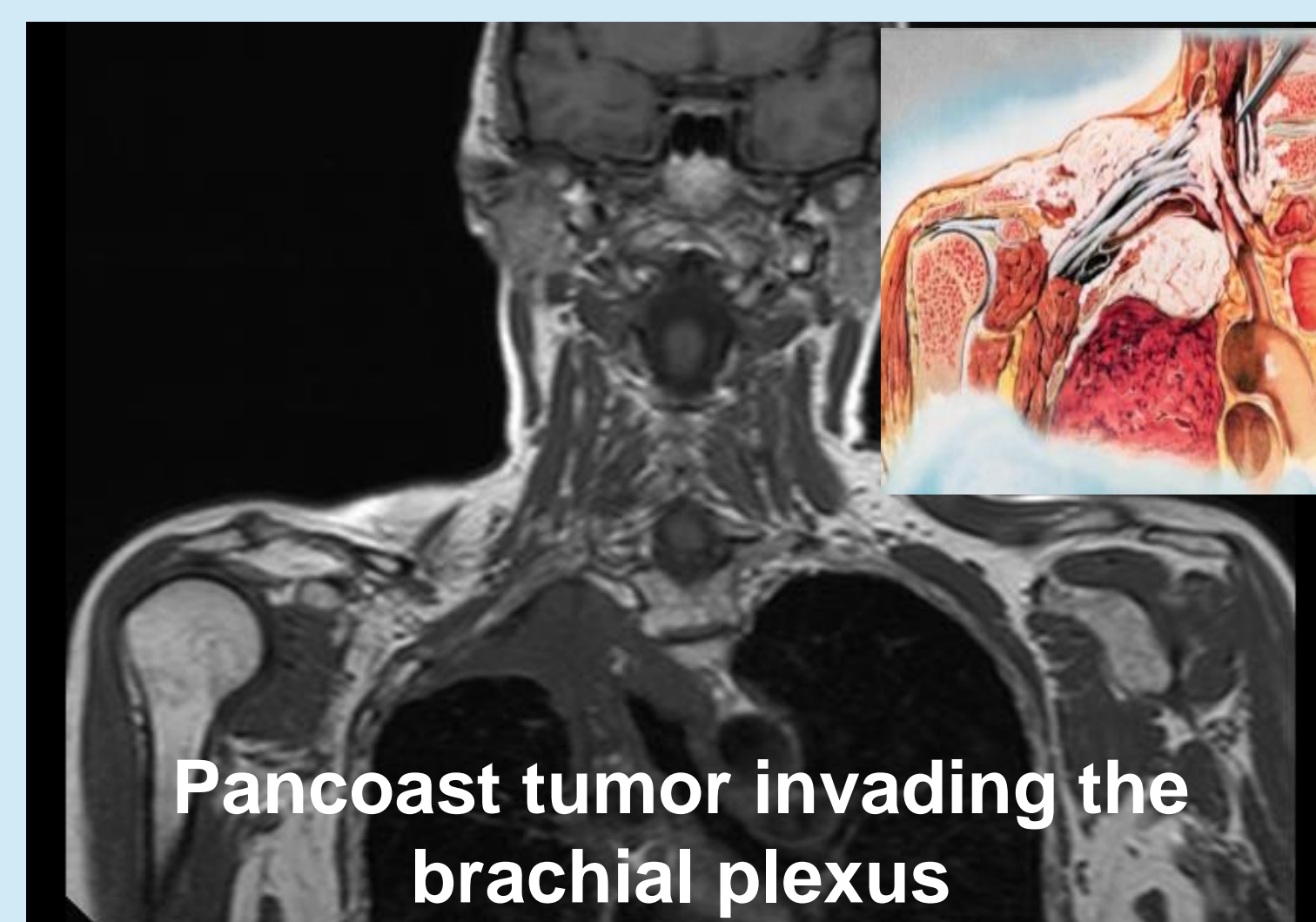
### Cancer Pain

Patients diagnosed with cancer report pain in average 50% cases. This prevalence is higher during treatment (59%) and in advanced stages (64%).

Opioid agents are analgesics strongly recommended to treat moderate to severe cancer-related pain by all scientific societies.

### Methadone for cancer pain

Methadone is an agent with particular pharmacological properties that provides analgesia where other opioids fail. In particular, methadone seems to possess analgesic properties in patients with neuropathic pain due to cancer related nerve damage (i.e peripheral neuropathy, rectal tumours, H&N cancer pain).



Pancoast tumor invading the brachial plexus



Peripheral neuropathy

The change of analgesic from a single opioid into methadone is called opioid rotation and requires careful calculation and slow titration to achieve adequate analgesia without causing opioid related side effects. This rotation is done by initiating with low doses of methadone while the primary opioid is slowly decreased.

Primary  
Opioid

Opioid rotation to Methadone

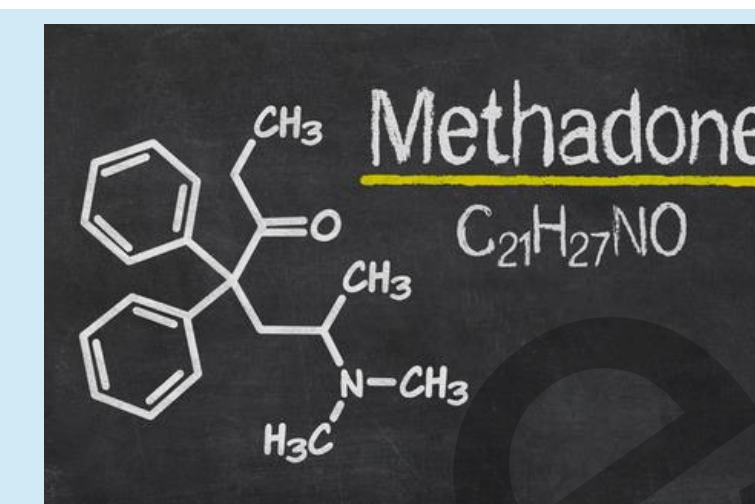
Methadone

### Coadjuvant methadone for cancer pain

Some patients experience satisfactory analgesia before completing the methadone rotation. This was explained by the co-administration of methadone and another opioid at lower doses. Small retrospective case series have demonstrated satisfactory analgesia with this combination with less side effects and lower consumption of PRN narcotics for pain management.

## HYPOTHESIS

In patients with moderate cancer-related pain, the addition of low dose methadone to another opioid significantly reduces pain severity compared to the addition of a placebo.



## OBJECTIVES

### Primary Objective

Reduction of average pain severity over the preceding 24 hours (measured with the Brief Pain Inventory: BPI).

### Secondary Objectives:

- Additional pain measurements: BPI (least, worst and now)
- Interference of pain on daily activities (measured by BPI)
- Cancer related symptoms measured by Edmonton Symptom Assessment Scale (ESAS)
- Total daily opioid dose (morphine equivalent daily dose: MEDD)
- Safety profile: drug related adverse events (DRAE)
- Patients' global impression of change (PGIC)

## METHODS / INTERVENTIONS (I)

### Patients included

- Adult patients presenting with moderate-severe cancer-related pain
- Cancer pain unsatisfactorily managed with opioids and coadjuvants



### Patients excluded

- Life expectancy <1 month
- Unstable opioid consumption for pain relief
- Severe kidney/liver impairment
- Patients receiving cancer treatment with potential analgesic effects <7 days before randomization or during study.



### Participating RCN Sites



MUHC Cancer Pain Clinic

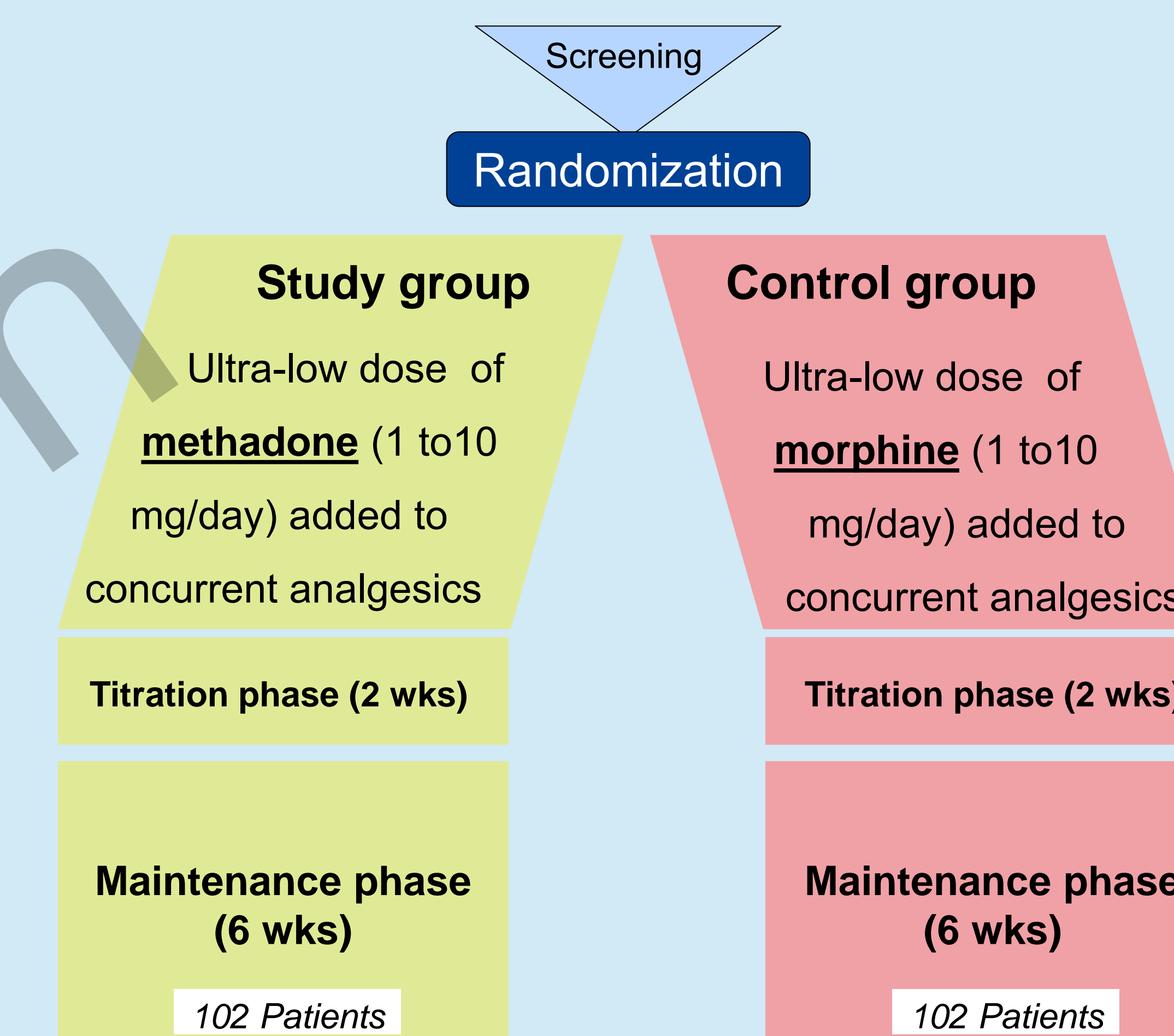


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## METHODS / INTERVENTIONS (II)

### Study design

Multicentre, double blind and randomized placebo-controlled clinical trial



## RESULTS

No results yet to be reported. Patient recruitment is on hold until final approval from health regulatory agencies to allow the use of controlled substances for research purposes.

## PATIENT IMPACT

A positive outcome would lead clinicians to implement low dose methadone combination as a routine tool to 1) enhance opioid analgesia, 2) decrease consumption of rescue analgesia with short acting opioid preparations and 3) avoid opioid induced side effects thus improving quality of life in patients with cancer pain.

## TRANSLATION ACROSS THE RCN

This research is a collaborative project between two RCN sites (RVH and JGH). Positive outcomes will be shared with the rest of RCN sites to encourage adopting this method into their routine clinical care.

A satisfactory collaboration across RCN sites could potentially encourage the creation of a new RCN tumour site ("Cancer Pain").