



ST VINCENT'S  
HEALTH AUSTRALIA



# Opioids and THC

Victorian Opioid Management ECHO  
Department of Addiction Medicine  
St Vincent's Hospital Melbourne 2021

UNDER THE STEWARDSHIP OF MARY AIKENHEAD MINISTRIES

# Is there a role for cannabis in pain mx?



- **Physiologically has potential to be less toxic analgesic option**
- **Very high therapeutic index**
  - Can be attributed in part to a lack of cannabinoid receptors in brainstem
  - Therefore lack of respiratory depression of significant adverse outcome
- **Compared to well established risks associated with escalating opioid use**
  - MED (**morphine equivalent dose**) of 50mg **doubles** risk of fatal overdose compared to MED of 20mg
  - MED of 90mg increase this risk by **10 times** [1]

[1] <https://www.cdc.gov/drugoverdose/deaths/prescription/index.html>

# Cannabinoids and pain modulation



- **Multiple proposed mechanisms for producing analgesia**

- Modulation of neuronal nociceptive (**pain**) processing
- Inhibition of pro-inflammatory molecule release
- Inhibition of mast cell activation (**inflammatory cascade**)
- Modulation of endogenous opioid receptors in primary afferent pathways

[2]

[2] <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6277878/>

# Cannabinoids and pain modulation



- **Not just limited to analgesia**

- May provide relief from symptoms commonly accompanying chronic pain
  - Nausea
  - Anxiety/depression
  - Insomnia [3]

[3] <https://pubmed.ncbi.nlm.nih.gov/18615144/>

# Cannabinoids with opioids - pre-clinical



- **Multiple pre-clinical studies have reported synergistic analgesic effects from cannabinoids with opioids [4], [5]**
  - Cannabinoid type 1 (CB<sub>1</sub>) receptor **antagonists** shown to potentially **reverse anti-nociceptive effects** of morphine demonstrating that endocannabinoid activity may affect morphine's action [6]

[4] <https://pubmed.ncbi.nlm.nih.gov/14706563/>

[5] <https://pubmed.ncbi.nlm.nih.gov/22048225/>

[6] <https://pubmed.ncbi.nlm.nih.gov/18469844/>

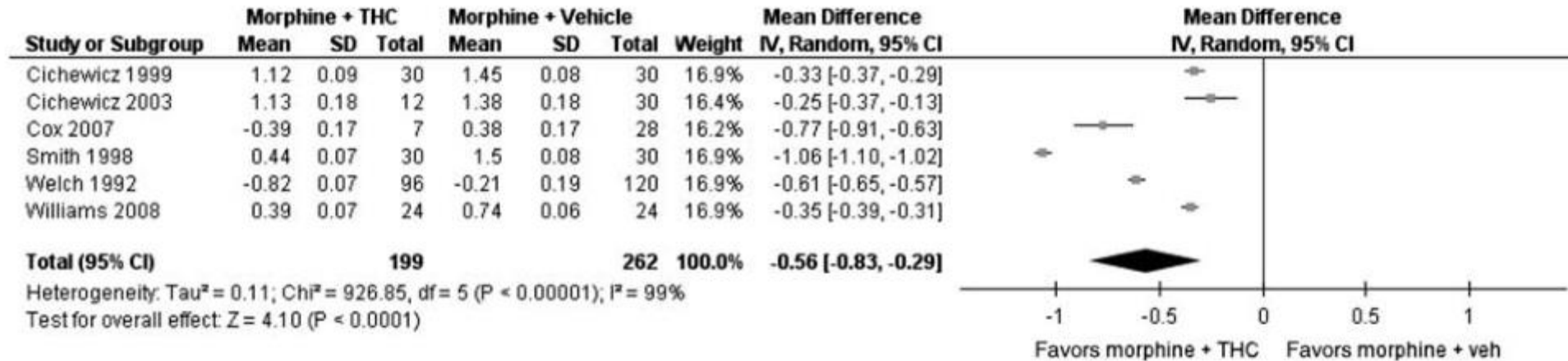
# Cannabinoids with opioids - pre-clinical



- **A systematic review in 2017 found 17 of 19 pre-clinical studies confirmed synergistic effects from opioid and cannabinoid co-administration**
  - Found ED50 (median effective dose) for morphine when combined with THC was **3.6 times lower** than morphine alone [7]

[7] <https://pubmed.ncbi.nlm.nih.gov/28327548/>

# Cannabinoids with opioids - pre-clinical



**Figure 2** Forrest plot for meta-analysis examining the opioid-sparing effect of delta-9-THC when co-administered with morphine. Note: all mean difference and SD values are of  $\log_{10}ED_{50}$ . THC, tetrahydrocannabinol.

[7] <https://pubmed.ncbi.nlm.nih.gov/28327548/>

# Cannabinoids with opioids - clinical



- **Sparsity of robust large scale, well controlled clinical trials in chronic non-cancer related pain management**
- **Two randomised placebo-controlled (n=177, n=360) trials evaluating cannabinoid (delta-9-THC and nabiximol respectively) efficacy in patients with active cancer-related pain**
  - In both studies **no change** in median amount of breakthrough opioid medication was identified in either cohort [8], [9]

[8] <https://pubmed.ncbi.nlm.nih.gov/19896326/>

[9] <https://pubmed.ncbi.nlm.nih.gov/22483680/>



# Cannabinoids with opioids - clinical



- **Observational study of 600 opioid-using patients who started medical cannabis were monitored over 6 months; at the end of the observational period:**
  - 26% of clients had **stopped** using opioids
  - Additional 55% of patients had reduced their average opioid dose by 30% [10]

[10] <http://www.sciencepublishinggroup.com/journal/paperinfo?journalid=653&doi=10.11648/j.ajpn.20190703.14>

# Complexities for future research



- **No clear consensus on optimal dose of cannabis to achieve optimal pain control**
  - Large range of how individuals absorb and metabolise cannabinoids
- **Diverse range of cannabinoid products with potentially different interactions with other medications [11]**

[11] <https://www.frontiersin.org/articles/10.3389/fphar.2021.633168/full>

# References

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- [1] <https://www.cdc.gov/drugoverdose/deaths/prescription/index.html>
- [2] <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6277878/>
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- [4] <https://pubmed.ncbi.nlm.nih.gov/14706563/>
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- [9] <https://pubmed.ncbi.nlm.nih.gov/22483680/>
- [10] <http://www.sciencepublishinggroup.com/journalpaperinfo?journalid=653&doi=10.11648/j.ajpn.20190703.14>
- [11] <https://www.frontiersin.org/articles/10.3389/fphar.2021.633168/full>

