Innovations

The effect of varenicline on cannabis use in cannabis users who also smoked tobacco

David Newcombe[1,2], Natalie Walker[1,3], Janie Sheridan[1,4], Susanna Galea[1,5]

[1]*The Centre for Addiction Research, University of Auckland, Auckland, New Zealand*
[2] *School of Population Health, University of Auckland, Auckland, New Zealand*
[3] *National Institute for Health Innovation, University of Auckland, Auckland, New Zealand*
[4]*School of Pharmacy, University of Auckland, Auckland, New Zealand*
[5]*Community Alcohol and Drugs Service, Waitemata District Health Board, Auckland, New Zealand*

AOD Provider Collaborative Research Symposium
19th June, 2014

CENTRE FOR ADDICTION RESEARCH
FACULTY OF MEDICAL AND HEALTH SCIENCES
THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau

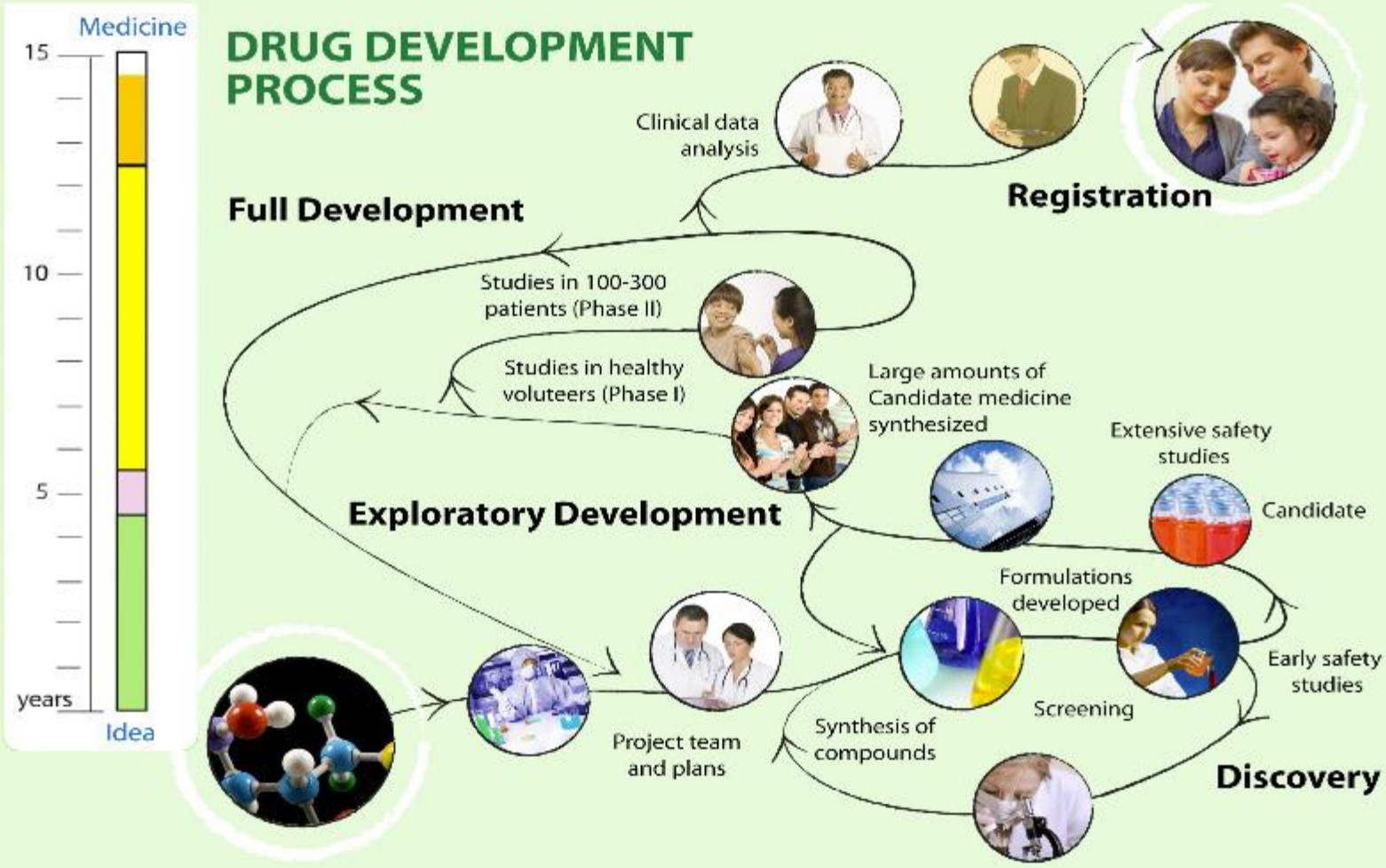
CENTRE FOR ADDICTION RESEARCH
FACULTY OF MEDICAL AND HEALTH SCIENCES
THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau

Overview

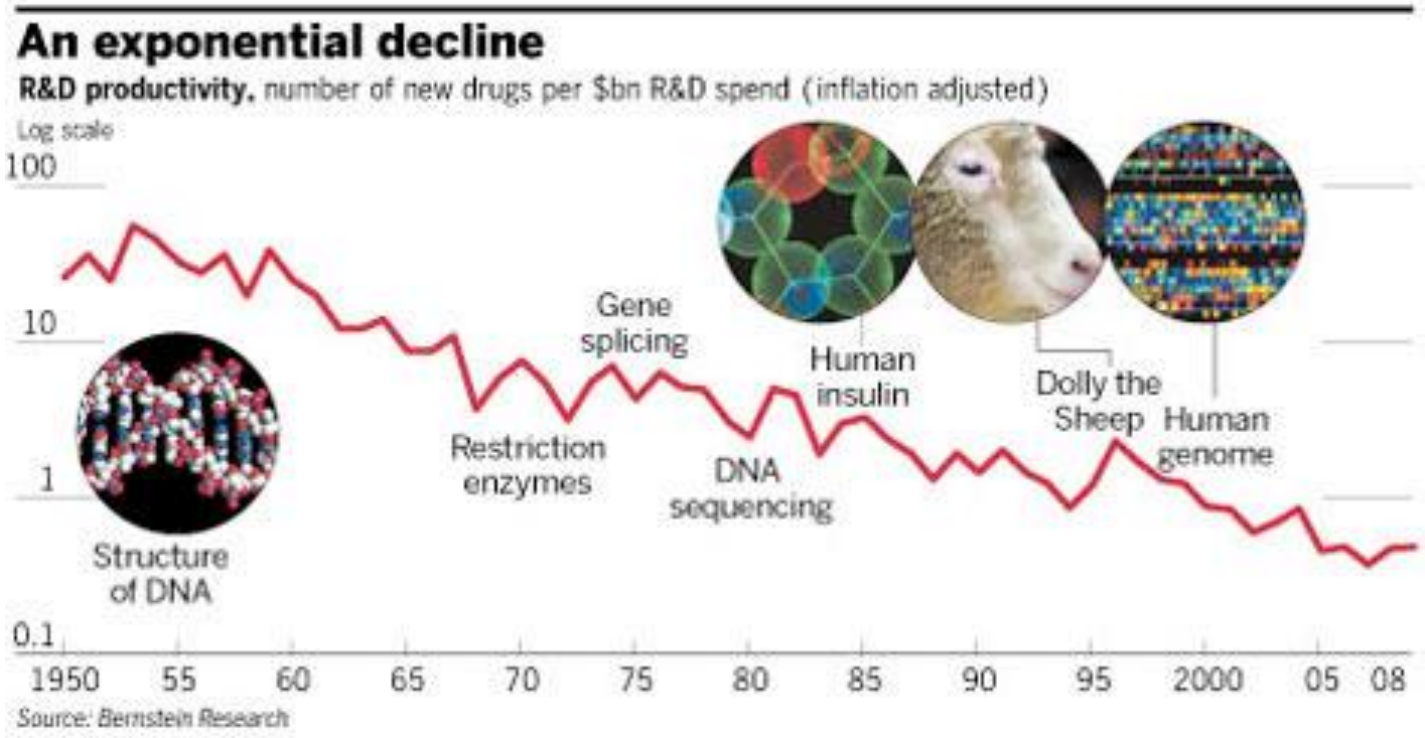
- Why is it important to be considering innovative ways to use current medicines
- Featuring the drug Varenicline (Champix®)
- The current study
  - Rationale
  - Overview of methods and results
- Discussion and implications

CENTRE FOR ADDICTION RESEARCH
FACULTY OF MEDICAL AND HEALTH SCIENCES
THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau

Innovation – Why?
The development of medicines



Decline in research



The Drug: Varenicline Tartrate

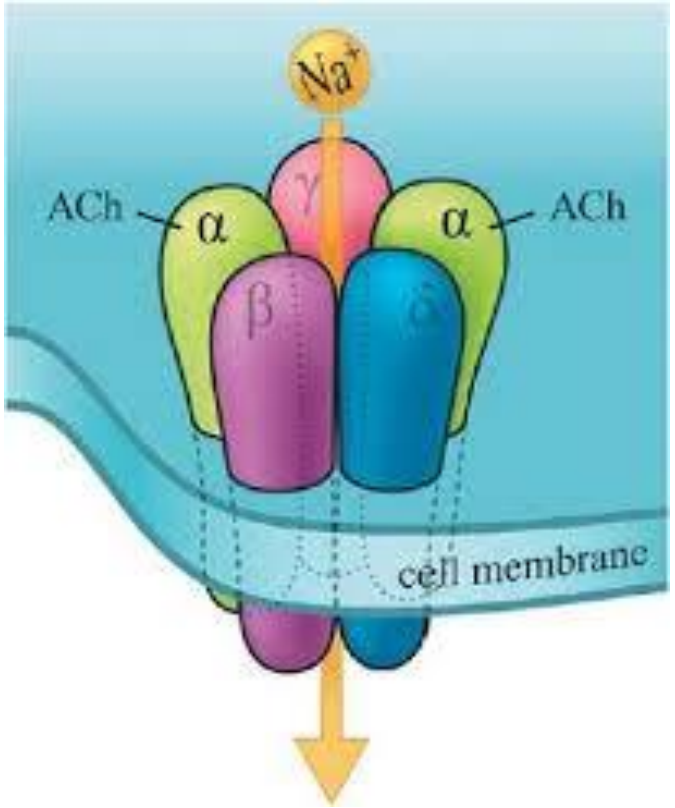
- Marketed by Pfizer as Champix® in Australasia and approved in 2006 (EU, USA)
- Recently funded by Pharmac
- History: Pfizer developed the drug based on extracts from the drug Cytisine (naturally extracted from genus *laburnum* and *cystisus)*
- Evidence of effectiveness: Cochrane Systematic review found it to be superior to bupropion (Zyban) and NRT in achieving abstinence and preventing relapse in smokers [1]

[1] *Cahill K, Stead LF, Lancaster T. Nicotine receptor partial agonists for smoking cessation. Cochrane Database Syst Rev 2008(1):CD006103*.

CENTRE FOR ADDICTION RESEARCH
FACULTY OF MEDICAL AND HEALTH SCIENCES
THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau

Varenicline - Mechanism of action

- Acts at a partial agonist at a number of nicotinic receptors (many subtypes)
- These receptors are abundant in brain reward centres
- Partial agonist action results in less activity than nicotine, but enough to reduce severity of tobacco withdrawal symptoms and reduce reward & satisfaction from smoking
- Common side effects – nausea/vomiting, headaches.



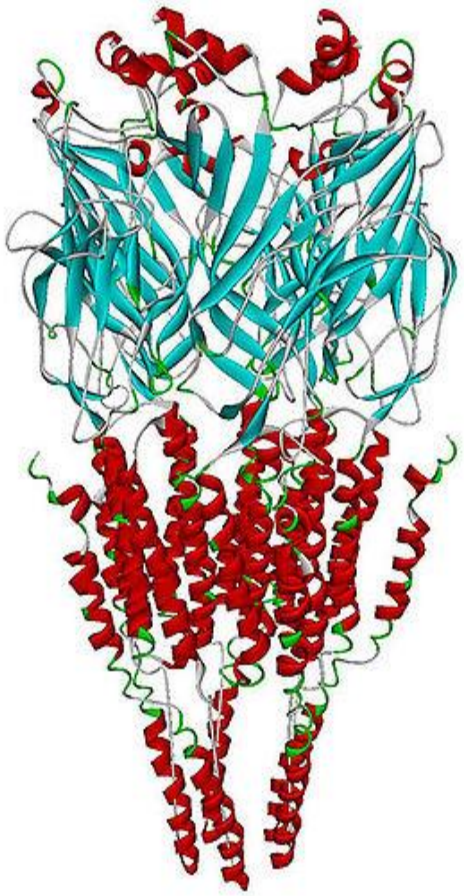
Study Rationale

- In NZ cannabis is the most commonly misused illicit drug - 12 month prevalence rate in 16-64 year age group was 15 %[2].
- It misuse is associated with many significant adverse effects and harms.
- Currently there is no pharmacological treatment available to treat cannabis dependence.
- Many cannabis smokers also smoke tobacco[3].
- Therefore a pharmacological agent that treats dependence on both drugs would be beneficial.

[2] *Ministry of Health. Drug Use in New Zealand: Key Results of the 2007/08 New Zealand Alcohol and Drug Use Survey Wellington: Ministry of Health, 2010.*
[3]*Arpana, A., Budney, A.J., Lynskey M.T., (2012). The co-ocurring use and misuse of cannabis and tobacco: a review. Addiction, 107 (7), 1221-1233* na et al, 2012

Pharmacological Rationale

- The primary active ingredient in cannabis (Tetrahydrocannabinol) and varenicline share a common mechanism of action by binding to the α_7 subtype of the nicotinic receptor [4].
- Therefore it is biological plausible that varenicline may have an effect on cannabis use.
- In absence of human data, conducted a preliminary case series.



[4] *Solinas M, Scherma M, Fattore L, Stroik J, Wertheim C, Tanda G, et al. Nicotinic alpha 7 receptors as a new target for treatment of cannabis abuse. J Neurosci 2007;27(21):5615-20*

Methods – Design

- Prospective case series – participants recruited from AOD clinic
  - Inclusion criteria:
    - Age ≥18 yrs.
    - **NOT smoking combination cannabis + tobacco**.
    - Dependent on tobacco with a desire to quit (but not necessarily cannabis).
    - CUDIT score ≥ 12.
    - Not currently suffering significant psychiatric disorder.
    - Written consent.

CENTRE FOR ADDICTION RESEARCH
FACULTY OF MEDICAL AND HEALTH SCIENCES
THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau

Methods - continued

- Procedure:
  - Medical assessment (including eligibility for subsidised Champix)
  - Interviews: Baseline – follow-up - 12 weeks
  - Intervention: 12 week supply of Champix
- Measures:
  - Baseline:
    - Substance use
    - Severity of Cannabis dependence (SDS)
  - Each assessment session:
    - SDS
    - amount/type of cannabis/tobacco
    - self efficacy
    - cannabis withdrawal
    - adverse events, treatment compliance.

Results – demographics and baseline

Subject #	Demographics Gender/age/ ethnicity	Tobacco use History (continuous use)	Cannabis use history (continuous use)	CUDIT Score	SDS cannabis
1	Female/49/ European	12 yrs	12 yrs	17	3
2	Male/31/ European	16 yrs	13 yrs	16	5
3	Female/39/ European	3 yrs	23 yrs	19	3
4	Male/37/Maori	3 yrs	29 yrs	25	9
5	Male/35/ European	2 yrs	2 yrs	16	3

Notes: CUDIT – Cannabis Use Disorders Identification Test (Adamson et al, 2010):
SDS – substance dependence scale – score of ≥4 indicative of dependence (Swift et al, 2008)

CENTRE FOR ADDICTION RESEARCH
FACULTY OF MEDICAL AND HEALTH SCIENCES
THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau

Results: Follow-up

#	Follow up; Time on Champix®	Self reported outcome	Reason for ceasing Champix®
1	Withdrew after 1st dose	• Dropped out	Nausea/vomiting ? Due to Champix
2	12 weeks FU: 4 weeks on Champix	• ↓ in use and enjoyment of t & c • ↓cannabis SDS - maintained at zero	Feeling flat
3	5 weeks	• ↓ in use and enjoyment of t & c • Reduction in enjoyment persisted • Cannabis SDS reduced to zero	Family stressors
4	5 weeks	• ↓in use and enjoyment of t & c • Cannabis SDS reduced to one	Nausea and vomiting
5	4 weeks: 2 weeks on champix	• Using the same amount of t as before; less c. • Reported less desire to use c. • No change in SDS	Bouts of nausea complicated initiation onto Champix. Short tempered and angry

CENTRE FOR ADDICTION RESEARCH
FACULTY OF MEDICAL AND HEALTH SCIENCES
THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau

Results: Follow-up

#	Follow up; Time on Champix®	Self reported outcome	Reason for ceasing Champix®
1	Withdrew after 1st dose	• Dropped out	Nausea/vomiting ? Due to Champix
2	12 weeks FU: 4 weeks on Champix	• ↓ in use and enjoyment of t & c • ↓cannabis SDS - maintained at zero	Feeling flat
3	5 weeks	• ↓ in use and enjoyment of t & c • Reduction in enjoyment persisted • Cannabis SDS reduced to zero	Family stressors
4	5 weeks	• ↓in use and enjoyment of t & c • Cannabis SDS reduced to one	Nausea and vomiting
5	4 weeks: 2 weeks on champix	• Using the same amount of t as before; less c. • Reported less desire to use c. • No change in SDS	Bouts of nausea complicated initiation onto Champix. Short tempered and angry

CENTRE FOR ADDICTION RESEARCH
FACULTY OF MEDICAL AND HEALTH SCIENCES
THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau

Discussion/implications

- Decreased amounts of cannabis used
- Decreased enjoyment from using cannabis
- Reduced desire for use of cannabis.
- Temporal relationship between commencement of Champix® and reduction in desire to use.
- Reasons for dropout - Nausea, vomiting, feeling flat & angry.

Results are suggestive of a link between the Champix® and reduced cannabis use.

What next ?

- Results are very preliminary !
- Champix® is not currently indicated for the treatment of cannabis dependence!
- However, we think the findings from this study are sufficient to support a larger study to explore its effectiveness.

Acknowledgements

- Community Alcohol & Drug Service
  - In particular Dr Jo Fleury for medical assessments
- Research assistance: Donna Watson – Client interviews and follow up
- Clients who participated in the study

Thank You