NDARC
National Drug & Alcohol Research Centre

The Difference is Research

A non-inferiority trial of cytisine versus varenicline for smoking cessation

NHMRC Project Grant (APP1108318): 4 years @ $1.9 mill

UNSW SYDNEY | Australia's Global University

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NSW GOVERNMENT | cancer institute NSW

Background

- Cytisine – Plant-based alkaloid
- Developed in Bulgaria – early 1960s
- Current availability: Central and Eastern Europe
- Approval status: OTC smoking cessation mediation
- MOA: nAChRs partial agonist
- Affordability
- Treatment duration

Current evidence

- Nine controlled and seven uncontrolled studies
- Three systematic reviews

Three high-quality studies

Study	Population	Safety	Efficacy
Cytisine vs. NRT[1]	1310 New Zealand smokers	Nausea, vomiting and sleep disorders	Cytisine is superior to NRT
Cytisine vs. placebo[2]	740 smokers	Gastrointestinal disorders, dizziness and somnolence	Cytisine is superior to placebo
Cytisine vs. placebo[3]	171 Kyrgyzstan smokers	Dyspepsia, nausea and headache	Cytisine is superior to placebo

1. Walker et al. *New Engl J Med* 2015
2. West et al. *New Engl J Med* 2011
3. Vinnikov et al. *J Smoking Cessation* 2008

Aim & Design

- **Aim:** To evaluate the cost-effectiveness of cytisine vs varenicline for smoking cessation in Australian smokers interested in quitting
- **Study design:** Single-blind randomised non-inferiority clinical trial
- **Study setting:** Recruitment via Quitline/advertisements
- **Number of participants:** 1266 (633 in each arm)
- **Check-in calls:** 3-during active treatment phase
- **Study duration:** 7 months follow-up

Eligibility

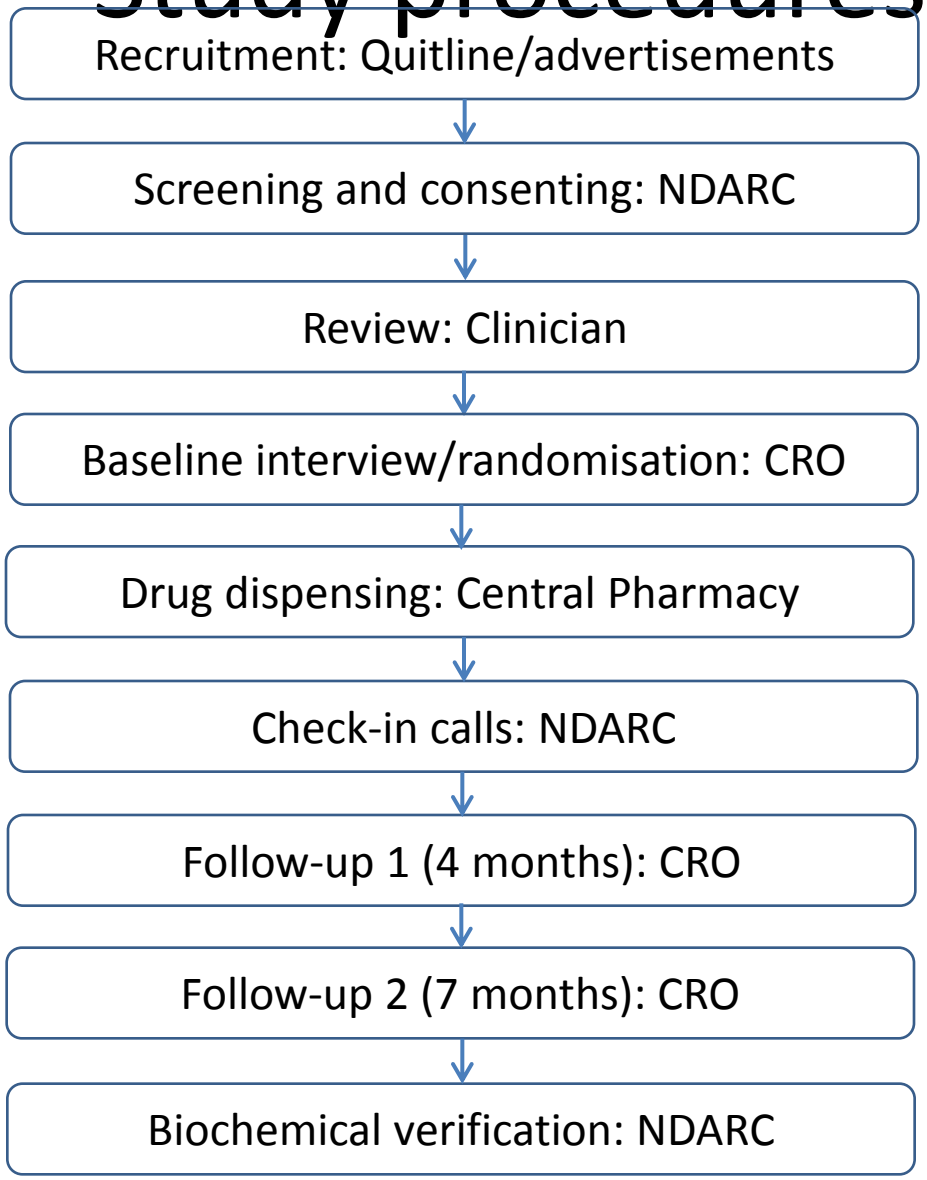
Inclusion criteria

- ≥18 years of age
- Current daily smoker
- Want to quit
- Willing to use cytisine/varenicline
- Verbal informed consent
- Access to a telephone
- Willing to complete follow-ups

Exclusion criteria

- Pregnant or breastfeeding
- Current use of cessation medications
- Participating in another program
- Hypersensitivity to active substance/excipients
- People with arrhythmia, heart attack, stroke, or severe angina
- People with pheochromocytoma or hyperthyroidism

Study procedures



Study arms

Intervention arm:

- Cytisine: 25 days supply
- Quitline support
- Quit day: 5th day

Control arm:

- Varenicline: 12 weeks supply
- Quitline support
- Quit day: 8th day

Medication delivery: via mail

Outcomes

Primary outcome

- Biochemically verified 6-month continuous abstinence (≤5 cigarettes from quit date)

Secondary outcomes

- Nicotine dependence: HSI
- DASS
- QoL: EQ5D
- Health resource use
- Financial Stress
- Mood and Physical Symptoms Scale
- Alcohol Use Disorders Identification Test (AUDIT-C)
- Adverse events

Safety outcomes

Adverse events

- Any untoward medical occurrence
- Not necessarily have to have causal relationship with treatment
- Unfavourable /unintended sign

A SAE is any untoward medical occurrence that at any dose

- Results in death
- Is life-threatening
- Requires inpatient hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant disability/incapacity,
- Congenital abnormality/birth defect
- Is an important medical event

Discussion point

- Tobacco treatment hiding in plain sight