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

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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. NRT¹  | 1310 New Zealand smokers   | Nausea, vomiting and sleep disorders| Cytisine is superior to NRT            |
| Cytisine vs. placebo² | 740 smokers                  | Gastrointestinal disorders, dizziness and somnolence | Cytisine is superior to placebo |
| Cytisine vs. placebo³ | 171 Kyrgyzstan smokers       | Dyspepsia, nausea and headache       | Cytisine is superior to placebo |

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

Recruitment: Quitline/advertisements

Screening and consenting: NDARC

Review: Clinician

Baseline interview/randomisation: CRO

Drug dispensing: Central Pharmacy

Check-in calls: NDARC

Follow-up 1 (4 months): CRO

Follow-up 2 (7 months): CRO

Biochemical verification: NDARC
Study arms

**Intervention arm:**
- Cytisine: 25 days supply
- Quitline support
- Quit day: 5\textsuperscript{th} day

**Control arm:**
- Varenicline: 12 weeks supply
- Quitline support
- Quit day: 8\textsuperscript{th} 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