The Risk of Adverse Cardiovascular Events from Varenicline Against the Benefits in Mortality from Smoking Cessation

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Introduction

- Smokers significantly higher mortality, tobacco cancers, and respiratory disease
- Combining behavioral counseling & pharmacotherapy highest cessation rates
- Varenicline outcomes in controlled trials significantly higher than placebo, sustained release bupropion, or single use NRT
- Meta-analysis by Singh: higher adverse CV events from varenicline, authors suggest harms outweigh benefits
- Quantification of potential varenicline benefits on patient outcomes, such as mortality, not well described

Aim

- To begin to calculate a balance of risks and benefits from varenicline that are meaningful to patient encounters
- To calculate the absolute risk increase from any excess cardiovascular events in varenicline users versus expected mortality reduction from varenicline-attributable tobacco cessation
- Use scenario of a 50 year old woman presenting to clinician

Method

Assumptions*

Two groups of 1,000 women smokers aged 50
one group receives standard course of varenicline, other receives placebo for cessation

Adverse cardiovascular events accrue only year 1
Mortality benefit at ten years is meaningful to patients
Initial CV risk from Framingham data
Assume that Singh reports true as published- that excess cardiovascular events in varenicline users versus expected mortality reduction from varenicline-attributable tobacco cessation
One year spontaneous cessation quit rate among smokers have 85.6 deaths/10,000 person-years

Results

Potential Risks
- Baseline risk of an adverse CV event in a year is 0.4%, or 4 out of the 1000 women
- If Singh study true, varenicline group would have average absolute risk of CV events of 0.69%, or absolute risk increase of 0.29%, and just less than 7 of the 1000 women taking varenicline would have an adverse CV event in first year
- Number needed to harm (inverse of the absolute risk increase of 0.29%)
- 1 additional woman might have a adverse CV event over a year for every 345 women taking varenicline, an increase that does not increase in future years

Potential Benefits
- Placebo group
  - 80 in placebo group quit smoking & 920 continue to smoke x 10 years
  - 79 of 920 still smoking expected to die
  - 4.6 of those that quit expected to die
  - Total 83.6 expected to die over 10 years
- Varenicline group
  - 217 in varenicline group quit smoking & 783 continue to smoke x 10 years (137 additional women quit as a result of the medication)
  - 67 of the 783 still smoking expected to die
  - 12.4 of those that quit expected to die
  - Total 79.4 expected to die over ten years

Summary

- Absolute Mortality Benefit from one-time varenicline use
  - 83.6 - 79.4 = 4.2 deaths
- Number needed to benefit
  - 1 additional life potentially saved over ten years for every 238 people who take one course of varenicline

Limitations

- CV events in two groups is taken at year one
- Calculations do not account for changes in smoking status over time
- Balance differs men or women of different ages

Conclusions

- Risks do not occur in a vacuum
- Clinicians could discuss benefits in more concrete terms "Just over 4 additional lives are saved over ten years at a cost of approximately 3 additional adverse cardiovascular event that would occur in the first year"
- Cost-effectiveness analysis & Markov modeling would allow broader analysis of benefits vs harms

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