Cost-Effectiveness of the “Polypill” for Secondary Prevention of CVD

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The Economics of Vulnerable Populations, at Home and Abroad
Background: CVD and Global Health

- Cardiovascular disease (CVD) is the leading cause of morbidity and mortality worldwide.

- Low- and middle-income countries (LMIC) face more than 75% of the global burden.

- WHO Global Action Plan for Non-Communicable Disease
  - Reduce premature mortality by 25% by 2025
  - Increase NCD medication prescription to cover 50% of eligible population.
Prescription Rates Low in LMIC

A Coronary heart disease
- No drug
- One drug
- Two drugs
- Three or more drugs

B Stroke

Yusuf Lancet 2011, PURE Study
Polypill/Fixed Dose Combination (FDC)

- Combine multiple CVD medicines into one pill
- Advantages
  - Improves adherence (as in HIV, TB)
  - Easier to prescribe
- Disadvantages
  - Difficult to titrate
- Argument for usage in LMIC
Polypill/FDC: Policy Implications

- 2012: WHO rejected polypill application for its Model List of Essential Medicines
  - No evidence on **efficacy**
  - No evidence on **safety**
  - No data on **cost-effectiveness**
Polypill/FDC: The Evidence

- Two RCTs for Secondary Prevention
  - FOCUS: Argentina, Brazil, Paraguay, Italy, Spain
  - UMPIRE: India, UK, Netherlands
- Improved adherence
- Demonstrated safety
- Improved BP, LDL-C

UMPIRE JAMA 2013
Question: Is the polypill cost-effective relative to usual care for secondary prevention of CVD in LMICs?
Study: Cost-effectiveness of polypill

Study Aim: To evaluate the cost-effectiveness of the polypill in China, India, Mexico, Nigeria, and South Africa

- Polypill may:
  - Reduce costs associated with acute events
  - Increase costs from prescription, prolonged survival
Analyses

1. What is the cost-effectiveness of polypill prescribed at current rates compared with current prescription?

2. What should we expect if we achieve WHO goals for secondary prevention of CVD?
   - Individual medicines prescribed to 50% of eligible
   - Polypill prescribed to 50% of eligible
Methods

- Microsimulation: adults aged 30-80 years in each country with prior ischemic heart disease or stroke.

- Perspective: Health system
- Analytic Horizon: Lifetime
- Future costs and life years discounted at 3% per year

- Probabilistic Sensitivity Analysis: Vary all input parameters among pre-defined distributions 1000x
Methods

Outcomes

- Major cardiovascular events: MI, stroke, CVD death
- Disability-adjusted life years averted
- Direct medical costs in International Dollars
- Cost-effective defined as 1x GDP/capita

\[
\text{ICER} = \frac{\text{Cost}_{\text{New therapy}} - \text{Cost}_{\text{Old therapy}}}{\text{Effectiveness}_{\text{New therapy}} - \text{Effectiveness}_{\text{Old therapy}}}
\]
Assumptions About Polypill

- Increased adherence compared to individual components
- As efficacious as its individual components
- Doses can be titrated
- Cost is 100% of the sum of its individual components
Sensitivity Analyses For The Polypill

- Increased adherence compared to individual components
- 80% efficacy compared to its individual components
- Doses can be titrated
- Cost is 200% of the sum of its individual components
Cost-Effectiveness of the Polypill in LMIC

Willingness to Pay Threshold
- 1x GDP/Capita

Scenario
- Base Case
- 2x Cost
- 80% Effective

Cost-Effectiveness of the Polypill vs Usual Care
- Not Cost-Effective: >1x GDP/Capita
- Cost-Effective: <1x GDP/Capita
- Cost-Saving

ICER (Int$/DALY averted)

China
- $14,500

India
- $17,000

Mexico
- $13,200

Nigeria
- $6,000

South Africa
- $6,100
Cost-Effectiveness of the Polypill in LMIC
Decrease in DALYs by treatment strategy

- China
- India
- Mexico
- Nigeria
- South Africa

Cost-Effectiveness of the Polypill in LMIC
Limitations

- Current modeling does not reflect programmatic costs of scaling up prescription rates
- Cost-effectiveness is distinct from affordability
Conclusions

- Cost-effectiveness of the polypill may be better in countries with more developed health systems.

- Impact of increasing prescription may be greater in countries with less health infrastructure.
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Supplemental Slides
Adherence

- **Usual Care**
  - Starts at 100% prescription, then declines according to the literature (steady state year 3)

- **Polypill**
  - Starts at 100% of prescription, declines exponentially

\[ y_{adherence} = a + (1-a) \times e^{-1.3 \times t} \]
Medication Prescription

- PURE Study
  - Marginal distribution of medication usage by drug class
  - Proportion of individuals taking 1, 2, or 3+ medications

- Calibration to determine correlation structure
  - Preserve marginal distribution and proportion taking n number of medications
  - Goodness of fit defined by root mean squared distance
  - Optimization function: Limited memory BFGS-B

- Problem not identified – multiple solution sets do not change results
Cost-Effectiveness of the Polypill in LMIC
Data Sources

- Demographics and Epidemiology:
  - UN population division
  - GBD 2015
- IHD and CVA transition probabilities:
  - Observational studies
  - Registries: RENAISSCA II, BRIG, ACCESS, CREATE
- Effectiveness of interventions
  - Meta-analyses of CVD medication RCTs
- Adverse effects of interventions
  - Meta-analyses of CVD medication RCTs
  - UMPIRE, FOCUS
- Adherence to medications:
  - Current prescription levels: PURE
  - Patient adherence over time: meta-analyses of observational data
  - Improvement in adherence with polypill: UMPIRE, FOCUS
- DALYs
  - Global Burden of Disease 2015
- Costs
  - WHO CHOICE
  - MSH International Drug Price Indicator Guide
  - Personal Correspondence
Model Validation

Cost-Effectiveness of the Polypill in LMIC