

- disease. *N Engl J Med*. 2006; **354**: 1567 – 1577.
3. Table 2: Cause specific mortality and morbidity. World Health Statistics. 2009. 8-8-2012. Available from: URL: [http://www.who.int/whosis/whostat/EN\\_WHS09\\_Table2.pdf](http://www.who.int/whosis/whostat/EN_WHS09_Table2.pdf) (Accessed: 8 August, 2012).
  4. Indian Polycap Study (TIPS), Yusuf S, Pais P, Afzal R, Xavier D, Teo K, et al. Effects of a polypill (Polycap) on risk factors in middle-aged individuals without cardiovascular disease (TIPS): a phase II, double-blind, randomised trial. *Lancet*. 2009; **373**: 1341 – 1351.
  5. PILL Collaborative Group, Rodgers A, Patel A, Berwanger O, Bots M, Grimm R, et al. An international randomised placebo-controlled trial of a four-component combination pill (“polypill”) in people with raised cardiovascular risk. *PLoS ONE* [Electronic Resource]. 2011; **6**: e19857.
  6. Soliman EZ, Mendis S, Dissanayake WP, Somasundaram NP, Gunaratne PS, Jayasingne IK, et al. A Polypill for primary prevention of cardiovascular disease: a feasibility study of the World Health Organization. *Trials* [Electronic Resource]. 2011; **12**: 3.
  7. Malekzadeh F, Marshall T, Pourshams A, Gharravi M, Aslani A, Nateghi A, et al. A pilot double-blind randomised placebo-controlled trial of the effects of fixed-dose combination therapy (“polypill”) on cardiovascular risk factors. *Int J Clin Pract*. 2010; **64**: 1220 – 1227.
  8. Sepanlou SG, Farzadfar F, Jafari E, Danaei G. Cardiovascular disease prevention using fixed dose pharmacotherapy in iran: updated meta-analyses and mortality estimation. *Arch Iran Med*. 2012; **15**: 531 – 537.
  9. Namazi MH, Mohagheghi A, Ostovaneh MR. Prevention of cardiovascular diseases in developing countries. *Arch Iran Med* 2012; **15**: 528 – 530.
  10. Wald DS, Wald NJ. The polypill in the primary prevention of cardiovascular disease. *Fundam Clin Pharmacol*. 2010; **24**: 29 – 35.
  11. Viera AJ, Sheridan SL, Edwards T, Soliman EZ, Harris R, Furberg CD. Acceptance of a Polypill approach to prevent cardiovascular disease among a sample of U.S. physicians. *Prev Med*. 2011; **52**: 10 – 15.
  12. Ebrahim S, Davey SG. Multiple risk factor interventions for primary prevention of coronary heart disease. *Cochrane Database Syst Rev*. 2000; **(2)**: CD001561.

## Polypill for Primary Prevention: Has The Time Arrived?

### Authors' Reply

Since the introduction of the concept of Polypill for cardiovascular disease (CVD) prevention, many studies have been conducted to determine whether it can be recommended as routine primary prevention of CVD. In the previous issue of the *Arch Iran Med* (2012; **15**(9): 531 – 537) we reported the estimated effectiveness of such a combination using updated meta-analyses of the component drugs.<sup>1</sup> Our estimates of the relative reduction in CVD mortality are more conservative than those previously reported,<sup>2-5</sup> because we estimated the effects of Polypill components on clinical endpoints rather than modeling their effects through reductions in blood pressure and serum cholesterol and we used a more conservative assumption for the combined effects of multiple treatments. None-the-less we may still have overestimated the achievable effects particularly, because adherence to treatment in the general practice settings is expected to be less than that reported in randomized trials.

Particular aspects of the cardiovascular disease epidemiology

and health system characteristics in Iran may support large scale population-based administration of Polypill: CVD constitute 53% of deaths above age 30 in Iran<sup>6</sup>; 54% of these deaths are attributable to high blood pressure and 22% to high serum cholesterol.<sup>7</sup> The pills are produced locally at a low cost and an extensive primary health care network can enhance the feasibility and coverage of the policy.

However, we agree with Nirantharakumar and Marshal that before the use of Polypill can be recommended as a strategy for primary prevention of CVD on a national scale, its safety and acceptability should be evaluated in large scale randomized trials and its cost-effectiveness should be rigorously examined. It should also be noted that the coverage of the primary health care system in urban areas may need to be strengthened (possibly using family physicians) before such a national strategy can be successfully implemented. We also reiterate our emphasis that medical interventions should be combined and balanced with effective lifestyle interventions in a comprehensive national CVD prevention strategy.

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## References

1. Sepanlou SG, Farzadfar F, Jafari E, Danaei G. Cardiovascular disease prevention using fixed dose pharmacotherapy in iran: updated meta-analyses and mortality estimation. *Arch Iran Med*. 2012. **15**: 531 – 537.
2. Soliman EZ, Mendis S, Dissanayake WP, Somasundaram NP, Gunaratne PS, Jayasingne IK, et al. A Polypill for primary prevention of cardiovascular disease: a feasibility study of the World Health Organization. *Trials*. 2011; **12**: 3.
3. PILL Collaborative Group, Rodgers A, Patel A, Berwanger O, Bots M, Grimm R, et al. An international randomised placebo-controlled trial of a four-component combination pill (“polypill”) in people with raised cardiovascular risk. *PLoS One*. 2011; **6**: e19857.
4. Wald DS, Morris JK, Wald NJ. Randomized polypill crossover trial in people aged 50 and over. *PLoS One*. 2012; **7**: e41297.
5. Wald NJ, Law MR. A strategy to reduce cardiovascular disease by more than 80%. *BMJ*. 2003; **326**: 1419.
6. Naghavi M, Abolhassani F, Pourmalek F, Lakeh M, Jafari N, Vaseghi S, et al. The burden of disease and injury in Iran 2003. *Popul Health Metr*. 2009; **7**: 9.
7. Farzadfar F, Danaei G, Namdaritabar H, Rajaratnam JK, Marcus JR, Khosravi A, et al. National and subnational mortality effects of metabolic risk factors and smoking in Iran: a comparative risk assessment. *Popul Health Metr*. 2011; **9**: 55.