

## Editorial

## Prevention of Cardiovascular Diseases in Developing Countries

See the pages: 531 – 537

**Cite this article as:** Namazi MH, Mohagheghi A, Ostovaneh MR. Prevention of cardiovascular diseases in developing countries. *Arch Iran Med.* 2012; **15**(9): 528 – 530.

According to WHO reports, nearly 80% of non-communicable diseases (NCDs) deaths - 29 million- in 2008 occurred in low- and middle-income countries, of those about 48% are estimated to have occurred under the age of 70. Cardiovascular diseases (CVDs) alone constitute about 39% of this huge death toll.<sup>1,2</sup> The cumulative lost output associated with NCDs, is estimated to be about US\$7 trillion over the period 2011-2025 through escalation of health-care costs and productivity losses in developing countries.<sup>1,2</sup> Cardiovascular diseases are the most common NCDs and the leading cause of death and disability (Figure 1 and 2, Table 1 and 2) in low and middle income countries including Iran.<sup>3,4</sup> Management of CVDs is expensive, and the costs are increasing as new therapies became available.<sup>5,6</sup> There is now sufficient evidence that it is possible to cost effectively prevent CVDs by controlling the modifiable risk factors such as hypertension, hyperlipidemia and diabetes. This highlights an urgent need for feasible strategies to prevent morbidity and mortality due to CVDs in low- and middle-income countries.<sup>5-8</sup>

Among proposed strategies, the concept of a polypill for CVD prevention has been much disputed since it was first suggested by Wald and Law in 2003.<sup>3</sup> Several types of formulations have been tested, in short term, for both primary and secondary prevention of CVDs, and several research groups across the globe are now working on this concept.<sup>8-15</sup> The notion is not without its critics, some disagreeing and think that the approach to give a polypill to all is far too radical. A number of others believe that the polypill is best employed as a treatment for secondary prevention; other

opponents contend that individual risk assessment and reduction should be the main strategy in preventive cardiology.<sup>8</sup>

The most recent study<sup>11</sup> which focused on the short term effect of a polypill given to healthy subjects solely on the basis of age (> 50 year) for the primary prevention of CVDs has shown the largest reduction in cholesterol level and blood pressure (BP) of any polypill study to date.<sup>9,10,12,14</sup> The reduction in BP and LDL cholesterol level were 12% and 39% (to levels typical of people aged 20), respectively during the 12-week study. They predicted that persistent decline in BP and LDL cholesterol of this extent would reduce stroke by 64%, and ischemic heart disease events by 72%. If healthy people receive polypill regularly from the age of 50 for long term, an estimated 28% would be protected from myocardial infarction and stroke during their lifetime and this will result in gain of average of 11 years of life, free of cardiovascular events. Side effects were more frequent with the polypill than placebo (29% vs 13%,  $p = 0.01$ ), although none were serious enough to cause discontinuation. Myalgia was more common with the polypill compared to placebo (11% vs 1.2%, respectively).

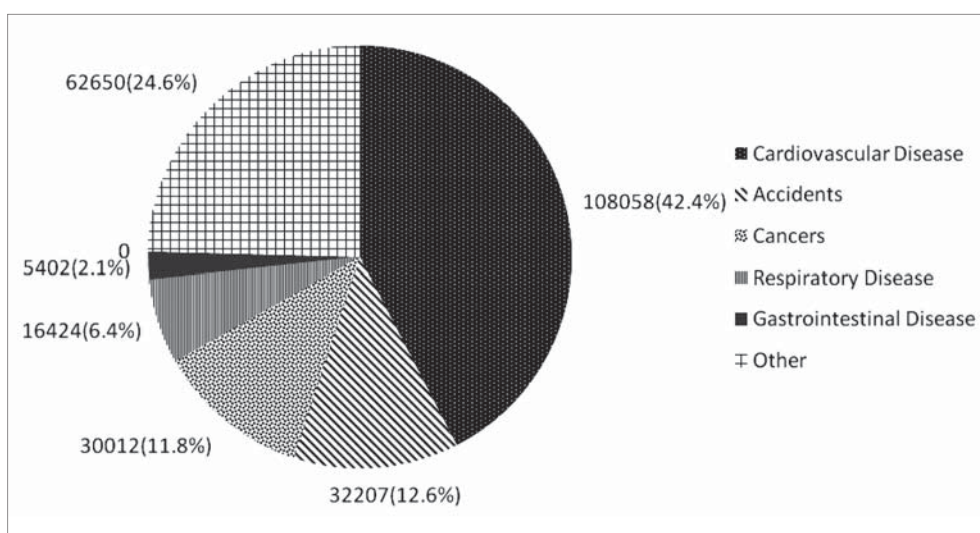
The meta-analysis by SG Sepanlou, et al. in the current issue of AIM<sup>16</sup> has clearly shown that the standard polypill formulation can reduce mortality due to ischemic heart disease and stroke by 30 – 53%, which means prevention of 28500 (95% CI: 21700, 34100) deaths from ischemic heart diseases (IHD) and 12700 (95% CI: 8800, 15900) deaths from stroke annually in Iran.<sup>16</sup> In other words, polypill might prevent one in three and one in four of premature deaths (deaths occurring before the age of 70) from IHD

**Table 1.** Estimated number of cause specific total deaths in all age groups according to the data from 29 provinces in Iran, 2010

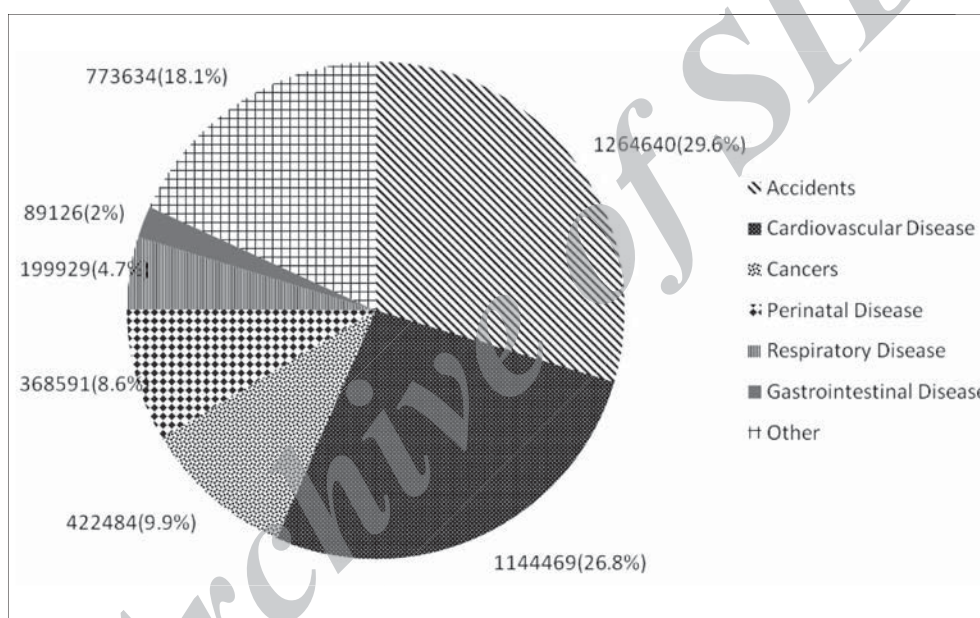
	Female	Male	Total
Cardiovascular Disease	48741(48%)	59317(38.9%)	108058(42.4%)
Accidents	7333(7.2%)	24874(16.3%)	32207(12.6%)
Cancers	11545(11.3%)	18467(12.1%)	30012(11.8%)
Gastrointestinal Diseases	2167(2.1%)	3235(2.1%)	5402(2.1%)
Respiratory diseases	6837(6.7%)	9587(6.3%)	16424(6.4%)
Other	25622(25%)	37001(24.2%)	62650(24.6%)
Total	102245	152481	254753

**Table 2.** Estimated years of life lost due to cause specific deaths according to data from 23 provinces in Iran, 2003

	Male	Female	Total
Accidents	982242(36.5%)	282398(17.9%)	1264640(29.6%)
Cardiovascular Disease	634099(23.5%)	510371(32.5%)	1144469(26.8%)
Cancers	236751(8.8%)	185733(11.8%)	422484(9.9%)
Perinatal Disease	207736(7.7%)	160855(10.2%)	368591(8.6%)
Respiratory Disease	109247(4%)	90682(5.8%)	199929(4.7%)
Gastrointestinal Disease	50862(1.9%)	38264(2.4%)	89126(2%)
Other	470412(17.5%)	303222(19.3%)	773634(18.1%)
Total	2691349	1571525	4262873



**Figure 1.** Estimated number of cause specific total deaths in all age groups according to the data from 29 provinces in Iran, 2010.



**Figure 2.** Estimated years of life lost due to cause specific deaths according to data from 23 provinces in Iran, 2003

and stroke, respectively. Further studies is now going on in Iran<sup>15,17</sup> to compare the lifestyle modification with polypill for primary and secondary prevention of CVDs and to check for feasibility and efficacy of the polypill administration through the extensive primary health care network in Iran. One of the main concerns in polypill concept is the adherence to regular intake of polypill among healthy subjects in general population, which is obviously much less than what is observed in clinical trials. However, the ongoing study in Iran is designed as a pragmatic trial which is nested in Golestan cohort study and might estimate the adherence in general population more realistically.<sup>18</sup> Polypill is now being manufactured by Iranian pharmaceutical companies with a cost as low as 5 cents per pill, however, further studies are also needed to estimate the cost-effectiveness of a national-scale population based intervention with detailed comparison of various treatment strategies to minimize the potential risk.

Mohammad Hassan Namazi MD<sup>1</sup>, Abbas Mohagheghi MD<sup>2</sup>, Mohammad Reza Ostovaneh MD<sup>3</sup>

<sup>1</sup>Department of cardiology, Moddraz Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran, <sup>2</sup>Department of cardiology, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran, <sup>3</sup>Digestive Disease Research Institute, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran.

## References

1. Noncommunicable diseases (NCD). WHO, 2012. Available from: URL: <http://www.who.int/gho/ncd/en/index.html> (Accessed Date: 6/26/2011).
2. NCD mortality and morbidity. World Health Organization, 2012. Available from: URL: [http://www.who.int/gho/ncd/mortality\\_morbidity/en/index.html](http://www.who.int/gho/ncd/mortality_morbidity/en/index.html) (Accessed Date: 6/26/2011).
3. Wald NJ, Law MR. A strategy to reduce cardiovascular disease by

- more than 80%. *BMJ*. 2003; **326**:1419.
4. Sarraf-Zadegan N, Sayed-Tabatabaei F, Bashardoost N, Maleki A, Tonchi M, Habibi H, et al. The prevalence of coronary artery disease in an urban population in Isfahan, Iran. *Acta cardiologica*. 1999; **54**:257.
  5. Rastegarpanah M, Malekzadeh F, Thomas GN, Mohagheghi A, Cheng KK, Marshall T. A new horizon in primary prevention of cardiovascular disease, can we prevent heart attack by "heart polypill"? *Arch Iran Med*. 2008; **11**:306 – 313.
  6. Malekzadeh F, Pourshams A, Marshall T. The preventive polypill--much promise, insufficient evidence. *Arch Iran Med*. 2007; **10**:430 – 431.
  7. Asadi-Lari M, Sayyari A, Akbari M, Gray D. Public health improvement in Iran—lessons from the last 20 years. *Public Health*. 2004; **118**:395 – 402.
  8. Gaziano TA, Opie LH, Weinstein MC. Cardiovascular disease prevention with a multidrug regimen in the developing world: a cost-effectiveness analysis. *The Lancet*. 2006; **368**:679 – 686.
  9. Yusuf S, Pais P, Afzal R, Xavier D, Teo K, Eikelboom J, 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.
  10. 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.
  11. Wald DS, Morris JK, Wald NJ. Randomized Polypill Crossover Trial in People Aged 50 and Over. *PLoS One*. 2012; **7**:e41297.
  12. 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.
  13. Majed M, MoradmandBadie S. A pilot double-blind randomised placebo-controlled trial of the effects of fixed-dose combination therapy ('polypill') on cardiovascular risk factors. *Arch Iran Med*. 2011; **14**:78 – 80.
  14. An international randomised placebo-controlled trial of a four-component combination pill ("polypill") in people with raised cardiovascular risk. *PLoS One*. 2011; **6**:e19857.
  15. Navabakhsh B, Malekzadeh R. Commented summary on Pilot Double-blind Randomized Placebo-controlled Trial of the Effects of Fixed-dose Combination Therapy ('polypill') on Cardiovascular Risk Factors. *Arch Iran Med*. 2011; **14**(6): 433 – 435.
  16. 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**(9):531 – 537.
  17. POLY IRAN in Primary and Secondary Prevention of Cardiovascular Disease in Middle-aged and Elderly Iranian. Available from: URL: [http:// clinicaltrials.gov/ct2/show/NCT01271985](http://clinicaltrials.gov/ct2/show/NCT01271985) (Accessed Date: 7/1/2011).
  18. Relton C, Torgerson D, O'Cathain A, Nicholl J. Rethinking pragmatic randomised controlled trials: introducing the "cohort multiple randomised controlled trial" design. *BMJ*. 2010; **340**:c1066.