The PolyIran Study: Update

Fixed-Dose Combination Therapy

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Disclosure Statement of Financial Interest

I, Nizal Sarrafzadegan DO NOT have a financial interest/arrangement or affiliation with any healthcare related companies that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

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Golestan Cohort

- 50,000 subjects
- >40 y/o on enrolment (2005)
- So far followed for 8-9years
- Main focus: Was esophageal cancer

Follow-up Cohort Report, 2010

The total number of **Deaths**: 1600.

Mortality rate: **1030/**100,000 person years.

Cause of Death		Number (%)		Cause of Death	Number (%)
Cardiovascular	MI	481	541 (33.8%)		
	Other	60			
Cancer			334 (20.9%)	Pending	17 (1.1%)
CVA			276 (17.3%)	Unknown	38 (2.4%)
Vehicle Accident			69 (4.3%)	Other	127 (7.9%)
Pulmonary related			57 (3.6%)		
Infectious diseases			53 (3.3%)		
Liver related			36 (2.3%)		
Renal			35 (2.2%)		
Neurologic			9 (0.6%)		
Hematologic			8 (0.5%)		
				Total	1600 (100%)

Polypill Pilot study

- 475 subjects free of CVD aged more than 50 years
- Randomized, double-blind, placebo controlled
- 12 months follow up
- Polypill: Aspirin 80, HCTZ 12.5, Atorvastatin 20, Enalapril 2.5
- Aim:
  - Tolerability
  - Compliance
  - Side effects
  - Effectiveness
  - Feasibility

Table 2 Changes in primary and secondary outcomes adjusted for baseline differences

Measurement	Visit	Intervention (mean)	*N*	Control (mean)	*N*	GLM mean difference	p value
Systolic BP	Baseline	124.8	241	130.3	234	−4.5	< 0.001
	Final visit	121.1	241	129.0	234		
Diastolic BP*	Baseline	78.4	240	81.2	234	−1.6	0.032
	Final visit	77.6	240	81.2	234		
Total Cholesterol	Baseline	5.26	241	5.26	234	−0.63	< 0.001
	Final visit	4.37	241	4.99	234		
LDL-cholesterol	Baseline	2.97	241	3.02	234	−0.46	< 0.001
	Final visit	2.37	241	2.87	234		
HDL-cholesterol*	Baseline	1.14	240	1.10	234	0.01	0.575
	Final visit	1.24	240	1.21	234		
Triglycerides*	Baseline	1.42	240	1.48	234	−0.16	0.005
	Final visit	1.42	240	1.60	234		
Fasting glucose*	Baseline	5.16	240	5.16	234	−0.17	0.008
	Final visit	5.15	240	5.31	234		

*For each of these variables, one data item was missing from the database.

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Changes in the main study

1) Participants: Those with and without CVD

2) Polypill formulation: Polypill 2 was added(Valsartan 40mg replace Enalapril 5mg)

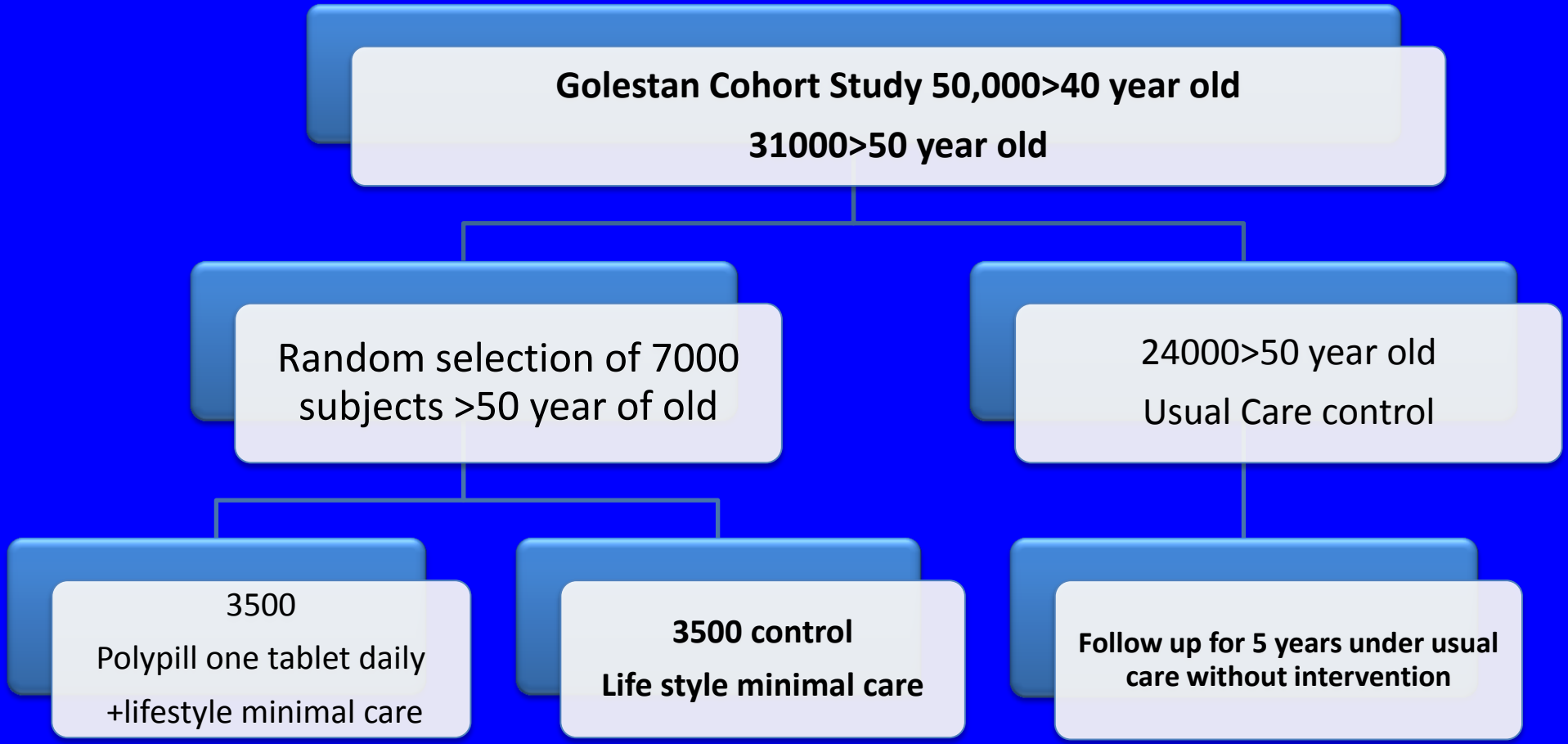
3) Comparison: Polypill vs. minimal care

4)Outcomes: CVD fatal and non-fatal events/other MCVE as primary, risk factors changes/non- CVD deaths as secondary ones.

5) Study design: Pragmatic RCT

6-Monitoring: Internal and external, interim analysis 2 years after last enrolment

PolyIran Study



PolyIran study:

- Villages were randomised to the control or intervention arm in January 2011 by statisticians in Birmingham.

- In February 2011, local study representatives started recruiting individuals from each of the villages, knowing the allocation status of each village.

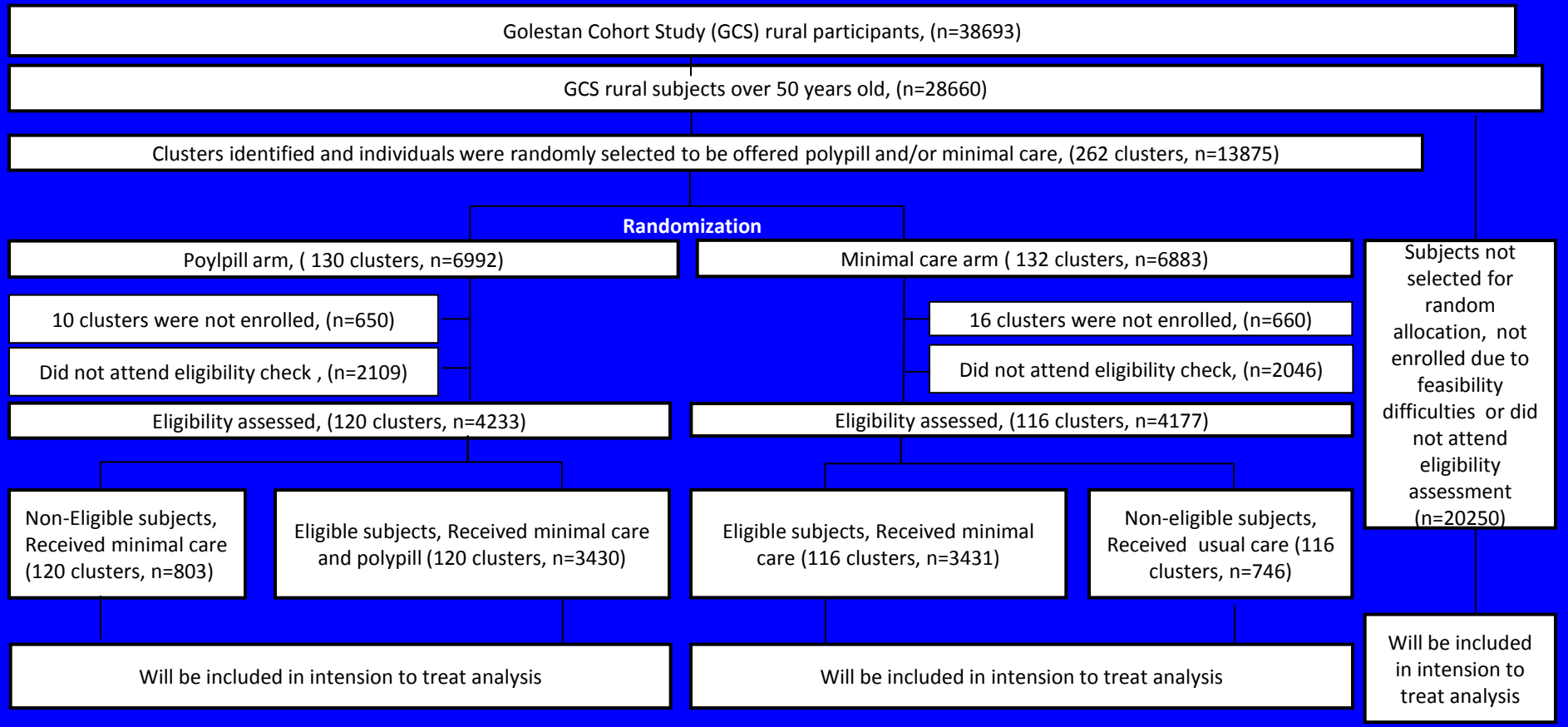
PolyIran Enrollment and Follow-up

- Totally **8410** subjects were enrolled to the study and the enrolment phase of the study was completed on April 15th 2013
- The follow-up phase began on Thursday, May 26th, 2011 and has been continued since then.
- The protocol was to follow intervention arm at months 1, 2, 3, 6, and then every 6 months after that; and to follow control arm at months 3, 6, and then every 6 months after that.

Text Messages

- Text messaging service was used:
  - To improve adherence to Polypill tablets (only intervention arm)
  - To encourage participants to modify their lifestyle (both intervention and control arms) in a way to prevent cardiovascular diseases.
- The protocol is to send a life style modification messages and messages to improve adherence every other week

Trial flow chart



Reasons for exclusions

Reasons for which subjects did not meet the eligibility criteria, n(%)

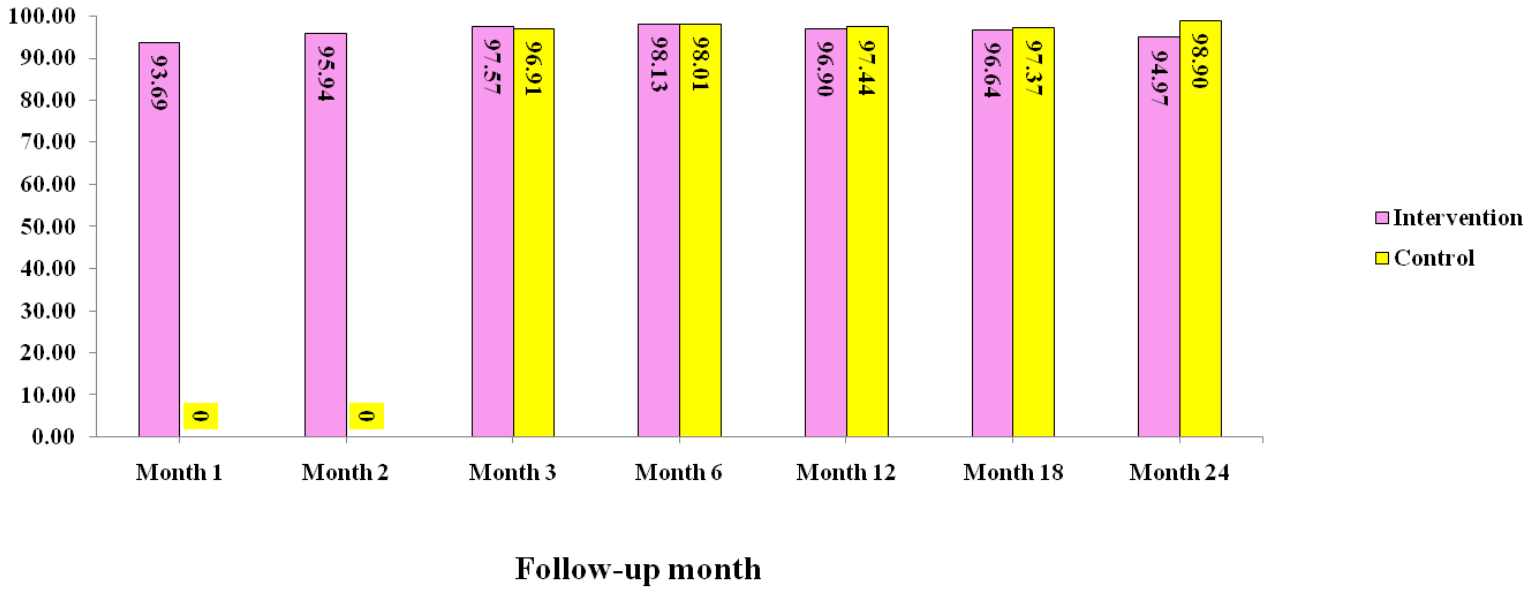
	Polypill arm	Control arm
Hypersensitivity to components of Polypill	11(1.4)	7(1)
History of angioedema	1(0.1)	1(0.1)
Peptic ulcer disease or gastrointestinal bleeding in last 3 months	13(1.7)	12(1.7)
Lactation or pregnancy	-	-
Bleeding disorders	1(0.1)	1(0.1)
Anticoagulation therapy	24(3.1)	13(1.8)
Alcohol consumption	2(0.3)	1(0.1)
Advanced liver disease	22(2.8)	16(2.2)
Uncontrolled epilepsy	10(1.3)	13(1.8)
Severe asthma	104(13.3)	136(19.1)
History of gout	2(0.3)	1(0.1)
Serum creatinine> 2 mg/dL	27(3.5)	30(4.2)
Glomerular filtration rate < 30 ml/min	51(6.5)	58(8.1)
Anemia	208(26.6)	184(25.8)
Blood pressure <90/60 mmHg	88(11.3)	36(5)
Medical/psychiatric disabilities	292(37.3)	299(41.9)
Non-availability	28(3.6)	2(0.3)
History of CVA	17(2.2)	27(3.8)

History of major cardiovascular events at baseline, n(%)

	Polypill arm	Control arm
Ischemic heart disease	472(11.15)	429(10.27)
Myocardial infarction	59(1.39)	63(1.51)
Heart failure	19(0.45)	17(0.41)
Stroke	37(0.87)	58(1.39)
Subjects with MCVE	522(12.33)	510(12.2)
Subjects without MCVE	3711(87.67)	3667(87.79)

MCVE: Major cardiovascular event

Figure 2. Proportion (%) of successful follow-up visits in Intervention and Control groups of the PolyIran trial (December, 2013)



Some Views of Isfahan

Thank You