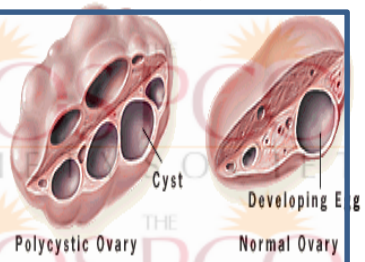
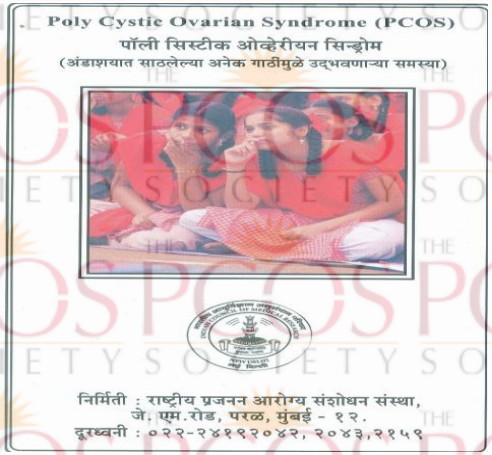
Research on PCOS at National Institute for Research in Reproductive Health (ICMR)



- **Epidemiological and Health Systems Research**
  - Community based studies on prevalence, risk factors and co-morbidities
  - Assessing current management practices and capacity building
- **Clinical**
  - Multidisciplinary management of PCOS
  - Cohort of infertile and adolescents reproductive and metabolic outcomes
- **Basic**
  - Genetic and epigenetic studies to understand the pathophysiology of PCOS using a multifaceted approach of genomics and proteomics
  - Development of animal model of PCOS to study cystogenesis
- **Bioinformatics** -mapping all the genes involved in the pathogenesis of PCOS

Community based studies on PCOS Challenges and Opportunities



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Community based study of PCOS prevalence among adolescents and young girls in Mumbai

- Systematic multistage random sampling method (Zone-Ward –Health post area- 80,000 population)
- Inclusion Criteria : Age 15- 24 yrs, 2 years post menarche and unmarried
- A sample size of 900 was calculated assuming a prevalence of 10% and precision of 2% at 95% confidence level
- Considering a non-response rate of 10%, the total was estimated to be about 1000 girls
- Eligible girls in selected study area - approx. 10,600 (census data)
- Household list obtained
- Every 10th household approached
- History at household after informed consent
- Medical examination at health post
- Blood collection on 3rd to 7th day of normal cycle
- USG abdominal -collective activity
- All enrolled cases screened - Probable cases – Diagnosis of exclusion
  - Controls –Reference

Joshi B et al., IJEM 2014

Participant Enrollment and Retention

Enrollment

- Only 3% girls had heard about PCOS
- Consent of parents/husbands
- Difficult to access high income groups
- Door to door survey in crowded slum – sensitive nature of questions
- Number of repeat visits
- Timings of the clinic
- Coordination for USG
- Girls were more concerned with cosmetic problems than menstrual
- Enroll only one from each household

Dropouts

- Stigma
- Parents refusal
- Got married or shifted residence
- No clinical symptoms -Not willing for investigations
- Inconvenient timing due to work or academic related activities

Strengths

- Involvement of local health post providers and CHVs
- Capacity building
- Provision of comprehensive adolescent services with supply of medicines
- Follow-up and counselling
- Proximity to investigation facilities

Caution

- Over-diagnosis
- Create anxiety

Continum of care- Referral services

Investigations required

Basic for PCOS diagnosis

- UPT
- **Total Testosterone**
- SHbg
- T4, TSH
- Prolactin
- 17 OHP

Diagnosis of MS

- FBS
- 2 hrs post 75 gms glucose
- Lipid profile

BMI- Criteria
Reference norms- ± 2SD

- Timing of blood collection
- Sample storage and transport to central facility- Cost and logistics
- Cost of Investigations – In house Rs. 2500/-per case

Pitfalls Of Ultrasonic Criteria ?
Significant intra-observer and inter-observer variability
Single sonologist

Determining Prevalence of PCOS among adolescents and young girls in Mumbai

Enrolled Participants (n=1000)

*Dropouts (N=222)

*After five rounds of home based health educative sessions with validated written information brochures

Completed all Investigations (n=600)

Completed investigations Partially (n=178)

Probable PCOS
Rotterdam = 149 (24.8%)
AES = 79 (13.2%)

Probable PCOS
Rotterdam = 20 (11.2%)

True PCOS
Rotterdam = 144 (22.5%)
AES = 76 (10.7%)

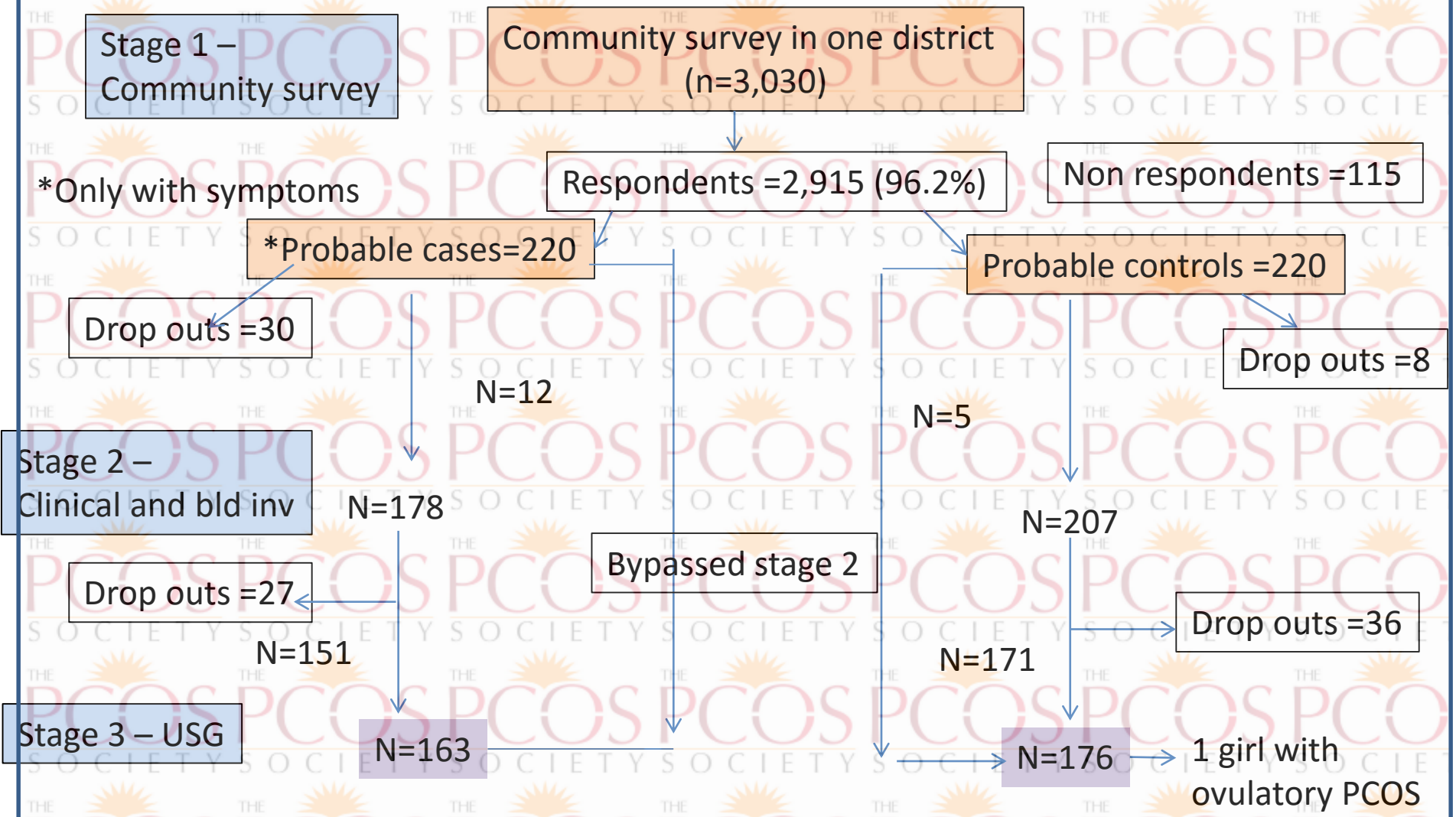
Counseling
Management
Followup-70%

Common Phenotypes –
Mild - 52.6% Frank -27.4%
Classic -13.3% **Ovulatory – 6.7%**

Salient findings

- **19% hyperinsulinemic**
- **History of oligomenorrhea**
- Specificity - 93.9%
- Sensitivity - 83.3%
- **72% were lean PCOS**
- **Metabolic syndrome -0.8%**
- **Mean 2hrs post glucose and LDL values significantly higher among obese and overweight**

Community based study in Srilanka



Prevalence-6.3% mainly reproductive phenotype
Rotterdam criteria

Kumarapeli V et al., 2008

Community based study -China

Invited participant 20,000 women

Initial rejecters 3114

Initial participants 16886 women

Completed questionnaire 15924

Normal 15030

Blood test Control 2732

PCOS 984

Blood Test 833

Prevalence-5.6% Rotterdam criteria

High prevalence of Metabolic disorders

- 10 Provinces
- 3 Strata
- 1 Township
- Villages in each township -3 strata of equal number of villages
- One village

Rong Li et al.,Human Reproduction 2013

Proposed ICMR Task force study on PCOS prevalence –Multi-centric study

- Through NIRRH Field Units/Medical Colleges -9 sites
- Involvement of Depts. of Community Medicine, OBGYN and Endocrionologist, Dermatologist, Psychiatry, Laboratory services
- Sample size -6300–Both Urban and Rural
- Multilayer stratified random sampling
- Purposive selection of rural setting- Ultrasound facilities (Observer dependency-??? –Follow NIH criteria –Miss ovulatory phenotypes?)
- Most reliable method for S. Testosterone levels -LCMS – centralized facility –cost of transport
- External team unknown to the community- need to involve local grass root level health providers
- Ensure basic management at PHCs with good referral linkages to tertiary facilities

➢ **Health economics of PCOS**

Birth cohort study in Australia

Flow chart of women involved in the study; from tracing through to the interview and clinical examination.

Prevalence-12%
Rotterdam criteria

National PCOS Guidelines
PCOS Australian Alliance 2011

Imputed figures for those who did not undergo inv.

Wendy M et al., Human Reproduction 2010

Cohort studies

- A large-scale, population-based retrospective cohort study in Taiwan among 3,566 PCOS vs 14,264 matched non PCOS. The adjusted hazard ratio of uterine cancer and breast cancer in subjects with PCOS were higher (HR: 8.42 [95% confidence interval: 1.62–43.89] and HR: 1.99 [95% confidence interval: 1.05–3.77], respectively) than that of the controls during the follow-up.

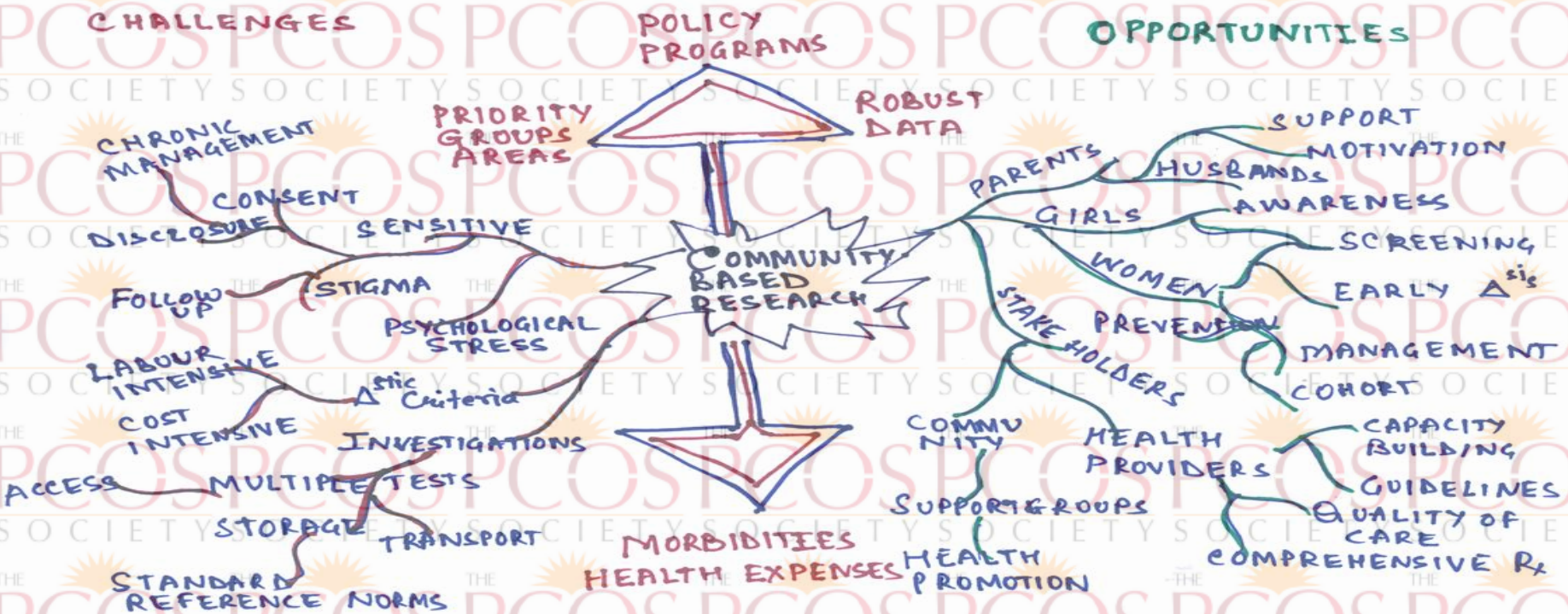
Cheng-Che et al., The Oncologist. 2015

- A long cohort of children born in the KEM Hospital since 1993 in the city of Pune and whose weights at birth were recorded in the labour ward register were followed up to determine the relationship between birth-weight and cardiovascular disease (CVD) risk factors and PCOS. Lower birth-weight was associated with increased insulin resistance. The highest levels of CVD risk factors were in children of low birth weight but high fat mass at 8 years

Pune Maternal Nutrition study Yajnik S et al., 2010

Way forward

Mind mapping



NCD-PCOS

Communicable diseases

Diverse Ethnicity

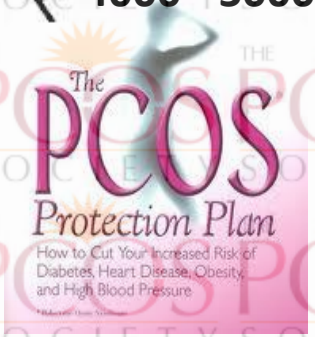
Diabetic capital

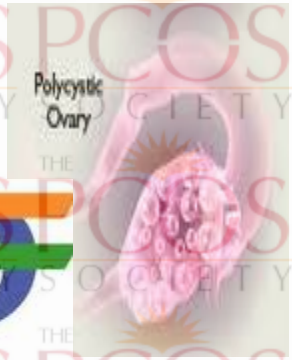
Acknowledgement

- Dr. Duru Shah and PCOS Society
- Co authors –Dr. Rama Vaidya and Dr. Sanjay Chauhan
- ICMR
- NIRRH –Director, Co- Scientists, Staff
- Study participants and gatekeepers

Economic burden to a woman affected with PCOS

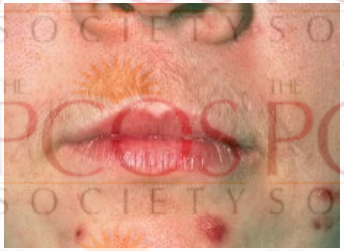
Metabolic & CVD
Per session
₹ 4000 - 50000





Lifestyle MRx

₹ 20- 50000/ yr



Cosmetologic therapies

Per session
₹ 7000

Initial evaluation
₹ 4000 - 5000

Menstrual disorders, infertility

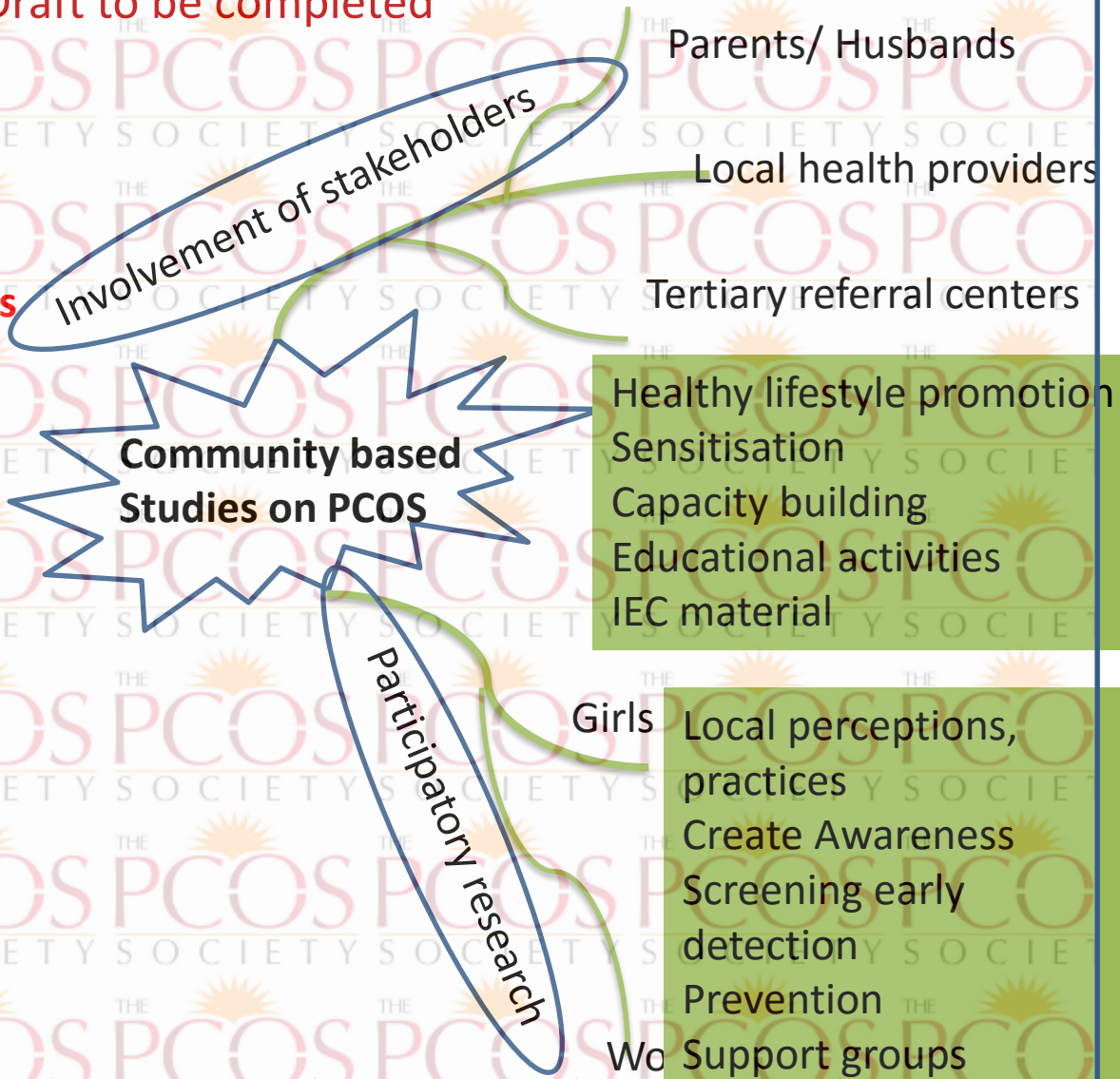
Per month
₹ 5000 – 1 L (IVF)

Mind mapping

Draft to be completed

Green – opportunities

Red will go on left side for challenges



Studies among defined population groups other than hospital settings

- Use of convenience samples eg.
  - recruiting women through publicity campaigns employee medical examinations
  - blood donors
  - school going girls etc.

- Non randomized
- Statistical evidence lacking to determine the representativeness of participants

Opportunities

- Influence policy and program- Australia National Health Program Awareness
- Participatory learning and involvement
- Local support group network
- Early screening
- Access to health services
- Health interventions
- Involvement of health system
- Capacity building

Community based prevalence studies

Country	Methodology and Sample size	Prevalence %
Australia Wendy *et al.*, 2009	Birth cohort **728** women predominately Caucasian women aged 27–34 years, born in Adelaide, South Australia	12
China *Rong Li et al.,2013*	10 provinces and municipalities multi-layer, stratified sampling method Rural: Urban ratio of 1:1 Women from 152 cities and 112 villages **20,000** women aged 19-45 yrs	5.6
Srilanka Kumarapeli V *et al.*, 2008	4 divisional secretariat areas of a district randomly selected Cluster sampling proportionate to population size **3,030** women aged 15-39 yrs	6.3 (Rotterdam)
India Joshi B et al 2014	1200 adolescent and young girls (15-24 yrs) from a defined selected geographical area in Mumbai	10.5(AES)
	A long cohort of children born in the KEM Hospital in the city of Pune and whose weights at birth were recorded in the labour ward register were followed up to determine the relationship between birth-weight and cardiovascular disease	

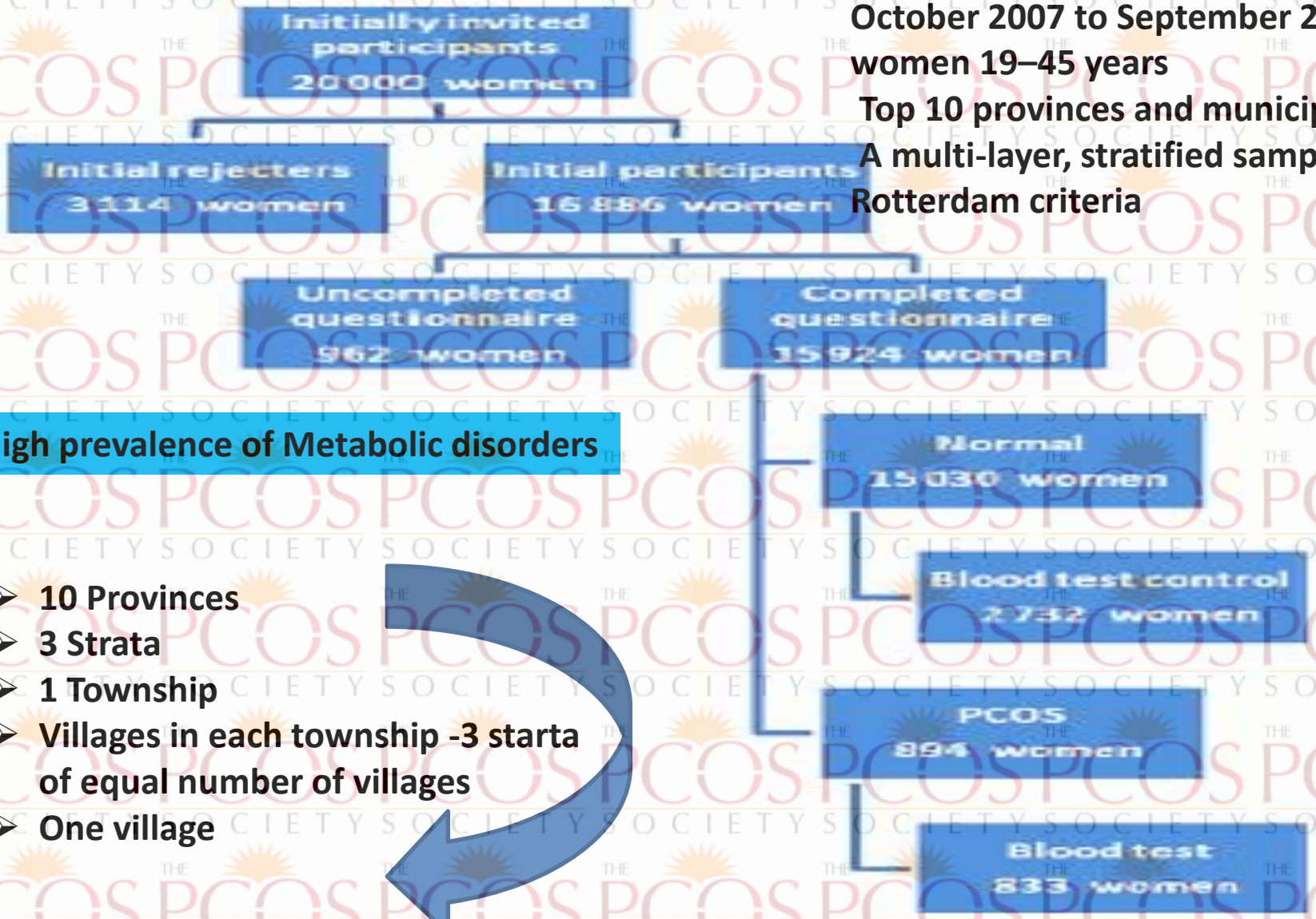
Community based study -China

October 2007 to September 2011, women 19–45 years

Top 10 provinces and municipalities

A multi-layer, stratified sampling

Rotterdam criteria



High prevalence of Metabolic disorders

- 10 Provinces
- 3 Strata
- 1 Township
- Villages in each township -3 starta of equal number of villages
- One village

Rong Li et al.,Human Reproduction 2013

PCOS Phenotypes* (n=600)

Mild (J) - 52.6% Frank(A,C,E) -27.4%

Classic(B, D,F) -13.3% Ovulatory(G,H,I) – 6.7%

Signs/Symptoms	A	B	C	D	E	F	G	H	I	J
Biochemical Hyper Androgenemia (FAI)	+	+	+	+	-	-	+	-	+	-
Hirsuitism	+	+	-	-	+	+	+	+	-	-
Oligomenorrhea	+	+	+	+	+	+	-	-	-	+
Polycystic ovaries on USG	+	-	+	-	+	-	+	+	+	+
PCOS (N=135)	8.1	-	8.9	5.2	10.4	1.5	1.5	8.1	3.7	52.6

*Ref: Norman RJ,et al., Polycystic Ovary Syndrome. Lancet 2007; 370 (9588): 685-97