# Basic Statistical Concepts
# &
# Study Design

**Workshop on ICH-GCP**

**13-14 February** 2020

# Outline

I. Research Question

II. Statistical Errors

III. Selection of Study Design

IV. Study Design & Statistical Concepts

# Research Question

**Dr. Khin Thet Wai**
**Director (Retd.), Chairperson,**
**IRB (DMR)**

# I. A good research question

**The definition of research question is key to research design.**

- **F**EASIBLE
- **I**NTERESTING
- **N**OVEL [NEW & ORIGINAL]
- **E**THICAL
- **R**ELEVANT

# Anatomy of a Good Research Question

**P**= Research Problem Identification : POPULATION

**(disease, condition, stage, severity)**

**I** = Intervention, Prognostic Factor or Exposure

**C** = Comparison

(two drugs, a drug and no medication or a placebo, or two diagnostic tests, two interventions for BCC)

**O** = Outcome

- What can you hope to accomplish, measure, improve or affect?
- Relief or elimination of symptoms?
- Reduce the number of adverse events?
- Improve function or test scores? Quality of life?

# Example

"What is the quality of life?“

The group of patients (e.g. age), the area (e.g. Germany), the disease (e.g. carcinoma breast), the condition (e.g. tumor stage 3), perhaps also the intervention (e.g. after surgery), and what endpoint (in this case, quality of life) is to be determined with which method (e.g. the EORTC QLQC30 questionnaire) at what point in time.

"What is the quality of life of patients with **CA breast**, tumor stage 3 eee 40-50 years age group in Myanmar after surgery with or without counselling if measured by EORTC QLQC30 questionnaire in 2017?”

# Example

- ***Study Population (P)***
- Patients co-infected with HBV and HIV, regardless of gender, age, the severity of infections and HBV genotype were included.
- ***Interventions (I)***
- Antiviral drugs (monotherapy or combination treatment) for the treatment of HBV infection were considered.
- ***Comparisons (C)***
- Data from an antiviral drug versus an alternative antiviral drug, combination treatment, or placebo were included.
- ***Study Outcomes (O)***
- Treatment success (virologic response) was defined as achieving undetectable levels of HBV DNA in patients at the end of 1 year (36–52 weeks).

# Statistics and Study Design

**Dr. Kyaw Lwin Show**
**Research Officer**
**Member, IRB (DMR)**

# II. Statistical Errors

| | |
|---|---|
| **STUDY DESIGN** | **No randomization in controlled trials**<br>**Inappropriate Control Group** |
| **DATA ANALYSIS** | **Unpaired Test for Paired Data** |
| **DATA PRESENTATION** | **SE but not SD**<br>**Pie charts for continuous variables** |
| **DATA INTERPRETATION** | Interpretation of poorly done study as a well done one |

# III STUDY DESIGN

Under estimated Significance of **Study Design**

**Subsequent Quality**

**Reliability of conclusion**

**Ability to publish a study**

## Six Main Considerations

- **The question to be answered**
- The study population
- The unit of analysis
- The type of study
- The measuring technique
- The calculation of sample size

# Choice of Study Design

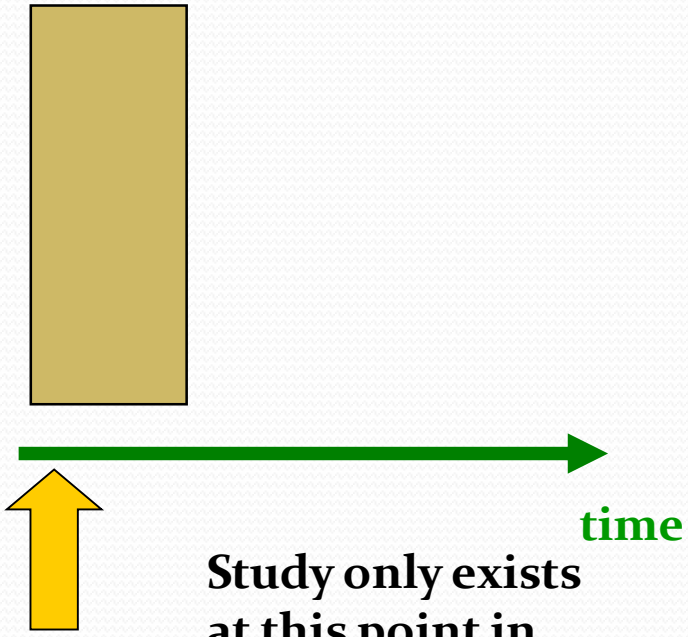
The choice of the study design is mainly determined by:

- Objectives of the study
- Available resources
- **Time frame allowed**

# Case reports and case series

- Detailed report of one or a series of patients
- Describe clinical characteristics of a well-defined group of patients without comparison group (e.g., pts. with a certain disease)

# Cross-sectional studies




- An "observational" design that surveys exposures and disease status at a single point in time
- Observe **prevalence** of a disease, not incidence of disease
- Can be usually performed in a short time
- Association can be investigated
- **Causality usually cannot be inferred**
- Can be useful for generating hypotheses

# B. Analytic/Observational Studies

To examine the relationships between **exposure** and **disease status** (or health outcome) in order to judge whether a particular exposure causes or prevents disease

**Cross-sectional Comparative Studies**

**Case-Control Studies**

**Cohort Studies**

# Case-Control Study

Tony Nengom et al. BMC Pediatrics (2017) 17:109
DOI 10.1186/s12887-017-0862-4

BMC Pediatrics

RESEARCH ARTICLE Open Access

## Assessment of cardiac function in children with congenital adrenal hyperplasia: a case control study in Cameroon

J. Tony Nengom[1*], S. Sap Ngo Um[1,2], D. Chelo[1,2], R. Mbono Betoko[1], J. Boombhi[1,3], F. Mouafo Tambo[1,4], A. Chiabi[1,4], S. Kingue[1,3] and P. Koki Ndombo[1,3]

**Abstract**

**Background:** High level of androgens found in congenital adrenal hyperplasia (CAH) seems to have a deleterious effect on heart function. We therefore evaluate cardiac function of children with CAH in comparison with a healthy group.

**Methods:** We carried out a case-control study in the single endocrinology unit of the Mother and Child Center of Chantal Biya's Foundation. Cases were matched for age and genotypic sex to 2 healthy controls. We analyzed the ejection fraction (LVEF), fractional shortening and left ventricular mass; output and cardiac index; E and A waves velocities, E/A ratio and the mitral deceleration time and diameter of the left atrium; tricuspid annular plane systolic excursion and pulmonary artery systolic pressure were also measured.

**Results:** We included 19 patients with a median age of 6.26 ± 3.75 years and 38 controls stackable distribution. The left ventricular mass of cases was greater than that of controls. A case of reversible cardiomyopathy on hormone replacement therapy was found.
For the cases, the average ejection fraction was 71.95 ± 7.88%; the average fractional shortening was 40.67 ± 7.02%. All these values were higher than those of controls, although the difference was not statistically significant. Diastolic left ventricular function was more impaired among the cases.
Right ventricular function was similar in both groups. These abnormalities were highly correlated to the late age at diagnosis and duration of treatment.

**Conclusion:** This study shows an altered cardiac function in CAH compared to healthy control and highlights importance of an early diagnosis of cases, a tight control of androgens levels and a regular monitoring of cardiac function.

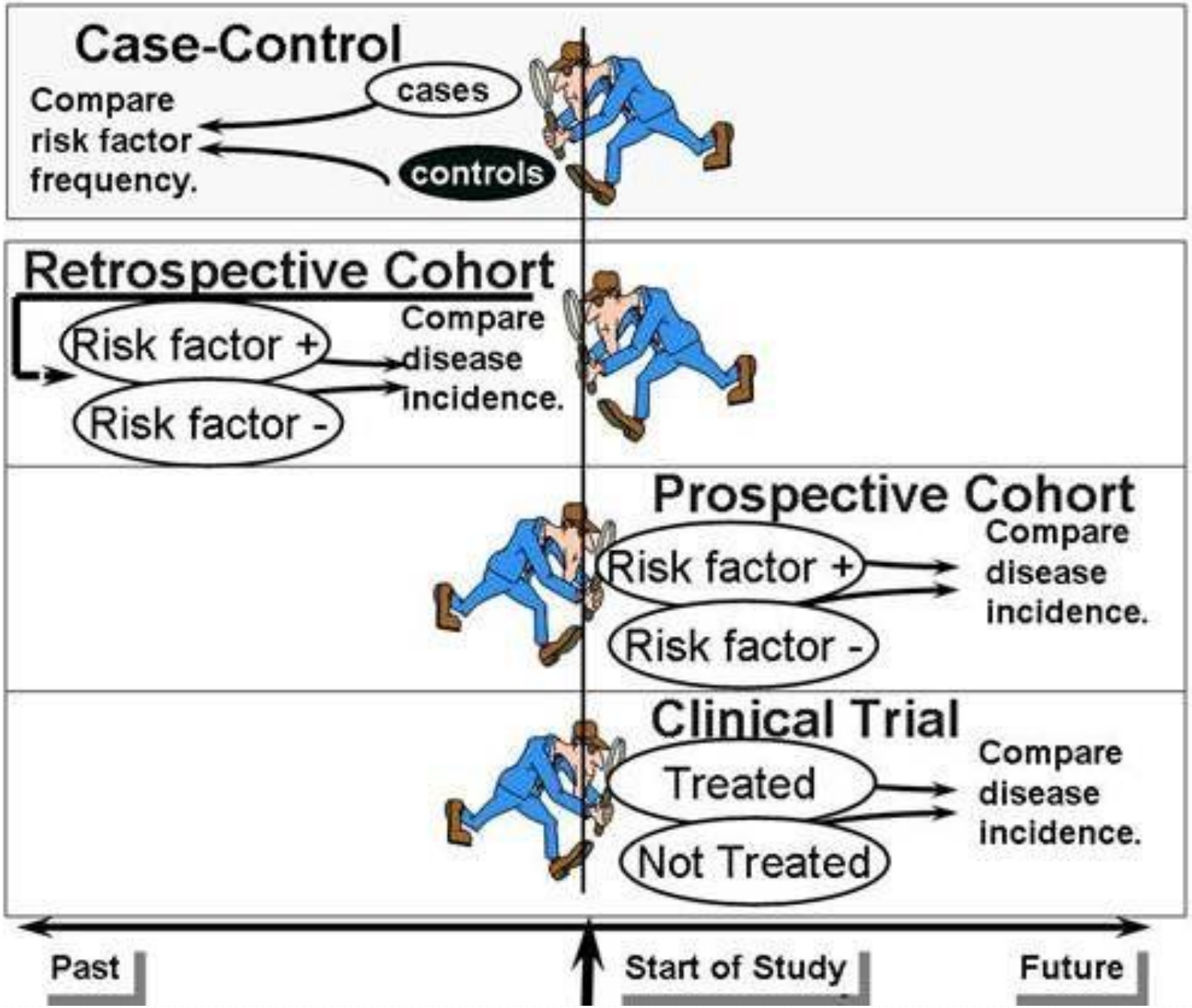
**Keywords:** Cardiac function, Congenital adrenal hyperplasia, Children

## Strengths

- Less expensive & time consuming
- Efficient for studying rare diseases

## Limitations

- Inappropriate when disease outcome for a specific exposure is not known at start of study
- Exposure measurements taken after disease occurrence
- Disease status can influence selection of subjects


Case-Control
Compare risk factor frequency.
cases
controls
Retrospective Cohort
Risk factor +
Risk factor -
Compare disease incidence.
Prospective Cohort
Risk factor +
Risk factor -
Compare disease incidence.
Clinical Trial
Treated
Not Treated
Compare disease incidence.
Past
Start of Study
Future

# Experimental Studies

**PHASE I:** Pharmaco kinetics & dynamics studies in a small number of healthy volunteers **(20-80)**

**PHASE II:** Standard treatment method has to be compared with placebo **(75-300)**

**PHASE III:** **W**hether the new drug is better than the standard drug (at least 2 RCTs required) **(1,000-2,000)**

**PHASE IV:**

Post-marketing product surveillance studies, conducted on patients in daily life; approved; evaluate the adverse effect and various additional indications of a new drug.

# Randomised Controlled Trials

- Self-controlled study: no independent control group
- Cross-Over Design: self-controlled & independent gps
- Parallel Group Design
- Factorial Design

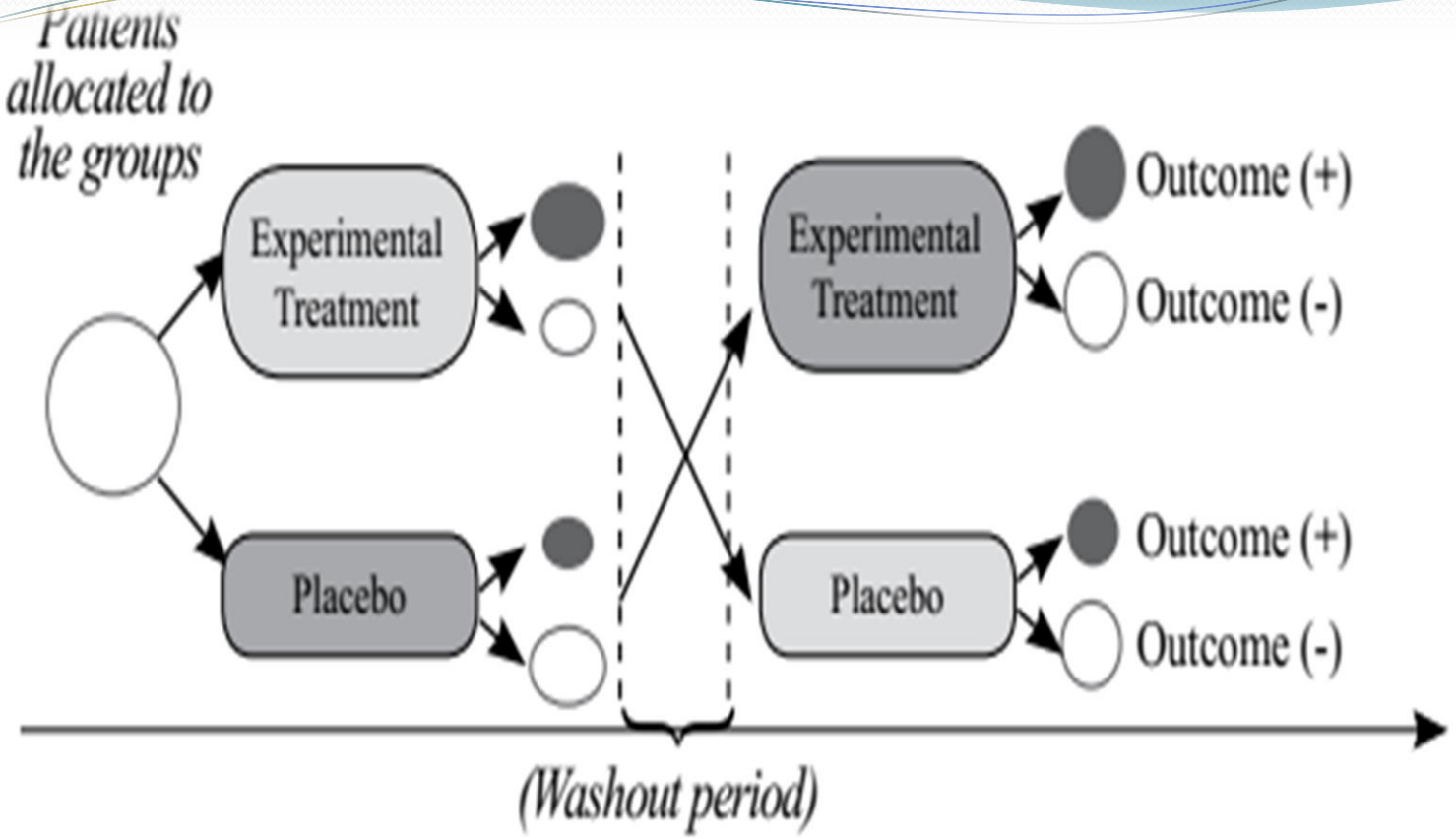



**FIG. 5.** Crossover study design

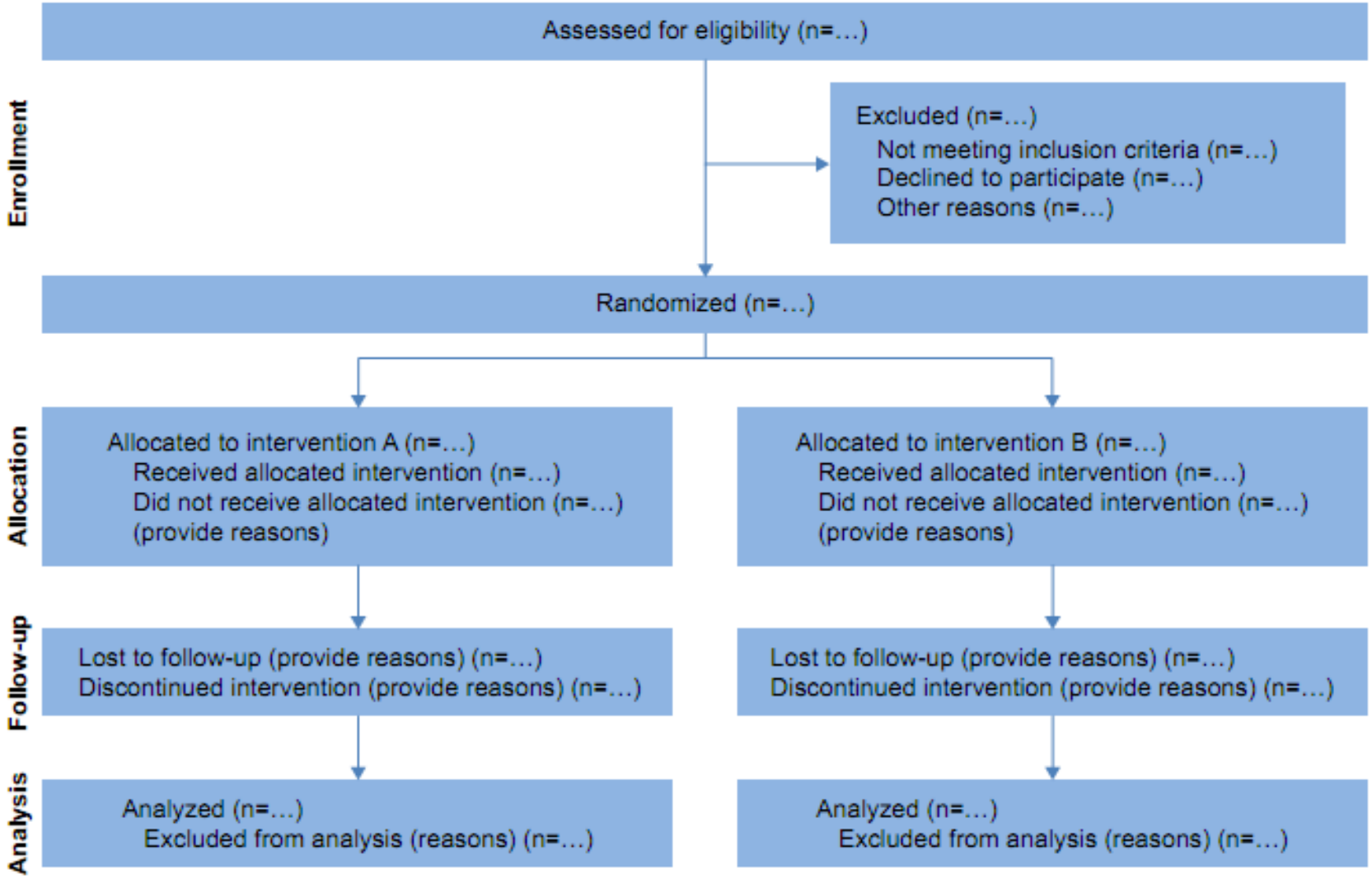
# Pros and Cons of the Crossover Trials

- A controlled trial where each participant has both therapies e.g is randomised *to treatment A* first then starts *treatment B*.

- **Advantages:**
  - all participants serve as own controls and error variance is reduced, thus reducing sample size needed
  - all participants receive treatment (at least some of the time)
  - statistical tests assuming randomisation can be used and blinding can be maintained

- **Disadvantages:**
  - all participants receive placebo or alternative treatment at some point
  - washout period lengthy or unknown
  - cannot be used for treatments with permanent effects

# Parallel Group Design



# RCT with Full Factorial Design

## Preventing falls among older people

Group-based Exercise

Home hazard Management

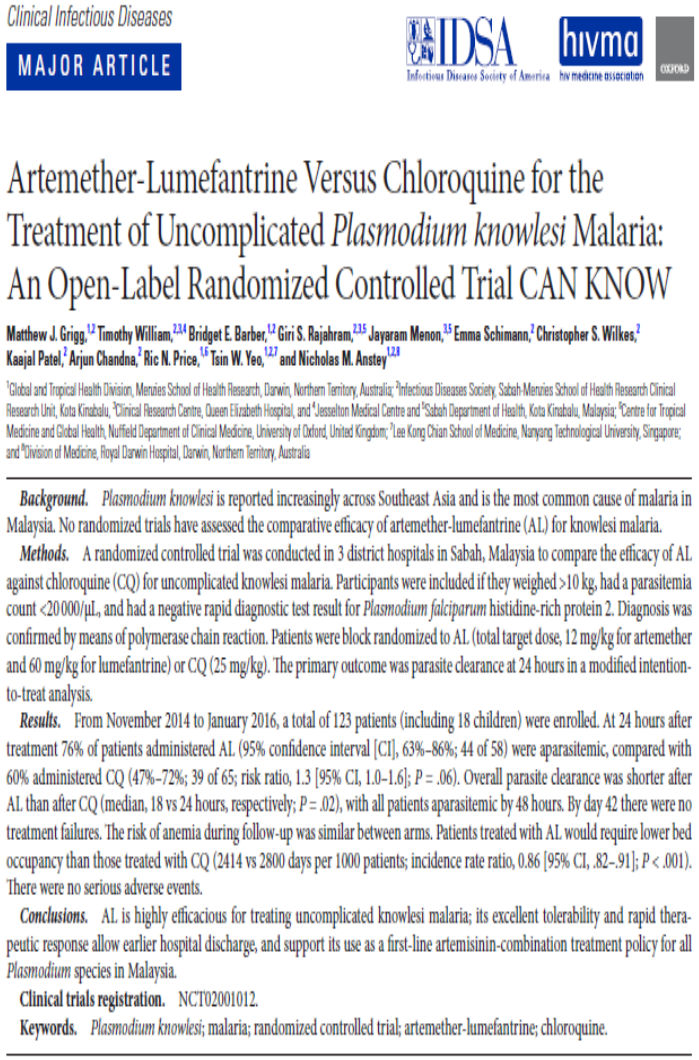
Vision Improvement

No Intervention

Self-reported time to first fall after intervention

# OPEN LABELLED RCT

- A design with subjects randomly assigned to "treatment" and "comparison" groups
- Provides most convincing evidence of relationship between exposure and effect
- Not possible to use RCTs to test effects of exposures that are expected to be harmful, for ethical reasons
- **The "gold standard" of research designs**



*Clinical Infectious Diseases*

MAJOR ARTICLE

## Artemether-Lumefantrine Versus Chloroquine for the Treatment of Uncomplicated *Plasmodium knowlesi* Malaria: An Open-Label Randomized Controlled Trial CAN KNOW

Matthew J. Grigg,[1,2] Timothy William,[2,3,4] Bridget E. Barber,[1,2] Giri S. Rajahram,[2,3,5] Jayaram Menon,[3,5] Emma Schimann,[2] Christopher S. Wilkes,[2] Kaajal Patel,[2] Arjun Chandna,[2] Ric N. Price,[1,6] Tsin W. Yeo,[1,2,7] and Nicholas M. Anstey[1,2,8]

[1]Global and Tropical Health Division, Menzies School of Health Research, Darwin, Northern Territory, Australia; [2]Infectious Diseases Society, Sabah-Menzies School of Health Research Clinical Research Unit, Kota Kinabalu, [3]Clinical Research Centre, Queen Elizabeth Hospital, and [4]Jesselton Medical Centre and [5]Sabah Department of Health, Kota Kinabalu, Malaysia; [6]Centre for Tropical Medicine and Global Health, Nuffield Department of Clinical Medicine, University of Oxford, United Kingdom; [7]Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore; and [8]Division of Medicine, Royal Darwin Hospital, Darwin, Northern Territory, Australia

***Background.*** *Plasmodium knowlesi* is reported increasingly across Southeast Asia and is the most common cause of malaria in Malaysia. No randomized trials have assessed the comparative efficacy of artemether-lumefantrine (AL) for knowlesi malaria.

***Methods.*** A randomized controlled trial was conducted in 3 district hospitals in Sabah, Malaysia to compare the efficacy of AL against chloroquine (CQ) for uncomplicated knowlesi malaria. Participants were included if they weighed >10 kg, had a parasitemia count <20 000/μL, and had a negative rapid diagnostic test result for *Plasmodium falciparum* histidine-rich protein 2. Diagnosis was confirmed by means of polymerase chain reaction. Patients were block randomized to AL (total target dose, 12 mg/kg for artemether and 60 mg/kg for lumefantrine) or CQ (25 mg/kg). The primary outcome was parasite clearance at 24 hours in a modified intention-to-treat analysis.

***Results.*** From November 2014 to January 2016, a total of 123 patients (including 18 children) were enrolled. At 24 hours after treatment 76% of patients administered AL (95% confidence interval [CI], 63%–86%; 44 of 58) were aparasitemic, compared with 60% administered CQ (47%–72%; 39 of 65; risk ratio, 1.3 [95% CI, 1.0–1.6]; $P = .06$). Overall parasite clearance was shorter after AL than after CQ (median, 18 vs 24 hours, respectively; $P = .02$), with all patients aparasitemic by 48 hours. By day 42 there were no treatment failures. The risk of anemia during follow-up was similar between arms. Patients treated with AL would require lower bed occupancy than those treated with CQ (2414 vs 2800 days per 1000 patients; incidence rate ratio, 0.86 [95% CI, .82–.91]; $P < .001$). There were no serious adverse events.

***Conclusions.*** AL is highly efficacious for treating uncomplicated knowlesi malaria; its excellent tolerability and rapid therapeutic response allow earlier hospital discharge, and support its use as a first-line artemisinin-combination treatment policy for all *Plasmodium* species in Malaysia.

**Clinical trials registration.** NCT02001012.

**Keywords.** *Plasmodium knowlesi*; malaria; randomized controlled trial; artemether-lumefantrine; chloroquine.

# Methods of minimizing BIAS

## *How to deal with bias – think ahead*

1. **Design stage** - minimize or avoid bias.
   - Avoid **selection bias** by including/excluding eligible subjects, by
     - Choice of source population
     - Choice of the comparison group

2. **Analysis stage -** determine presence or direction of possible bias and also account for confounding in analysis.

3. **Publication stage** - Potential biases typically described in "Discussion" section. Provide judgment and possible consequences of bias on results

# Methods of minimizing BIAS (contd.)

## Blinding

**EXAMPLE: PADMA28 trial**

**Blinding**

Staff at Padma AG, Switzerland not involved in patient recruitment or other trial activities will label and pack the study medication according to a standard operating procedure and based on the randomization list provided by CTU Bern. The randomization list will be kept electronically at CTU Bern in a password protected file. Study personnel involved in patient recruitment and testing will have no access to the list. The statistician responsible for the final analysis will also have no access to the list until the primary analysis of the trial is finished.

**OPEN LABEL**

**SINGLE BLIND**

**DOUBLE BLIND**

# Pros and Cons of the RCT

**Advantages:**

- unbiased distribution of confounders
- blinding more likely
- randomisation facilitates statistical analysis

**Disadvantages:**

- expensive: time and money
- volunteer bias
- ethically problematic at times

# Cluster randomized trial (CRT)

- A type of trial in which groups of subjects are randomized in contrast with a traditional clinical trial
- Randomize different communities, clinics, or cities to either get or not get a particular intervention
- **Cluster RCTs** are defined as having "groups or clusters of individuals rather than individuals themselves . . . randomized to intervention arms" (Eldridge & Kerry, 2012, p. 3).

Source: University of Chicago, 2013

# Examples of cluster randomized trial (CRT)

Lund et al. BMC Pregnancy and Childbirth 2014, 14:29
http://www.biomedcentral.com/1471-2393/14/29

BMC Pregnancy & Childbirth

RESEARCH ARTICLE Open Access

## Mobile phones improve antenatal care attendance in Zanzibar: a cluster randomized controlled trial

Stine Lund[1*], Birgitte B Nielsen[2], Maryam Hemed[3], Ida M Boas[1], Azzah Said[3], Khadija Said[3], Mkoko H Makungu[3] and Vibeke Rasch[1,4]

**Abstract**

**Background:** Applying mobile phones in healthcare is increasingly prioritized to strengthen healthcare systems. Antenatal care has the potential to reduce maternal morbidity and improve newborns' survival but this benefit may not be realized in sub-Saharan Africa where the attendance and quality of care is declining. We evaluated the association between a mobile phone intervention and antenatal care in a resource-limited setting. We aimed to assess antenatal care in a comprehensive way taking into consideration utilisation of antenatal care as well as content and timing of interventions during pregnancy.

**Methods:** This study was an open label pragmatic cluster-randomised controlled trial with primary healthcare facilities in Zanzibar as the unit of randomisation. 2530 pregnant women (1311 interventions and 1239 controls) who attended antenatal care at selected primary healthcare facilities were included at their first antenatal care visit and followed until 42 days after delivery. 24 primary health care facilities in six districts were randomized to either mobile phone intervention or standard care. The intervention consisted of a mobile phone text-message and voucher component. Primary outcome measure was four or more antenatal care visits during pregnancy. Secondary outcome measures were tetanus vaccination, preventive treatment for malaria, gestational age at last antenatal care visit, and antepartum referral.

**Results:** The mobile phone intervention was associated with an increase in antenatal care attendance. In the intervention group 44% of the women received four or more antenatal care visits versus 31% in the control group (OR, 2.39; 95% CI, 1.08-5.55). There was a trend towards improved timing and quality of antenatal care services across all secondary outcome measures although not statistically significant.

**Conclusions:** The wired mothers' mobile phone intervention significantly increased the proportion of women receiving the recommended four antenatal care visits during pregnancy and there was a trend towards improved quality of care with more women receiving preventive health services, more women attending antenatal care late in pregnancy and more women with antepartum complications identified and referred. Mobile phone applications may contribute towards improved maternal and newborn health and should be considered by policy makers in resource-limited settings.

**Trial registration:** ClinicalTrials.gov, NCT01821222.

**Keywords:** Antenatal care, Maternal health, Neonatal health, Mobile phones, mHealth, Zanzibar

Check for updates

Original Article

Asia Pacific Journal of Public Health
2016, Vol. 28(8) 765–775

DOI: 10.1177/1010539516675698
aph.sagepub.com
SAGE

## Effectiveness of Mindfulness Intervention on Psychological Behaviors Among Adolescents With Parental HIV Infection: A Group-Randomized Controlled Trial

**Myo-Myo Mon, MBBS, MPH[1,2], Tippawan Liabsuetrakul, MD, PhD[2], and Kyaw-Min Htut, MBBS[1]**

**Abstract**

This study aims to identify the effectiveness of mindfulness intervention on the psychological behaviors of adolescents with parental HIV infection and its associated factors in Myanmar. A total of 80 adolescents from 2 intervention townships and 80 adolescents from 2 control townships were enrolled in a group randomized controlled trial with assessments at baseline and 6 months follow-up. The mindfulness intervention involved monthly group sessions for 3 consecutive months led by an experienced mindfulness trainer. Three domains of psychological behaviors—namely, emotional, conduct, and social behaviors—were assessed at baseline and compared after 6 months. Multilevel regression analysis was used to determine the effectiveness of the intervention and associated factors for psychological behaviors. The intervention significantly improved emotional and conduct behaviors at 6 months ($P < .001$) but had no effect on social behavior. The significant effect of the intervention existed after adjusting for gender, family type, child age, and orphan status.

**Keywords**

adolescent health, parental HIV infection, mindfulness, psychological behaviors

### Introduction

Human Immunodeficiency Virus (HIV) and Acquired ImmunoDeficiency Syndrome (AIDS) affect children and adolescents in many significant ways, especially on their health. Previous studies have documented the direct and indirect consequences of HIV and AIDS on the rights of children and adolescents, including the psychological impact, and access to health care services.[1-3] Importantly, children and adolescents with parental HIV infection are at risk of developing behavioral problems.[4,5]

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Email: mmyomon@gmail.com

# Community trial

- Trials on communities rather than patients
- Usually quasi-experimental

(absence of randomization (or) control)

- Usually test of preventive measures

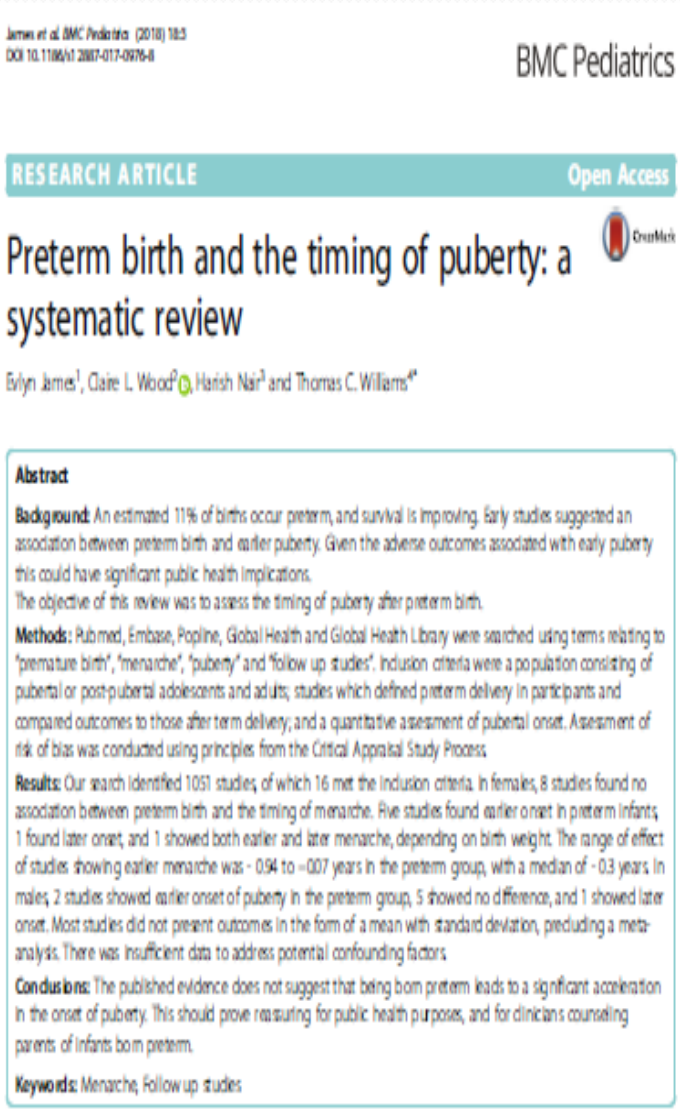
*Examples:*

- Iron-fortified salt and anemia in the community
- Impregnated bed net and malaria morbidity

# SYSTEMATIC REVIEWS

A **systematic review** is a means of identifying, evaluating and interpreting all available research relevant to a particular research question, or topic area, or phenomenon of interest.

Systematic reviews and meta-analyses are essential to summarize evidence relating to efficacy and safety of health care interventions accurately and reliably.



James et al. BMC Pediatrics (2018) 18:3
DOI 10.1186/s12887-017-0976-8

BMC Pediatrics

RESEARCH ARTICLE Open Access

## Preterm birth and the timing of puberty: a systematic review

Evlyn James[1], Claire L. Wood[2], Harish Nair[3] and Thomas C. Williams[4*]

**Abstract**

**Background:** An estimated 11% of births occur preterm, and survival is improving. Early studies suggested an association between preterm birth and earlier puberty. Given the adverse outcomes associated with early puberty this could have significant public health implications.
The objective of this review was to assess the timing of puberty after preterm birth.

**Methods:** Pubmed, Embase, Popline, Global Health and Global Health Library were searched using terms relating to "premature birth", "menarche", "puberty" and "follow up studies". Inclusion criteria were a population consisting of pubertal or post-pubertal adolescents and adults; studies which defined preterm delivery in participants and compared outcomes to those after term delivery; and a quantitative assessment of pubertal onset. Assessment of risk of bias was conducted using principles from the Critical Appraisal Study Process.

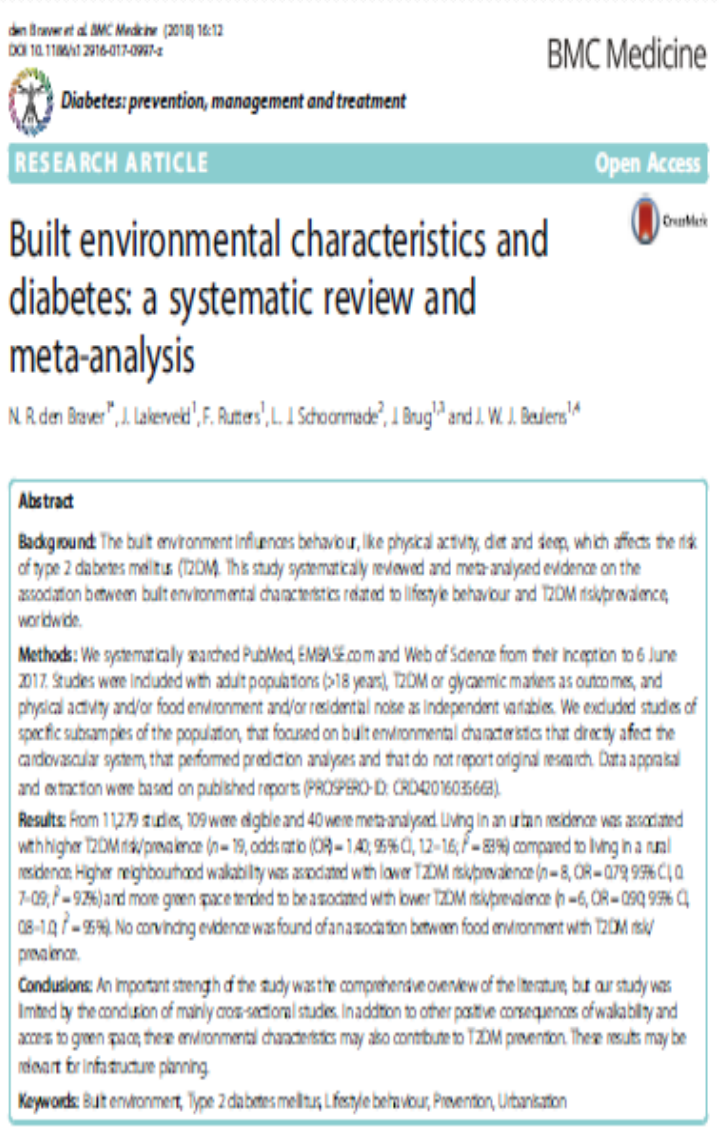
**Results:** Our search identified 1051 studies, of which 16 met the inclusion criteria. In females, 8 studies found no association between preterm birth and the timing of menarche. Five studies found earlier onset in preterm infants, 1 found later onset, and 1 showed both earlier and later menarche, depending on birth weight. The range of effect of studies showing earlier menarche was - 0.94 to −0.07 years in the preterm group, with a median of - 0.3 years. In males, 2 studies showed earlier onset of puberty in the preterm group, 5 showed no difference, and 1 showed later onset. Most studies did not present outcomes in the form of a mean with standard deviation, precluding a meta-analysis. There was insufficient data to address potential confounding factors.

**Conclusions:** The published evidence does not suggest that being born preterm leads to a significant acceleration in the onset of puberty. This should prove reassuring for public health purposes, and for clinicians counseling parents of infants born preterm.

**Keywords:** Menarche, Follow up studies

# SYSTEMATIC REVIEWS (Contd.)

- **Cochrane Systematic Reviews** are of primary research in human health care and health policy
- Internationally recognized as the **highest standard in evidence-based health care**
- Investigate the effects of interventions for prevention, treatment and rehabilitation
- Assess the accuracy of a diagnostic test for a given condition in a specific patient group and setting



den Braver et al. BMC Medicine (2018) 16:12
DOI 10.1186/s12916-017-0997-z

BMC Medicine

Diabetes: prevention, management and treatment

RESEARCH ARTICLE Open Access

Built environmental characteristics and diabetes: a systematic review and meta-analysis

N. R. den Braver*, J. Lakerveld, F. Rutters, L. J. Schoonmade, J. Brug and J. W. J. Beulens

**Abstract**

**Background:** The built environment influences behaviour, like physical activity, diet and sleep, which affects the risk of type 2 diabetes mellitus (T2DM). This study systematically reviewed and meta-analysed evidence on the association between built environmental characteristics related to lifestyle behaviour and T2DM risk/prevalence, worldwide.

**Methods:** We systematically searched PubMed, EMBASE.com and Web of Science from their inception to 6 June 2017. Studies were included with adult populations (>18 years), T2DM or glycaemic markers as outcomes, and physical activity and/or food environment and/or residential noise as independent variables. We excluded studies of specific subsamples of the population, that focused on built environmental characteristics that directly affect the cardiovascular system, that performed prediction analyses and that do not report original research. Data appraisal and extraction were based on published reports (PROSPERO-ID: CRD42016035663).

**Results:** From 11,279 studies, 109 were eligible and 40 were meta-analysed. Living in an urban residence was associated with higher T2DM risk/prevalence ($n = 19$, odds ratio (OR) = 1.40, 95% CI, 1.2–1.6; $I^2 = 89\%$) compared to living in a rural residence. Higher neighbourhood walkability was associated with lower T2DM risk/prevalence ($n = 8$, OR = 0.79, 95% CI, 0.7–0.9; $I^2 = 93\%$) and more green space tended to be associated with lower T2DM risk/prevalence ($n = 6$, OR = 0.90, 95% CI, 0.8–1.0; $I^2 = 95\%$). No convincing evidence was found of an association between food environment with T2DM risk/prevalence.

**Conclusions:** An important strength of the study was the comprehensive overview of the literature, but our study was limited by the conclusion of mainly cross-sectional studies. In addition to other positive consequences of walkability and access to green space, these environmental characteristics may also contribute to T2DM prevention. These results may be relevant for infrastructure planning.

**Keywords:** Built environment, Type 2 diabetes mellitus, Lifestyle behaviour, Prevention, Urbanisation

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2011

A Systematic Review and Meta-Analysis of the Effectiveness of Child-Parent Interventions for Children and Adolescents with Anxiety Disorders

Kristen Brendel
*Loyola University Chicago*





Georgia State University
ScholarWorks @ Georgia State University

Public Health Theses | School of Public Health

5-11-2013

A Systematic Review: Examining the Relationship Between Coffee Consumption and Breast Cancer

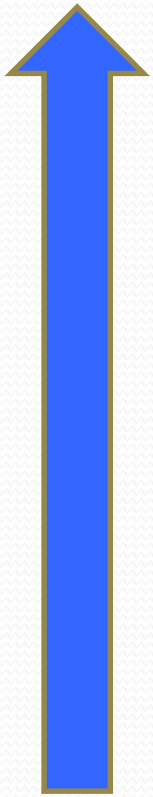
Lalini Pillay
*Institute of Public Health*



**FURTHER READINGS:** Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. (2009) The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration. PLoS Med 6(7): e1000100. https://doi.org/10.1371/journal.pmed.1000100

# Rating Evidence

- Systematic reviews
- Randomized clinical trials
- Non-randomized clinical trials
- Cohort study
- Case-control study
- Cross-sectional study
- Ecological study



# Network Meta-analysis (NMA)

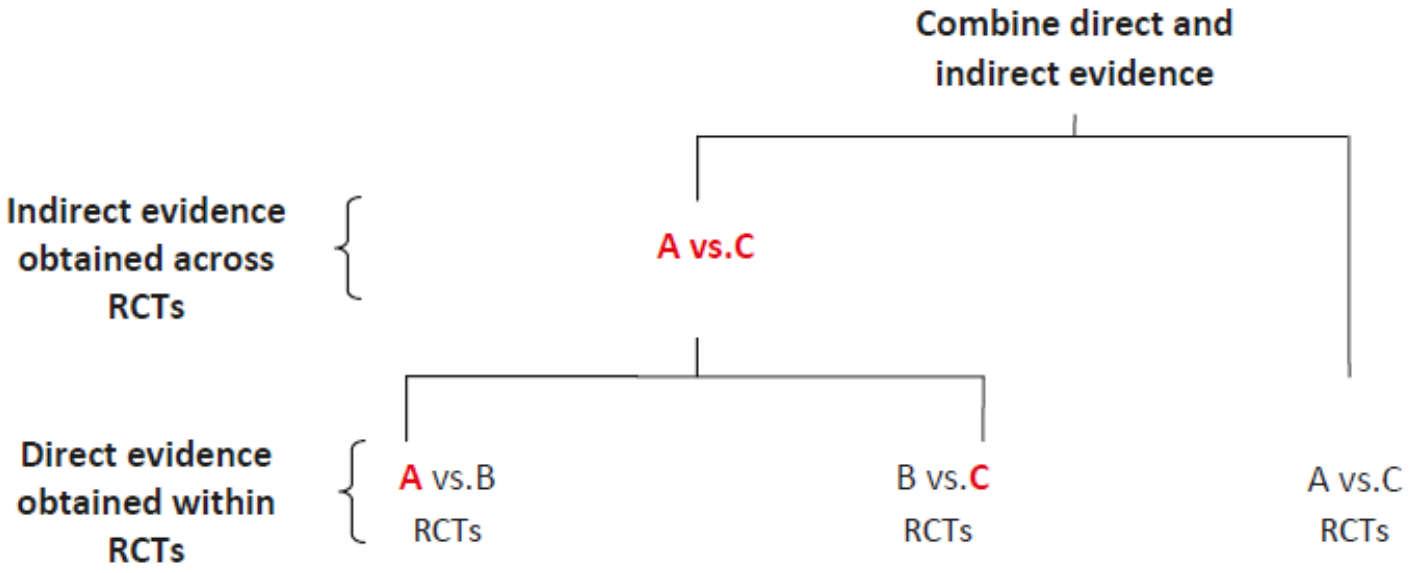
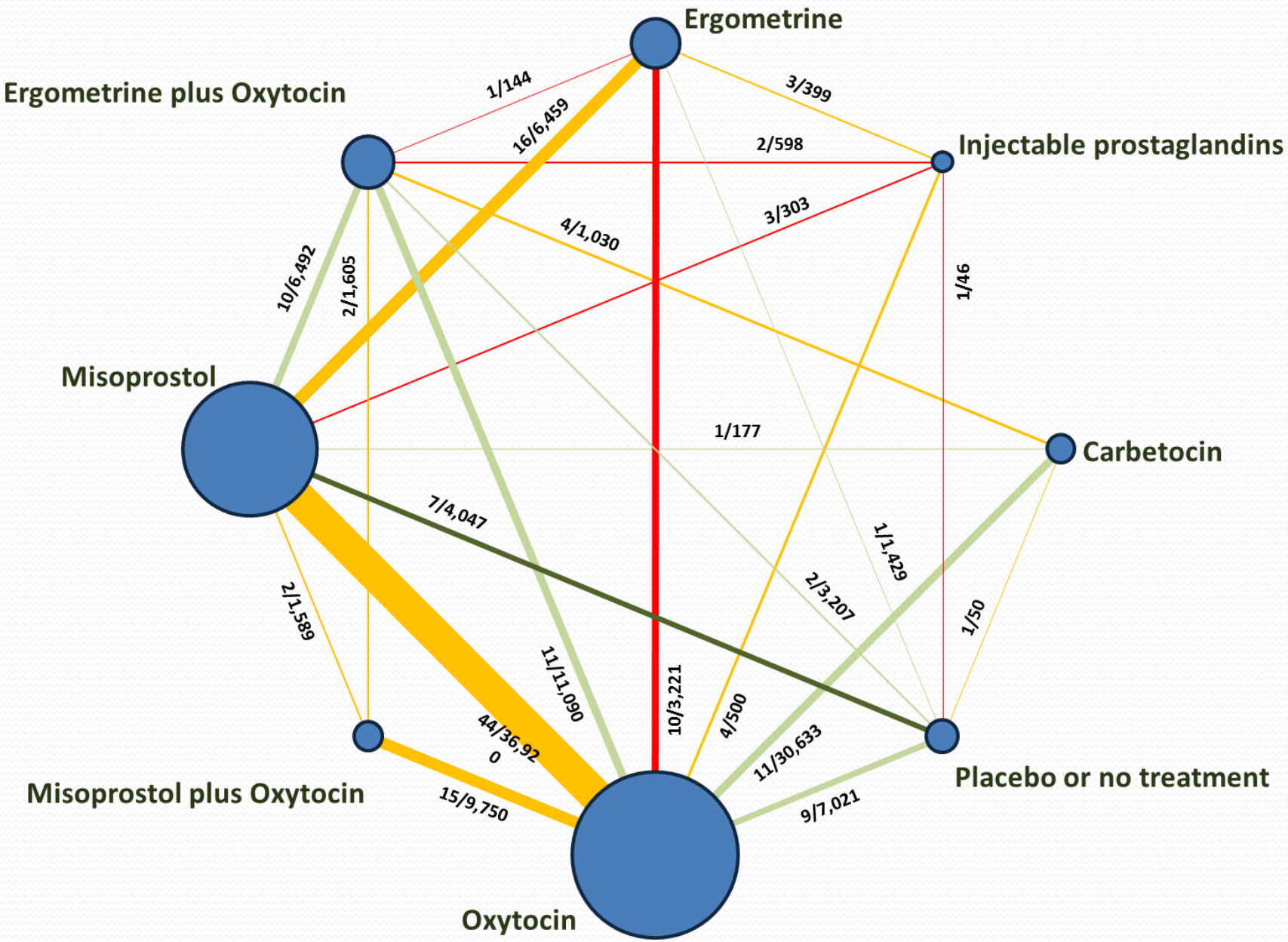
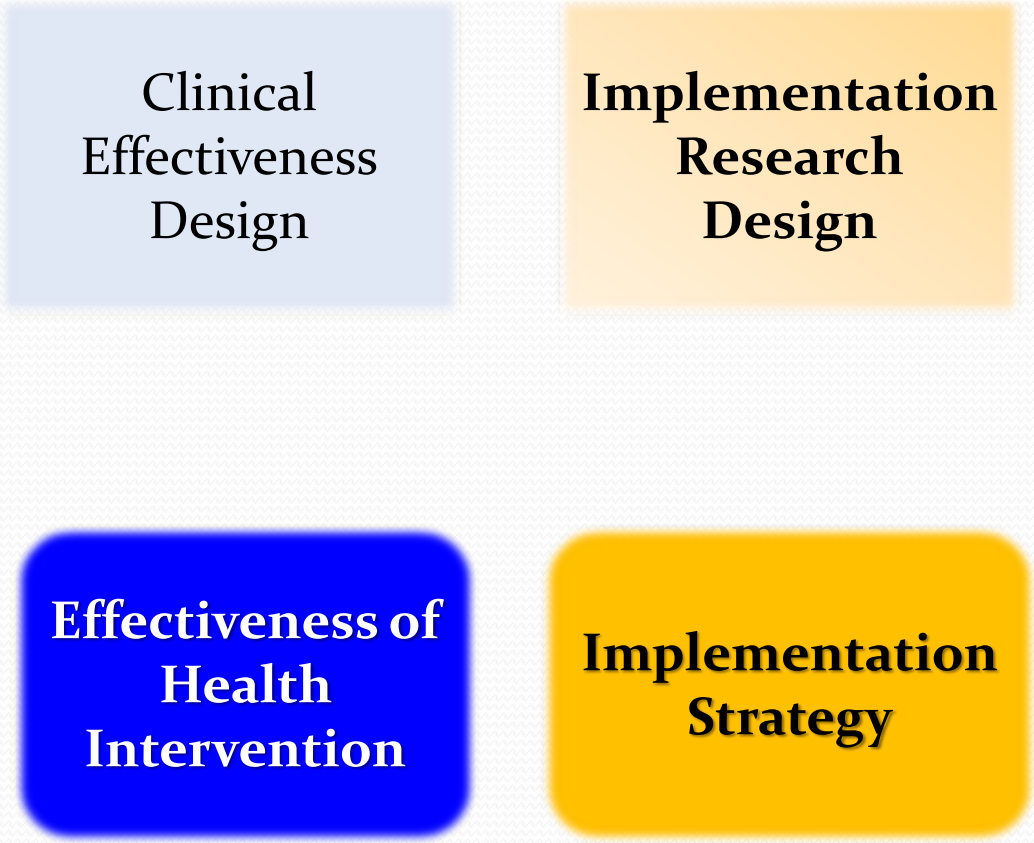



**Figure 1** Illustration of a network meta-analysis that combines direct evidence obtained within RCTs (A vs. B, B vs. C and A vs. C), and indirect evidence obtained across RCTs through a common comparator (A vs. B and B vs. C).


Ergometrine
Ergometrine plus Oxytocin
Injectable prostaglandins
Misoprostol
Carbetocin
Misoprostol plus Oxytocin
Placebo or no treatment
Oxytocin
1/144
16/6,459
3/399
2/598
4/1,030
3/303
10/6,492
2/1,605
1/46
1/177
7/4,047
1/1,429
2/3,207
1/50
2/1,589
11/11,090
44/36,92
0
10/3,221
4/500
11/30,633
15/9,750
9/7,021

# Effectiveness-implementation Hybrid Designs

- Combining Elements of Clinical Effectiveness and Implementation Research to Enhance Public Health Impact
- Important to assess **implementation outcome variables**
- **[Acceptability, Adoption, Appropriateness, Feasibility, fidelity, Implementation cost, Coverage, Sustainability]**



# IV. Study Design and Sampling Issues

Appreciation of statistical methodology often leads to the design of a study with increased precision and consequently, a smaller sample size.

***It is good design that is needed, not necessarily a large sample size.***

**Studies with poor design are unethical.**

# Study Design and Sampling Issues

Whatever the study design, a calculation must be performed before the start of the study to estimate the necessary number of units of analysis (for example, patients) to answer the main study question.

Sample size planning helps to ensure that the study is large enough, but not excessively large.

If the sample is small, the power will also be low, bringing the risk that real differences will not be identified.

**New knowledge is won from a single accurately performed, well designed study of adequate size.**

# Sample size re-estimation (SSR) in sample size adjustable (SSA)designs

- High degree of uncertainty in estimated event rates at the design stage
- Lack of availability of reliable parameter estimates to calculate the sample size
- Therefore **mid-course adjustment** is essential to reach a definitive conclusion.
- The original sample size could be revised based on estimates derived from interim data.
- SSR techniques offer potential for improving program efficiency by allowing mid-course sample size adjustment.

# Descriptive & Inferential Statistics

- **Descriptive Statistics**

  Summarize, describe or show data, and in the early stage of analysis help give a "feel" for the data.

- **Inferential Statistics**

  Inferential statistics allow **conclusions** or **comparisons** to be made from a sample or population, such as a group of patients.

# Choosing a right statistical test

| The **scale of measurement** of the test variable | CONTINUOUS | BINARY | CATEGORI -CAL |
| --- | --- | --- | --- |
| **The type of study design** | PAIRED | | UNPAIRED |

# References


- Röhrig B, du Prel J-B, Blettner M. Study Design in Medical Research. Review Article. Part 2 of a Series on the Evaluation of Scientific Publications. Dtsch Arztebl Int 2009; 106(11): 184–9 DOI: 10.3238/arztebl.2009.0184
- Gosho M, Nagashima K, Sato Y. Study Designs and Statistical Analyses for Biomarker Research. Review. Sensors, 2012, 12, 8966-8986;doi:10.3390/s120708966 ww.mdpi.com/journal/sensors
- Sample size re-estimation. www. Biopharmnet.com>doc12004-03
- Bossuyt PM, Cohen JF, Gatsonis CA, Korevaar DA; for the STARD group. STARD 2015: updated reporting guidelines for all diagnostic accuracy studies. Ann Transl Med 2016;4(4):85. doi: 10.3978/j.issn.2305-5839.2016.02.06
- CONSORT guidelines

# THANK YOU