# Establishing an Investigator Initiated Trial

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# News Headline 19th May 2009

"British man falls from 6000 feet and forgets to open his parachute. He is now resting at home with his wife"

# The wopflop trial: RCT of Working Open Parachutes versus FaiLure to Open Parachutes

Same plane at 10000 feet
on calm day
over central Australian desert
so weather/landing environment
not factors
at 2 minutely intervals

200 healthy law students/lawyers

Stratified by age, weight
gender

Randomly allocated

Double blind

Sham Parachute group

Working parachute group

Outcome

Outcome

Survival
Autopsy cause of death

# If I can’t get funding for that:

- Some people complain that not getting paid on time makes them unhappy
- But there are many confounders and people could be unhappy for lots of reasons
- We need a randomised trial to justify increasing resources in pay office so people can be paid on time

# The SPIT trial: RCT of Staff Paid Incorrectly versus on Time trial

Need a >50% difference in outcome to justify improving the service

1000 employees

Randomly allocated

Inclusion criteria:
all full/part time staff (stratified)
Exclusion criteria:
Head of department haematology

**Paid correctly but late**

**(10<x<14 days)**

**Paid correctly and on time**

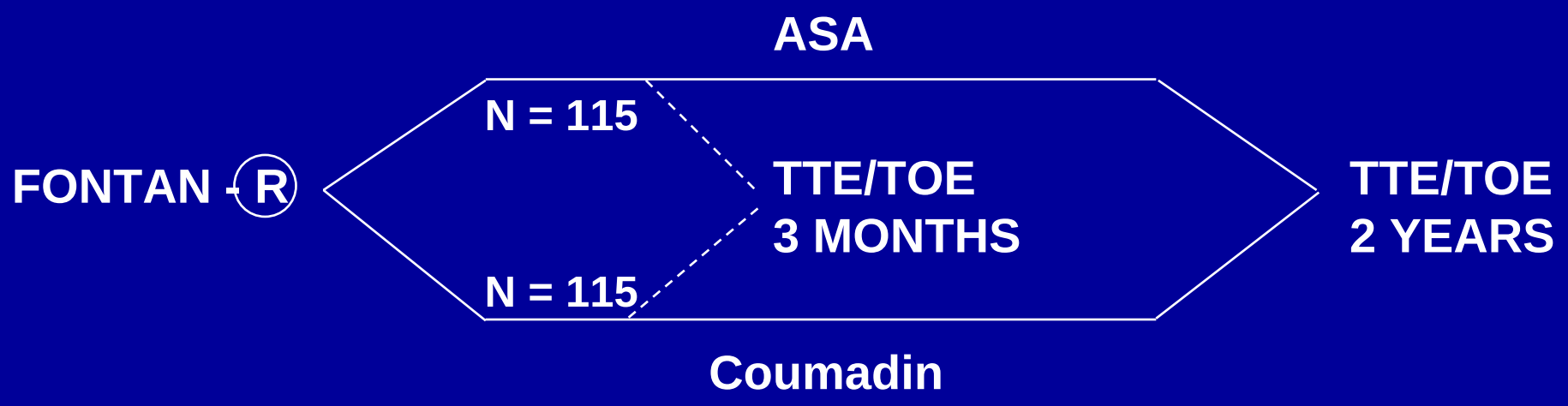
QoL measure

Work satisfaction rating

QoL measure

Work satisfaction rating

# FONTAN A




Heart & Stroke Foundation of Canada
NHF Australia

# Do I have a question worth studying?

- Clinical observation
- Effort to improve outcomes
  - Mortality
  - Morbidity
  - Quality of life
- Cost effectiveness
- Reduced side effects

# The question is the key element

# How do you develop the question?

- Clinical service
  - Post Fontan children on warfarin
- Discussion with colleagues
  - Initial informal chats
  - Survey through national groups
  - Understand their priorities, concerns
- Review of literature
  - Comprehensive systematic review
  - Publish in a journal your colleagues will read

# Developing the question

- Must be in equipoise
  - Based on the evidence
- Must be ethical based on current standard of practice
  - Especially in considering placebo groups
- Must be clear and specific and capable of being answered

# Am I the right person to develop the trial?

- Training
- Resources
- Time
- Desire
- Collaborative networks
- support

# Masters of Health Research Methodology McMaster University

- CHS-HRM 721 Fundamentals of health research and evaluation methods.
- CHS-HRM 702 Introduction to biostatistics.
- CHS-HRM 730 Research methods for randomised controlled trials.
- CHS-HRM 733 Statistical and methodological issues in controlled clinical trials.
- CHS-HRM 734 Data management in health research.
- CHS-HRM 751 Observational and analytical research methods.
- Major Thesis : *A randomised trial of prophylactic anticoagulation in children following Fontan surgery*

# Support

- Statistical
- Imaging
- Laboratory
- Randomisation
- Data management
- Administrative

# Collaborative networks

- Single centre
- Multi centre
- International

# CHS-HRM 799
# Acronyms for clinical trials

- Optimal acronym length
- Use of numbers for subsequent trials
- The value of rhyming syllables
- How to avoid offending religious or ethnic groups
- Acronyms for any language
- How much is too much innuendo
- Subliminal messages in trial acronyms
- How to design trial questions and budgets to fit your acronym

# Is it all in the name ?

## Long term prophylaxis after acute coronary syndromes

- AFTER
  - Aspirin/Anticoagulants Following Thrombolysis with Anistreplase (Eminase) and Recurrent Infarction
- CARS
  - Coumadin aspirin reinfarction study
- CHAMP
  - Combined Hemotherapy and Mortality Prevention study

# Is it all in the name ?

## Long term prophylaxis after acute coronary syndromes

- OASIS
  - Organization to Assess Strategies for Ischemic Syndromes
- APRICOT
  - Antithrombotics in the Prevention of Reocclusion in Coronary Thrombolysis
- TIMI, ASPECT, WARIS

# Developing the protocol

- Clinical service
  - Consider standard practice in terms of review visits, investigations, etc
- Discussion with colleagues
  - Workshops
  - Circulating Drafts and key questions
  - Protocolize every step
- Review of literature
  - Continue to keep up to date
  - Support each step of the trial especially outcome measures

# Developing the protocol

- Need to make your colleagues have ownership- a commitment to the cause
  - communication, communication and more communication
- Need to have patients on side
  - Use parent support groups
- Need to have expertise/experience
  - Getting from idea to implementable study is not easy.

# Funding

- Competitive
- Never enough
- How much good will can you rely on
- Need for pilot data
- Acknowledgment
- Commercial/Pharmaceutical industry

# Compromises

- Inevitable
- Separate manageable from deal breakers
- Make every effort to minimise known problems
- There will always be unknown
- One trial will never solve the world
  - We know that, but getting everyone else to understand is difficult

# A Multicentre Randomized Trial Comparing Heparin/Warfarin Versus Aspirin as Primary Thromboprophylaxis for Two Years After Fontan Procedure in Children

Paul Monagle[1], Andrew Cochrane[1], Robin Roberts[3], Barbara Szechtman[3], Michael Gent[3], Maureen Andrew[2], Brian W. McCrindle[2]

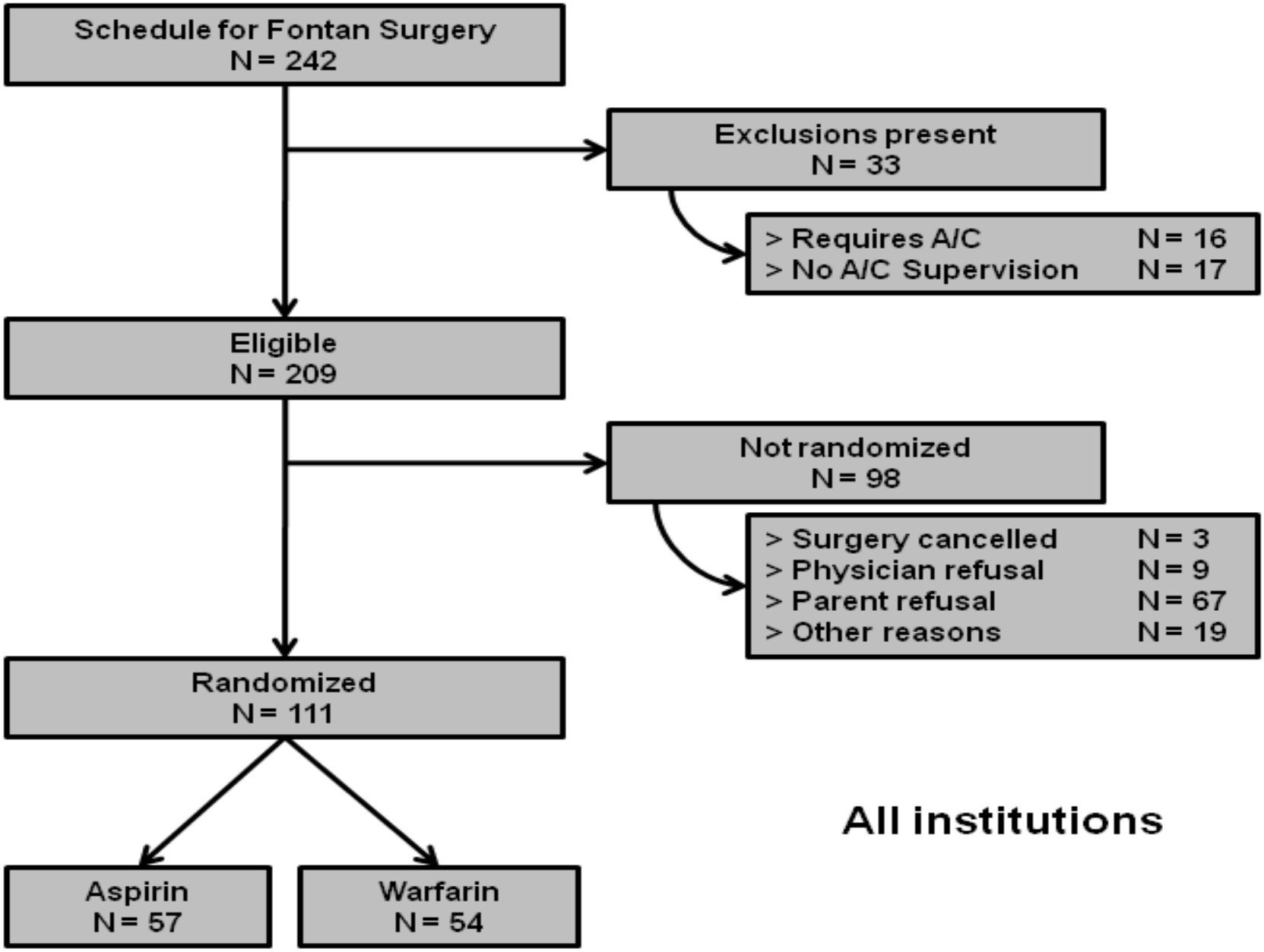
for the Fontan Anticoagulation Study Group

[1] University of Melbourne, Melbourne, Australia

[2] University of Toronto, Toronto, Canada

[3] McMaster University, Hamilton, Canada

HEART & STROKE FOUNDATION

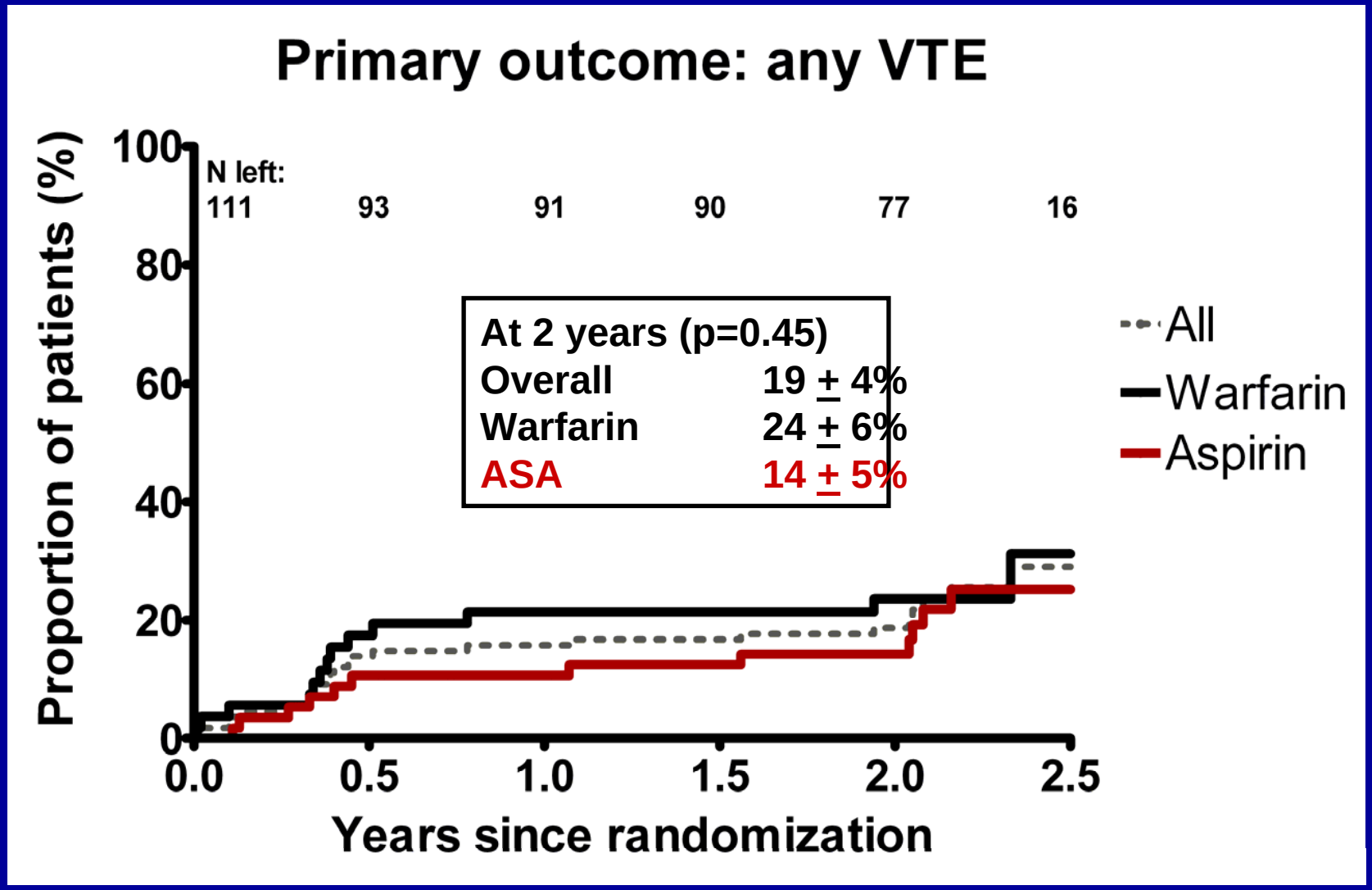


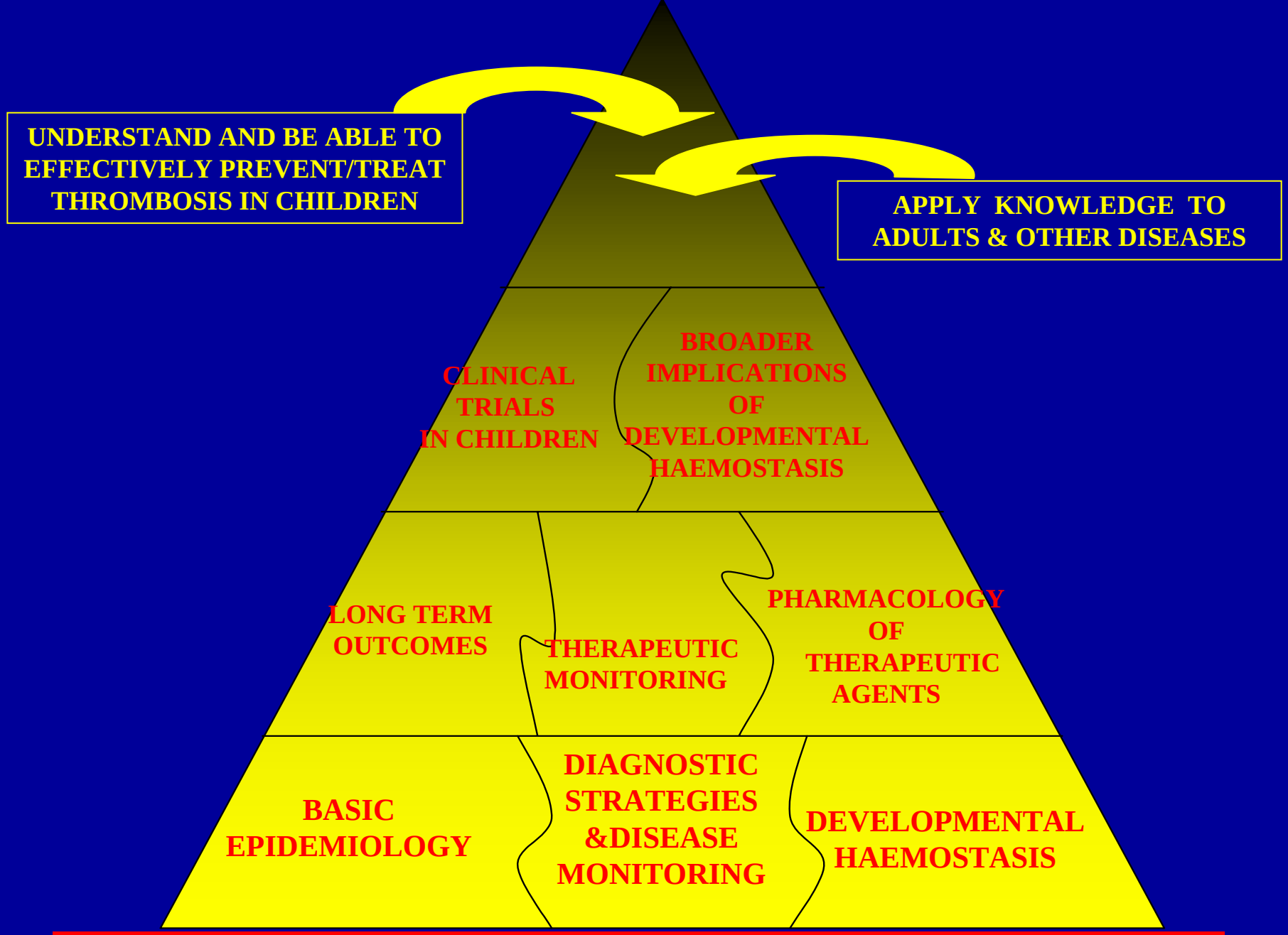

All institutions

# Results – First Endpoints

| | ASA n=57 | Warfarin n=54 |
|---|---|---|
| Patient withdrew | 0 | 2 |
| Death | 1 | 0 |
| Patient stopped drug | 2 | 3 |
| Physician stopped drug | 3 | 6 |
| Stopped after AE | 0 | 1 |
| Thrombosis | 12 (21%) | 13 (24%) |
| Clinical | 4 | 3 |
| Routine | 8 | 10 |

Results – Time-related freedom from thrombosis, all events, intention to treat






Clinical thrombosis and anticoagulation service

# Be determined- never give up