



Current Research in PPH and Uterotonics

Current Research in PPH Prevention and Uterotonics Quality

- PPH Prevention Studies:
 - Champion Trial – Heat Stable Carbetocin
 - IMOX Trial – Intramuscular oxytocics
 - Uterotonics Network Meta-analysis
- Uterotonics Quality:
 - Maternal health products quality audits – Nigeria
 - Clinical experience with the quality of oxytocin

Heat-Stable Carbetocin°

- Heat stable carbetocin (HSC) is a uterotonic medicine used to prevent PPH
- Carbetocin is registered and used in more than 80 countries. Since 1997
- HSC has proven efficacy and safety evidence, primarily in C-section
- Ferring's proprietary formula for HSC does not require cold-chain transportation or refrigerated storage (Data submitted for publication)
- The heat stable version has been introduced into 27+ countries to date including Australia, Europe and Mexico since 2015
- Carbetocin (manufactured by Ferring Pharmaceuticals) has been used in prevention of PPH for 20 years (since 1997) in over 10 million women, primarily following caesarean section
- Currently 11 national guidelines are recommending Carbetocin for active management of third stage of labour (AMSTL) (data on file)

* Brand names: PABAL, Duratocin, Lonactene

Heat stable carbetocin for preventing PPH

- Also known as the Champion Trial
- WHO-led, multi-centre randomised controlled trial
- To evaluate non-inferiority of Carbetocin RTS 100 µg IM versus oxytocin 10 IU IM for prevention of PPH and severe PPH after vaginal delivery
- 29, 658 women recruited across 23 sites in 10 countries
- Data collection completed end January 2018
- Results will be announced in October 2018
- Objectives – regulatory and PPH guidelines

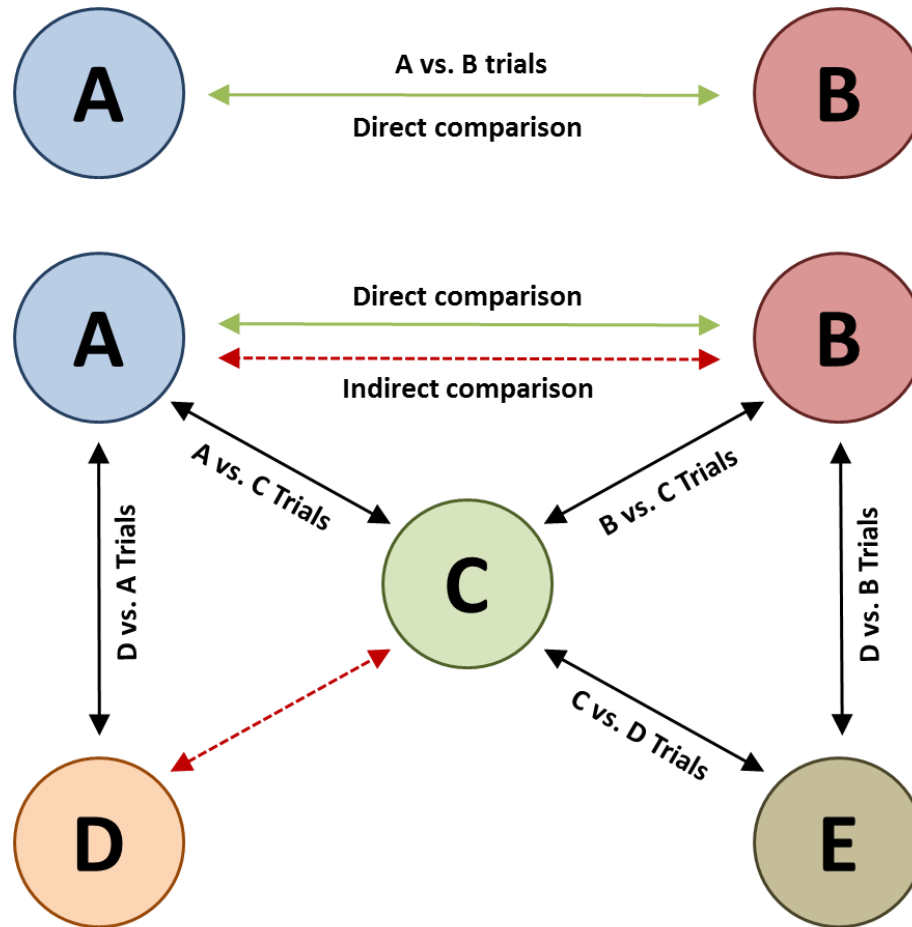
Intramuscular Oxytocics (IMOX)

- A Comparison Study of Intramuscular Carbetocin, Syntocinon and Syntometrine for the Third Stage of Labour Following Vaginal Birth
- North Bristol NHS Trust
- According to a survey, 71.4% of maternity units in the UK routinely administer Syntometrine (oxytocin/ergometrine) for preventing PPH while guidelines recommend Syntocinon (oxytocin)
- According to other studies:
 - Carbetocin slightly better at preventing PPH than Syntometrine and with less side-effects
 - Carbetocin may be as good as Syntocinon at preventing PPH
- No existing studies directly comparing effectiveness, side-effects and cost-effectiveness of the 3 drugs
- Over 6,000 patients
- Results to be published in 2018

Uterotonics Network Meta-Analysis

- Uterotonic Agents for Preventing PPH – Cochrane Review
- Assess clinical effectiveness and side-effect profile of uterotonic drugs to prevent PPH
- Generate clinically useful ranking of available uterotonics according to their effectiveness and side-effects.
- Purpose: reducing uncertainty about which is the most effective drug for preventing PPH

Uterotonics Network Meta-Analysis



Uterotonics Network Meta-Analysis

Primary Outcomes

500 mL

1000 mL

Secondary Outcomes

Death

Death or severe morbidity composite outcome

Additional use of uterotonics

Transfusion

Blood loss

Change in Hb

Side-effects

Nausea

Vomiting

Hypertension

Headache

Tachycardia

Hypotension

Abdominal pain

Fever

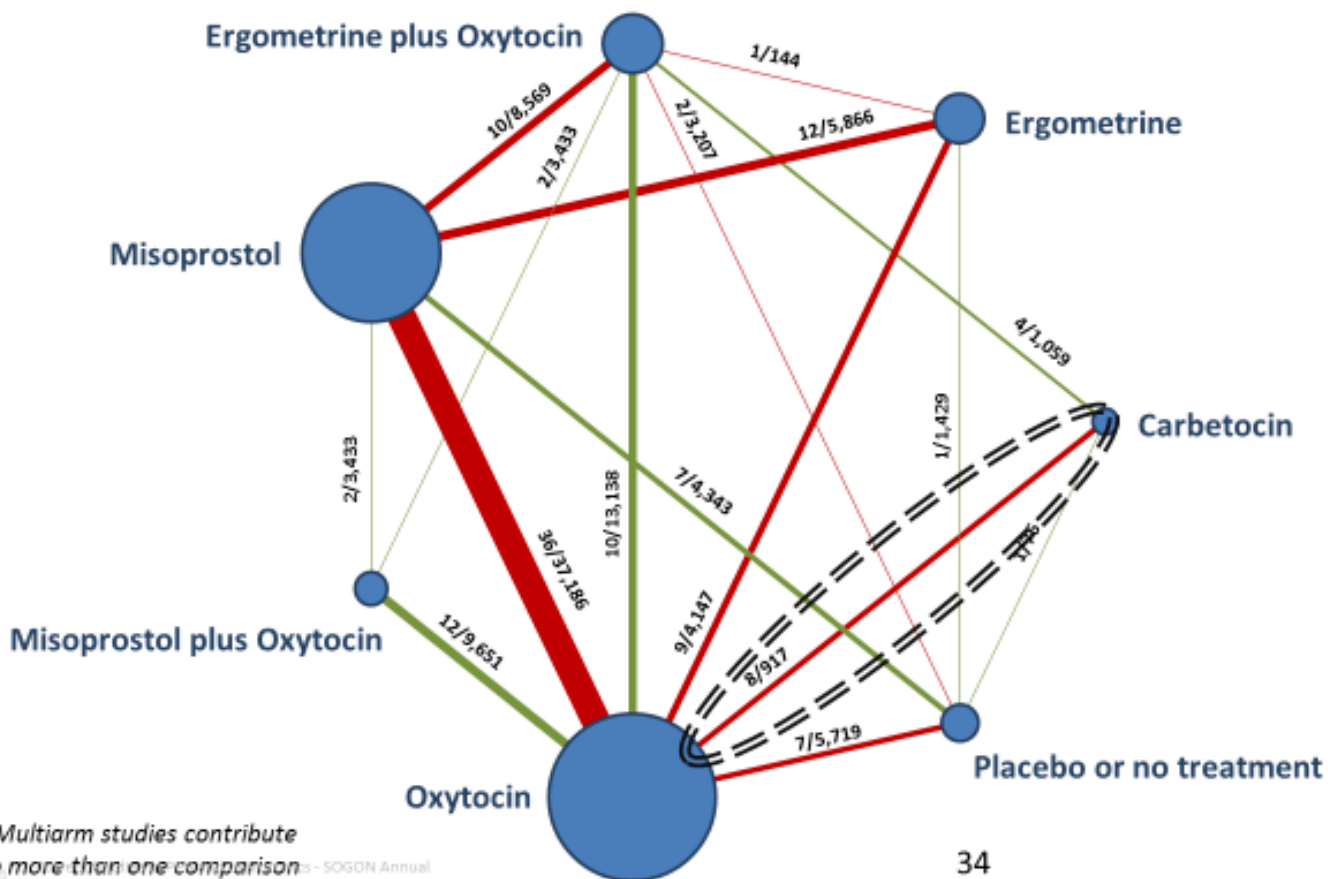
Shivering

Primary Outcomes (restricted to high quality studies only)

500 mL

Uterotonics Network Meta-Analysis

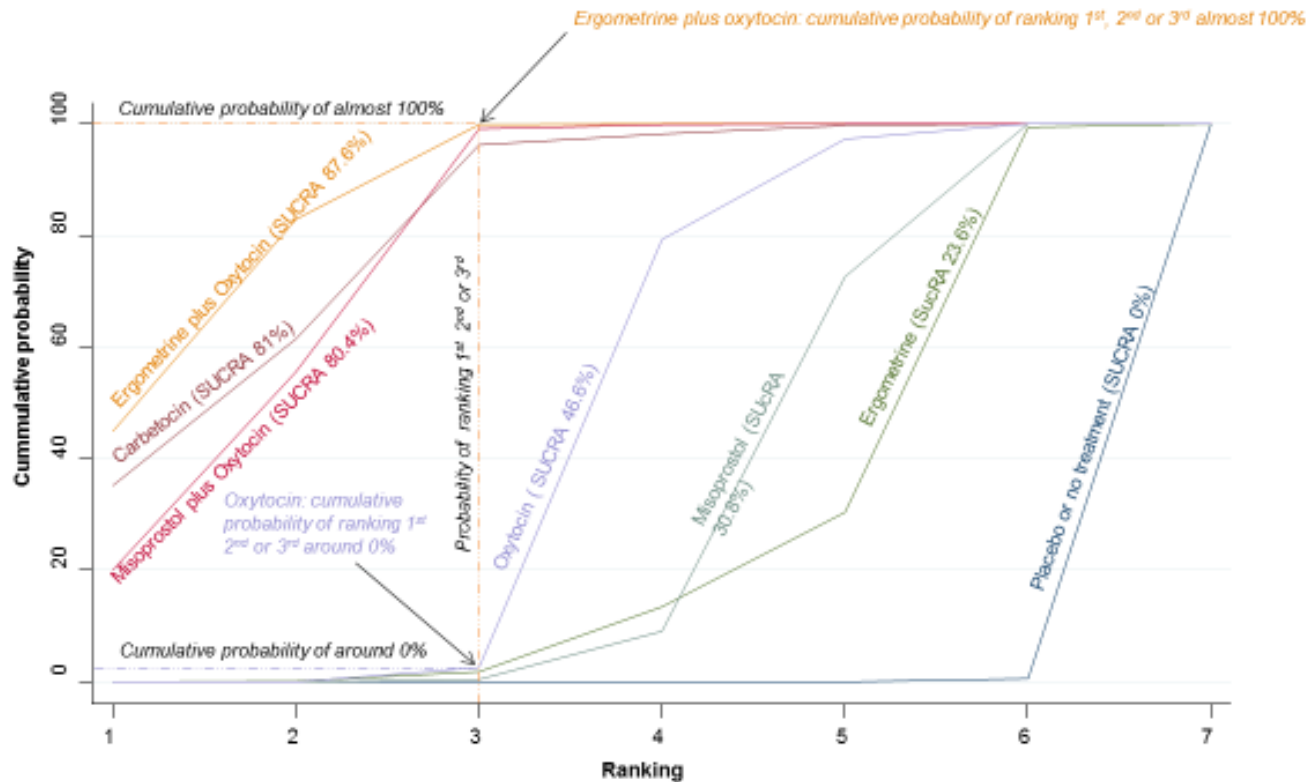
Network Diagram for PPH \geq 500 mL



* Multiarm studies contribute to more than one comparison - SOGON Annual Meeting, Sokoto - November 2017

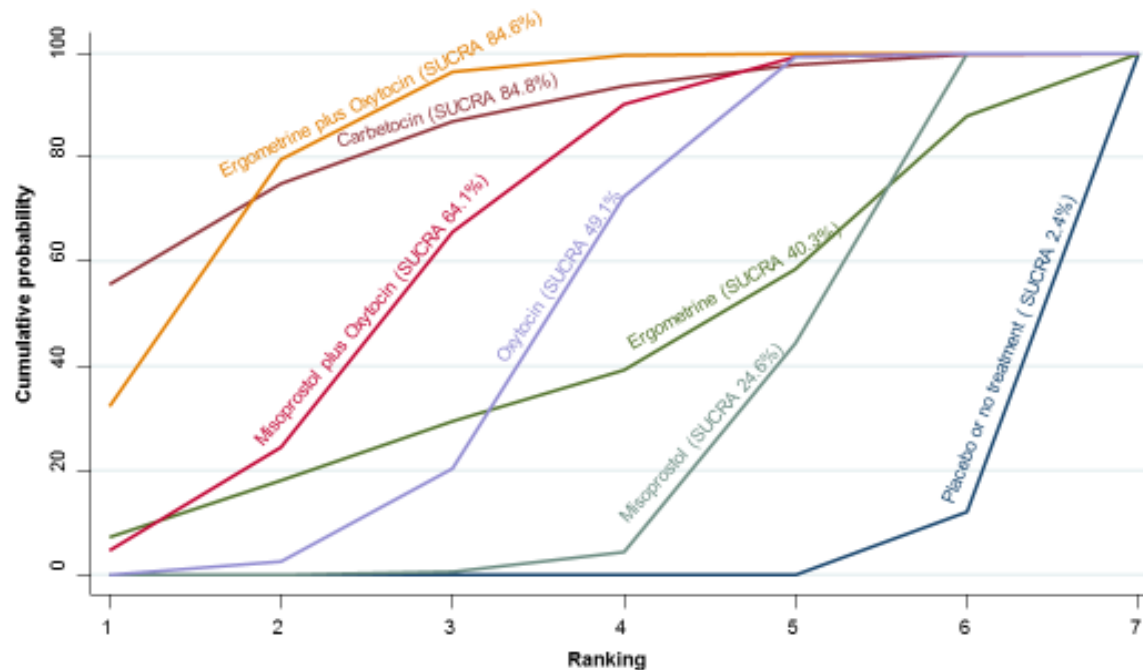
Uterotonics Network Meta-Analysis

Cumulative Rank Plot PPH ≥ 500 mL



Uterotonics Network Meta-Analysis

Cumulative Rank Plot PPH \geq 1000 mL



Uterotonics Network Meta-Analysis

- In 137 trials (>86,000 women)
- Most effective drugs for all blood loss outcomes
 - Syntometrine
 - Carbetocin
 - Oxytocin + Misoprostol combination (OxyMiso)
- **Oxytocin is not in the top 3**
- Worst drugs for side effects
 - Syntometrine
 - OxyMiso
- Most cost-effective drug is carbetocin (despite the unit cost for carbetocin being relatively more expensive)
- However, carbetocin loses its ranking in high quality studies
- WHO Champion trial will fulfil the gap

Safe Childbirth and Quality Medicines

- Results of Oxytocin, Misoprostol, Magnesium Sulfate and Calcium Gluconate Quality Audits, Nigeria
- Promoting the Quality of Medicines Program, USP
- The quality of oxytocin injection, misoprostol tablets, magnesium sulfate, and calcium gluconate injections was assessed across the six geopolitical zones of Nigeria.
- 159 samples of oxytocin
- HPLC Assay test for composition of active ingredient, and confirmation of registration with regulatory authority (NAFDAC)
- **74.2% of oxytocin injection samples failed the assay test**, with the northeast and southeast zones registering the highest failure rates. The percentage composition of the active ingredient varied between 0.0% and 163.7%

Clinical experience with the quality of oxytocin

- Cross-sectional study to assess HCP clinical experience with the quality of oxytocin (Lagos State, Nigeria)
- Lagos University Teaching Hospital
- RHSC Webinar available at rhsupplies.org for results



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