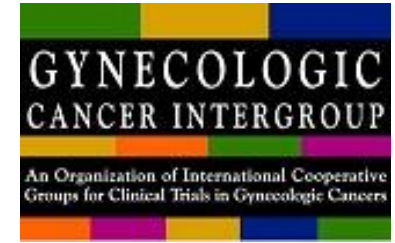




# **EXCISE – EXcisional treatment Comparison for In Situ Endocervical adenocarcinoma**



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## **Excisional treatment in women with cervical adenocarcinoma- in-situ (AIS): a prospective randomised controlled non- inferiority trial to compare AIS recurrence after loop electrosurgical excision procedure (LEEP) to cold knife cone biopsy (CKC)**

Cohen P.A, Sykes P, Stockler M, Eva L, Symcock B, Wrede C.D.H, McNally O, Leung Y,  
Brand A

GFIG Cervix Cancer Committee Meeting May 30<sup>th</sup> 2018

Sponsor: St John of God Healthcare, Australia

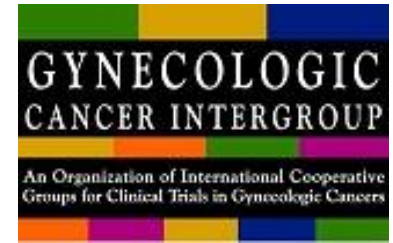
Funding: ANZGOG Fund for New Research

# Background and rationale

- AIS is the precursor to invasive cervical adenocarcinoma
- AIS on cytology and/or biopsy => a diagnostic excisional procedure to exclude invasive adenocarcinoma and treat AIS
- CKC vs. LEEP/LLETZ: both have pros and cons:
  - Against LEEP/LLETZ: incomplete excision, thermal artefact, maybe greater risk of a positive endocervical margin
  - For LEEP?LLETZ: avoid general anaesthesia, outpatient setting, lower morbidity, and reduced rates of obstetric complications
- There are NO prospective randomised studies to inform practice and clinical practice varies worldwide



# Aims and objectives



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**Aim:** to determine if the treatment of cervical AIS by LEEP is non-inferior to CKC with regard to 5-year recurrence rate in women managed conservatively

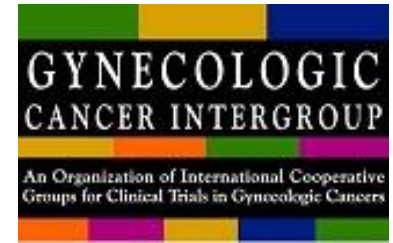
**Hypothesis:** LEEP will not be inferior to CKC with regard to AIS persistence and recurrence in conservatively managed women

**Primary objective:** to compare the 5-year recurrence rate of cervical AIS following LEEP to that after CKC, in conservatively managed women.

**Secondary objectives:** margin status and specimen dimensions, early and late complications (obstetric), QoL, cost-effectiveness



# EXCISE



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**Study population:** women aged 18 to 45 years diagnosed with AIS on cervical screening and/or colposcopically directed biopsy who are to receive excisional treatment

**Inclusion criteria:** lesion amenable to single pass excision; patients able to comply with follow-up and QOL assessments

**Exclusion criteria:** previous excisional/ablative treatment, cytology or clinical suspicion of invasion, on immunosuppressive agents, pregnancy, unsuitable for single pass excision

**Randomisation:** 1:1 (LEEP: CKC)

# Sample size calculation

- Estimated using a 2 group test of non-inferiority of proportions
- Primary end point is the AIS recurrence rate at 5 years and the comparison will be between CKC and LEEP, based on a 1-sided test for non-inferiority
- Assumes an 8% rate of AIS recurrence at 5 years after CKC, and a 5% non-inferiority margin (upper 95% confidence rate of AIS recurrence of 13% is still within the non-inferiority margin)
- Sample size needed is 730 (365 per group). Assuming a 10% drop-out rate, a total sample size of 810 participants (405 per group) would need to be randomised. One-sided Type I error is set at 5% with 80% power



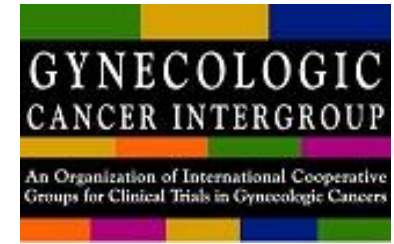
# Pilot status update



| Country     | Site                         | Date Activated | Patients Recruited |
|-------------|------------------------------|----------------|--------------------|
| New Zealand | Christchurch Womens Hospital | 06.07.2017     | 1                  |
| New Zealand | National Womens, Auckland    | 01.11.2017     | 3                  |
| Australia   | St John of God, Perth        | 10.10.2017     | 4                  |
| Australia   | King Edward Memorial, Perth  | 06.11.2017     | 1                  |
| Australia   | The Womens, Melbourne        | 07.05.2018     | -                  |



# EXCISE – EXcisional treatment Comparison for In Situ Endocervical adenocarcinoma



- Pilot to recruit 30 patients – aim to complete December 2018
  - Primary endpoint margin status
  - Randomisation 2:1 (LEEP:CKC)
  - Protocol published in BMJ Open 2017 August 28;7(8)e017576
- Australian NHMRC Grant Application March 2019 **subject to international support for a phase III study**
- Questions:
  - Non-inferiority margin – 5% or 7%?
  - Should margin status be the primary endpoint?
    - Advantage - primary endpoint reached rapidly
    - Disadvantage - sample size would need to be >2000 assuming a 25% +ve margin rate and 5% NI margin