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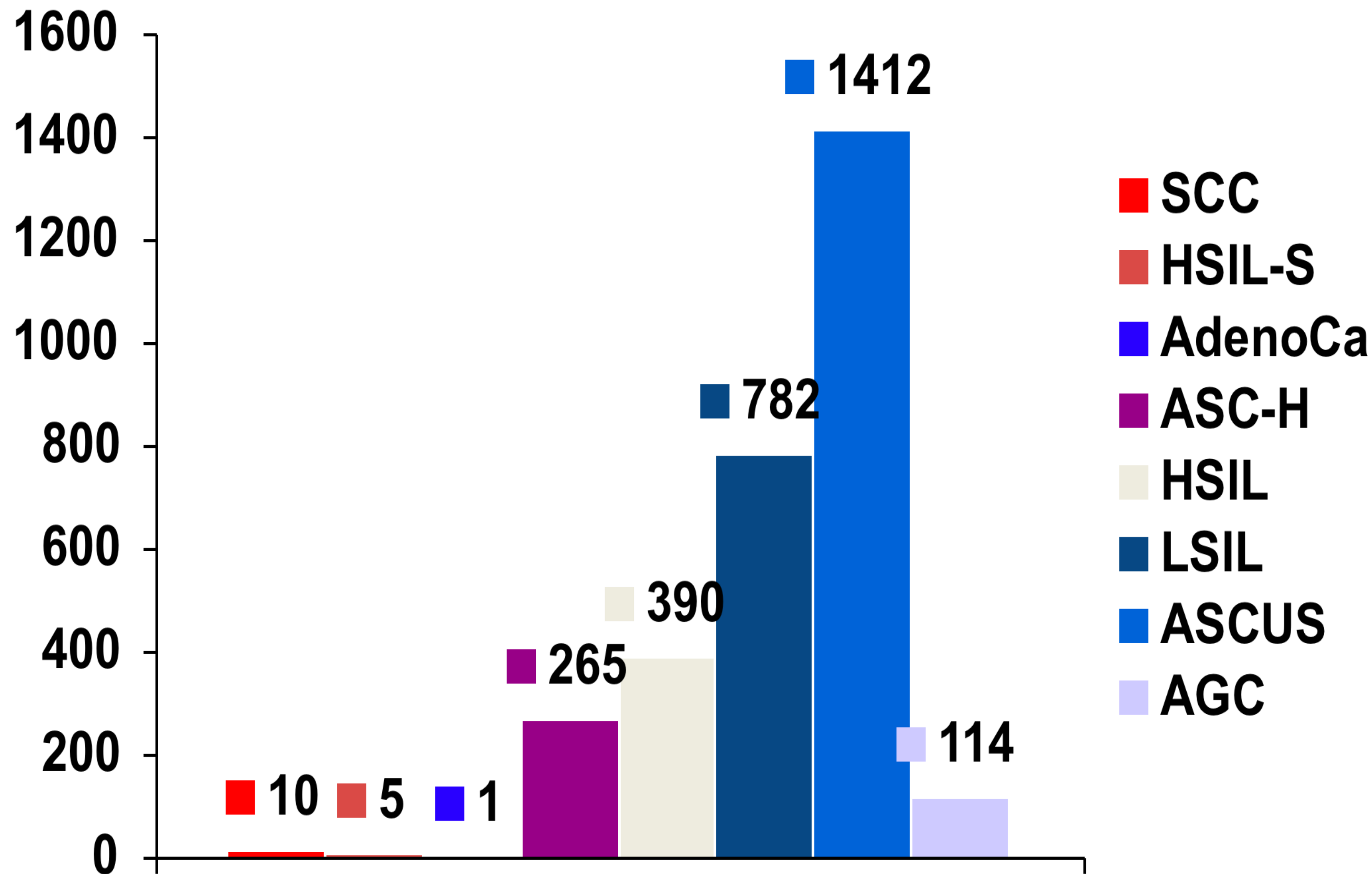
Management of the Glandular Abnormality

James Bentley
President Society of Canadian Colposcopists
Chief Division of Gynecologic Oncology
Dalhousie University

Capital Health

DALHOUSIE UNIVERSITY
Inspiring Minds

No. referred to colposcopy 2003: NSCCPP



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Ways to diagnose a glandular lesion

- Abnormal cytology i.e. AGC
- On biopsy/ excision done for CIN

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Bethesda 2001

B. Glandular Cell

1. Atypical
   a) Endocervical cells (NOS)
   b) Endometrial cells (NOS)
   c) Glandular cells (NOS)

   } AGC-NOS

2. Atypical
   a) Endocervical cells, favor neoplastic
   b) Glandular cells, favor neoplastic

   } AGC-N

3. Endocervical adenocarcinoma in situ (AIS)
4. Adenocarcinoma
   a) Endocervical
   b) Endometrial
   c) Extrauterine
   d) NOS
5. Other Malignant Neoplasms (specify)

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AGC cytology

Pathology finding[1]	
CIN 1	7%
CIN 2 or 3	36%
Adenocarcinoma in situ	20%
Cervical Cancer	9%
Endometrial Pathology	29%

Cytology[2]	Any high-grade lesion	High grade glandular
AGC-NOS	9-14%	0-15%
AGC-N	27-96%	10-93%

[1]Daniel A Int.J.Gynaecol.Obstet 2005; 91(3)238-242
[2] Wright T Emerging Issues on HPV infections 2006 p 140-146

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AGC cytology

Impact of age on rates of neoplasia in women with AGC

	CIN 2,3 OR AIS	Endometrial hyperplasia or neoplasia
Premenoausal	22-30%	3%
Postmenopausal	6-7%	19%

[2] Wright T Emerging Issues on HPV infections 2006 p 140-146

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Glandular Changes

- <0.5% of paps show AGC
- 3% of abnormal pap smears
- Ratio of AIS to CIN 3 1:50 on average
- 20-25% of invasive cancers are glandular

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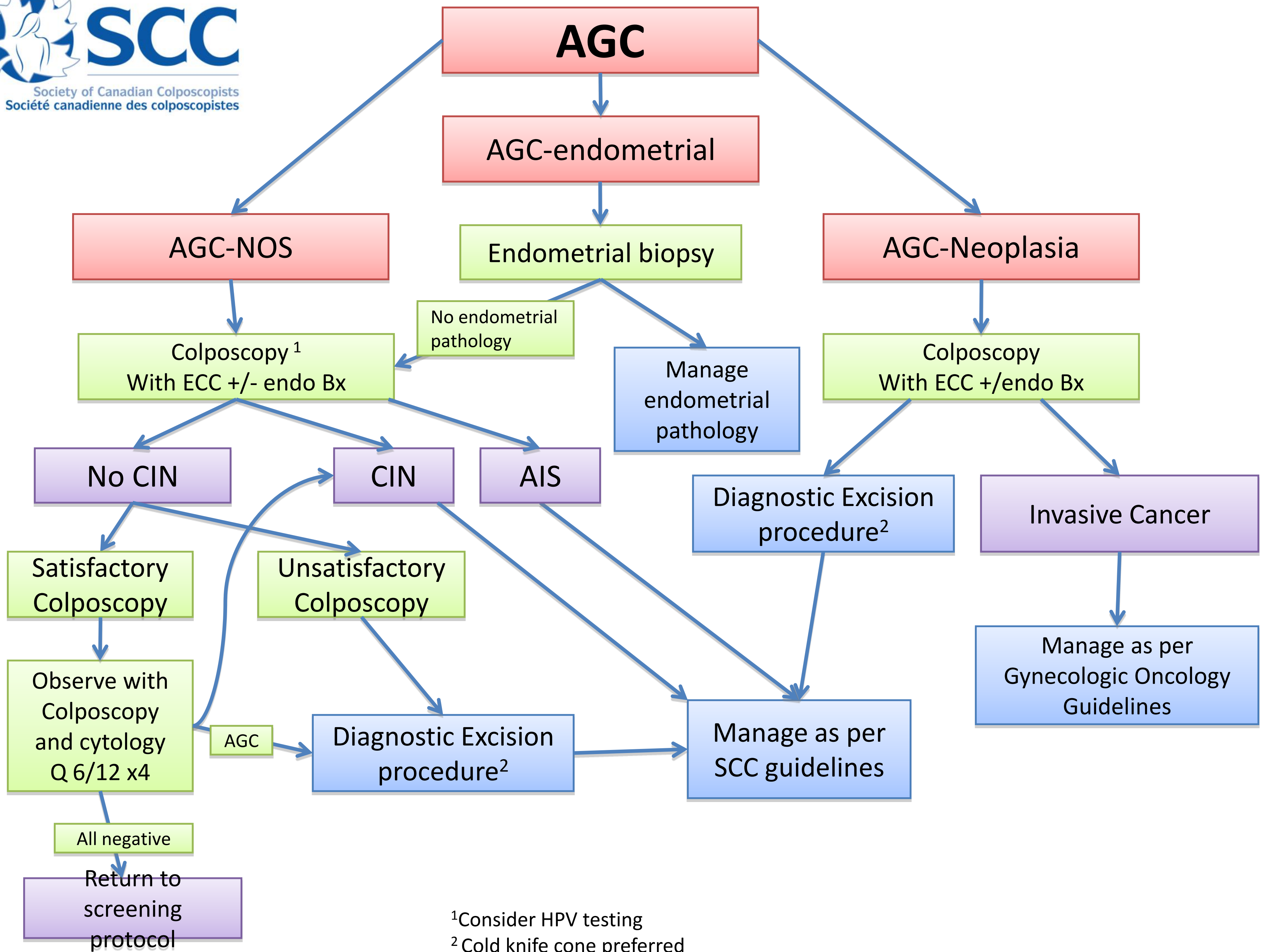
AGC= always get colposcopy!!!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AGC
AGC-endometrial
AGC-NOS
Endometrial biopsy
AGC-Neoplasia
No endometrial pathology
Colposcopy 1
With ECC +/- endo Bx
Manage endometrial pathology
Colposcopy
With ECC +/endo Bx
No CIN
CIN
AIS
Diagnostic Excision procedure2
Invasive Cancer
Satisfactory Colposcopy
Unsatisfactory Colposcopy
Manage as per Gynecologic Oncology Guidelines
Observe with Colposcopy and cytology Q 6/12 x4
AGC
Diagnostic Excision procedure2
Manage as per SCC guidelines
All negative
Return to screening protocol
1Consider HPV testing
2 Cold knife cone preferred

AGC-HPV Triage

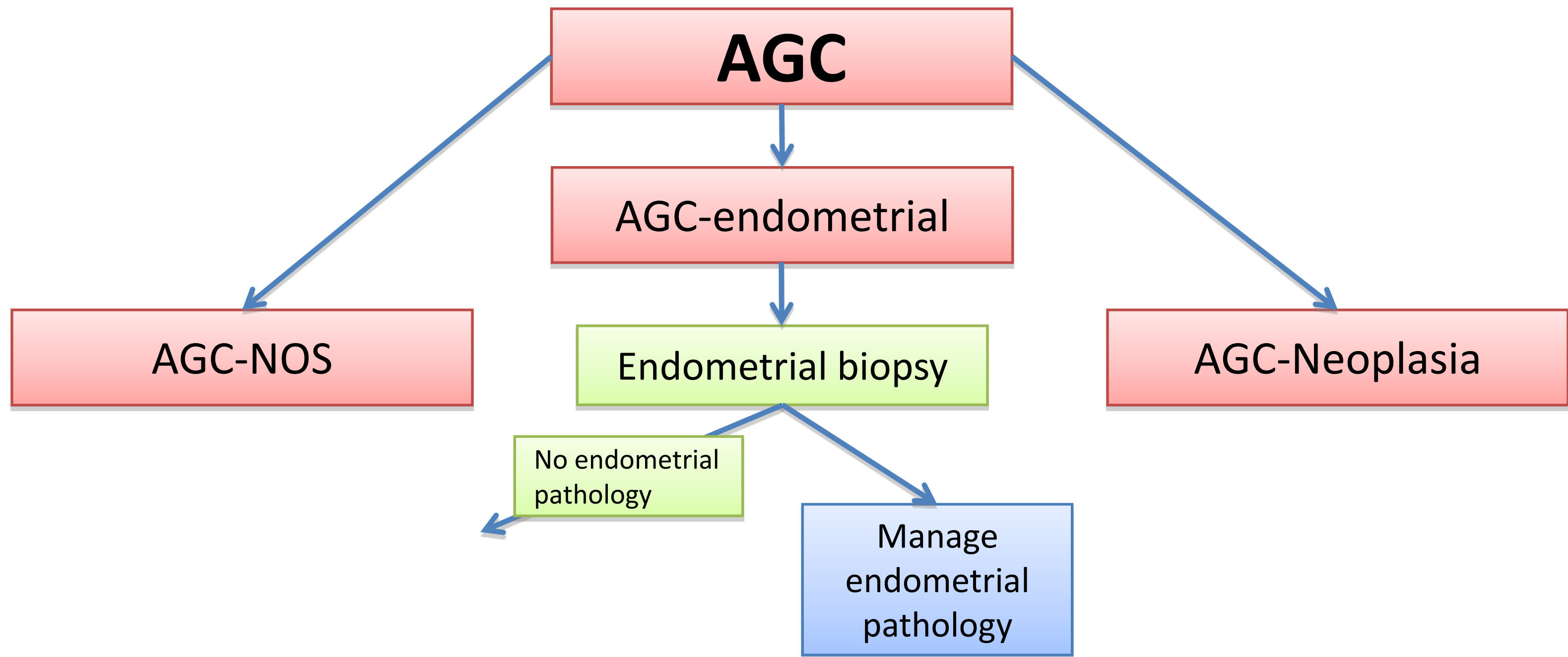
- Cases accessed from Newfoundland and New Brunswick.
- Based on 124 cases of 1325 AGC diagnoses.
- HPV test:
  - Sensitivity 88%
  - Specificity 87%
  - PPV 52%
  - NPV 98%
- HPV testing may be useful in AGC triage

- *Fontaine D, et al. Can HPV testing be useful in AGC triage?*
  - *Int HPV Conference, Vancouver, 2005*

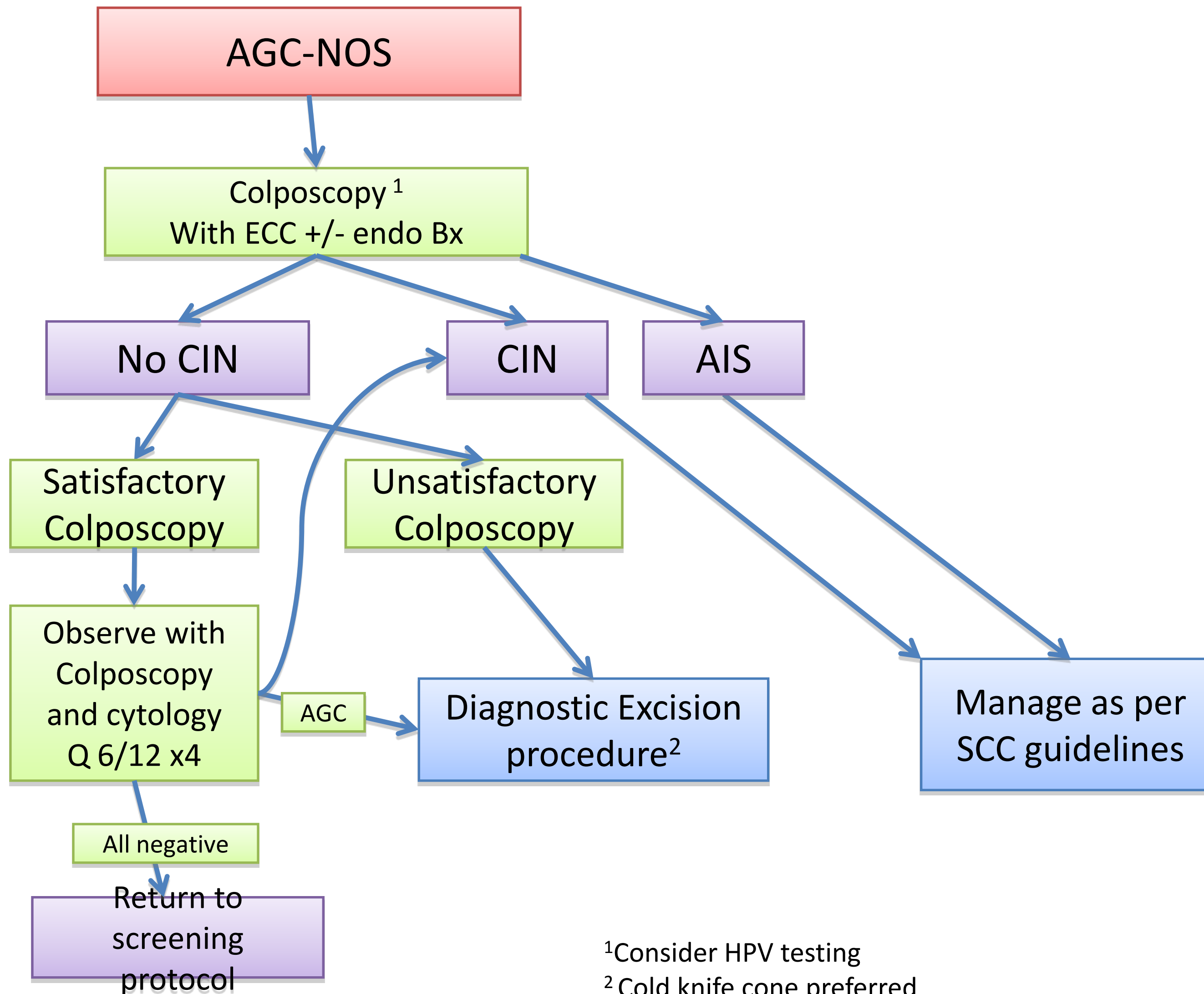
AGC-HPV Triage: Ontario Study

- 88 cases.
- 83% of women with CIN 2 or 3 were HPV positive.
- 100% with AIS, HPV positive
- 100% with cervical cancer, HPV positive
- Sensitivity of HPV test 90%, NPV 97%.
- HPV testing is useful in AGC triage

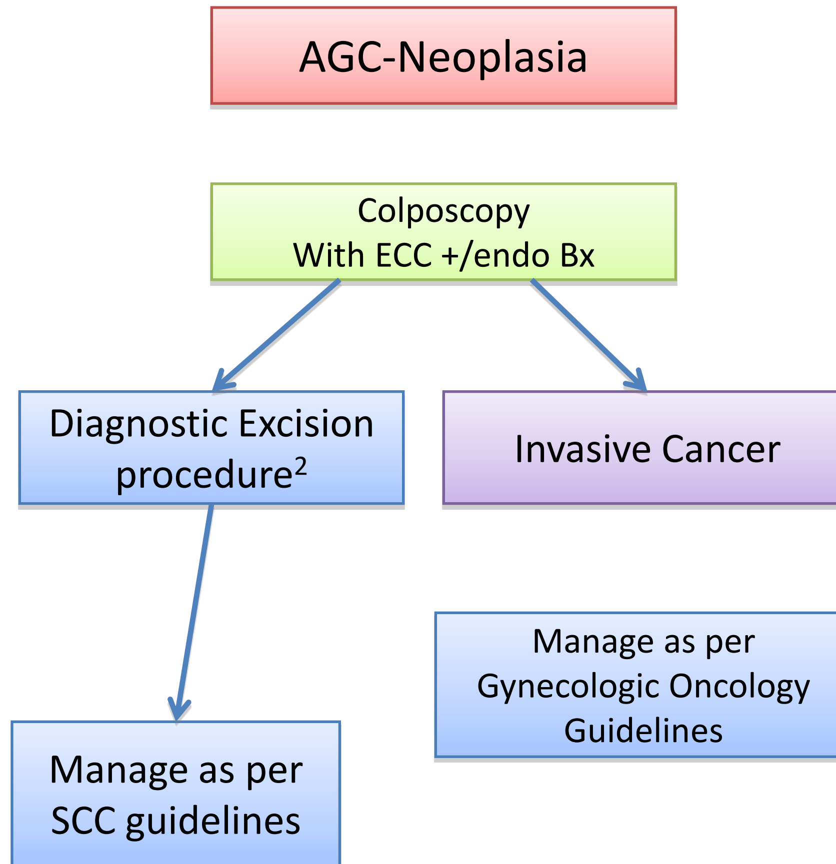
- *Murphy J, et al. Accuracy of HPV testing in identifying high risk cervical neoplasias among women with AGC in Pap smear.*
  - *Int HPV Conference, Prague, 2006*



AGC
AGC-endometrial
AGC-NOS
Endometrial biopsy
AGC-Neoplasia
No endometrial pathology
Manage endometrial pathology



[1] Consider HPV testing
[2] Cold knife cone preferred



[1]Consider HPV testing
[2] Cold knife cone preferred

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Identifying glandular lesions- challenges

- Difficulty with cytology
- Colposcopy inexperience
  - Rarity of lesions
- Size and location
  - 50 % involve the ectocervix, canal 5%, both 38%
  - 48% only involve one quadrant
  - Length < 15 mm
  - Bertrand et al: highest < 19.9mm in 78%, none higher than 29.9mm
- Skip lesions: 6.5 -15% of AIS
- Buried disease: 60 % below metaplastic or dysplastic epithelium
- Mixed disease: 50% occurs in coexistance with AIS, usually CIN 3

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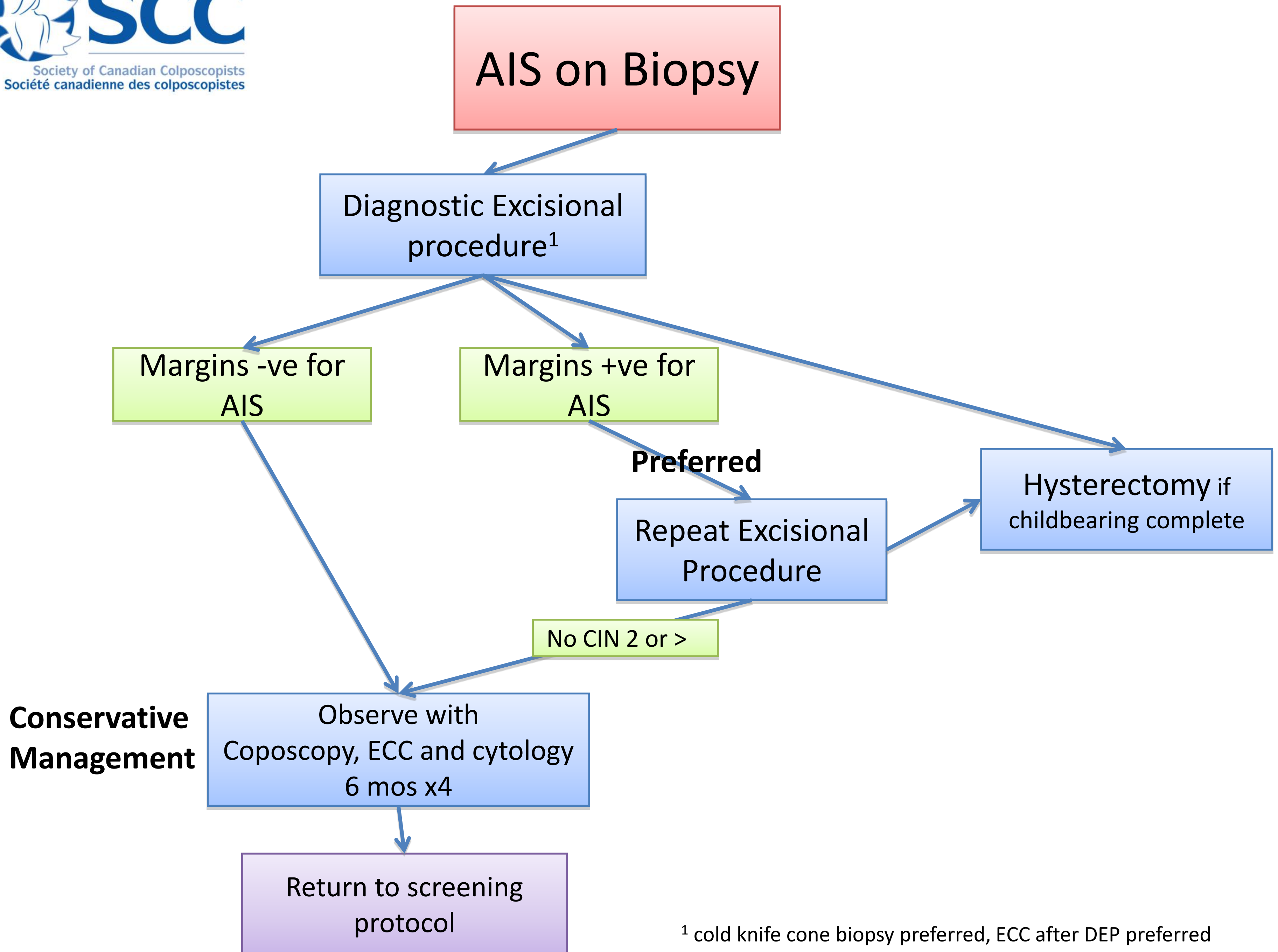
Colposcopic features of glandular lesions

- Lesion overlying glandular epithelium not in contact with the S-C junction
- Large crypt openings
- Papilliary like lesions
- Epithelial budding
- Variegated red and white lesions
- Waste-thread-like vessels
- Tendril-like vessels
- Root-like vessels
- Character writing-like vessels
- Single and multiple dots at the tips of papillary excrescences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AIS on Biopsy
Diagnostic Excisional procedure1
Margins -ve for AIS
Margins +ve for AIS
Preferred
Hysterectomy if childbearing complete
Repeat Excisional Procedure
No CIN 2 or >
Conservative Management
Observe with Coposcopy, ECC and cytology 6 mos x4
Return to screening protocol
1 cold knife cone biopsy preferred, ECC after DEP preferred

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Management of Adenocarcinoma in Situ (AIS)

- When suspected or on Bx prior to therapy treatment:
  - Laser cone or cold knife cone[1]
    - "Cone" should be cylindrical and at least 25 mm in long[2]
    - With negative endocervical margin residual ACIS 9.5-23%[1]
  - Definitive therapy is extra-facial hysterectomy
- AIS found unexpectantly in LEEP specimens with negative margins[3]
  - May be followed expectantly, with colposcopy and ECC
  - 0 recurrences in 28 patients

[1] SOGC Clinical Practice Guidelines JSOGC;1999:77, 699-706

[2] Bertrand M, Am J Obstet Gynecol;1987:157,21-5

[3] Bryson P Gynecol Oncol;2004:93,465-468

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AIS with a desire for fertility

- Need negative margins
- If margins negative residual disease in hysterectomy specimen 12.5%
- If conservative management cytology/ colposcopy +/- ECC q 6/12 x 4 then annually
- No need for hysterectomy after family complete

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AIS with positive margins

- If +ve risk of residual is 46%
- Risk of adenocarcinoma 16.7%
- Need repeat with negative margins

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Conclusions

- AGC always needs colposcopy
- AGC is usually an indicator of CIN
- AIS may be identified colposcopically
- AIS warrants a large cold knife cone
- Use algorithms to guide management and follow-up