Cryotherapy has No Place in Colposcopy Practice
• No financial disclosures

• No conflicts of interest
? Precision ? Personalized Medicine
? Best Evidence Based Practice
Principals of Surgical Management

• CIN1 should be treated with the same radicality as CIN3
• The whole TZ should be treated or excised and not just the area CIN can be identified
• CIN can involve crypts so destruction or excision should be to at least 7 mm
• All patients are at risk of cancer in the future and should be followed up
More residual disease with Cryotherapy

Graph of Relative Risk (95% CI)

HIGH GRADE DISEASE  Cryotherapy versus Laser Ablation: Residual Disease

• 77 papers—equivalent to 28,827 cases of treated CIN—were included in the meta-analysis. Cryotherapy achieved cure rates of 94.0% (CIN1), 92.0% (CIN2), and **85.0% (CIN3)**. Use of the double-freeze method and absence of endocervical involvement significantly increased cure rates. Minimal side effects

• Cryotherapy is an effective, safe, and acceptable treatment for CIN in low-resource settings, enabling availability
Mapping out Transformation Zone for Excisional / Ablative Treatment

- SCJ in canal
- Transformation Zone

Tailoring treatment according to location of TZ
Type I TZ / Adequate Colposcopy

is completely ectocervical and fully visible
TZ has an endocervical component and is fully visible, 

Adequate colposcopy Not suitable for ablation
Will both lesions be treated adequately by Cryotherapy probes?
Cervical Crypts

4mm depth

Squamous Metaplasia in Crypts

Maximum depth 5 mm
Surgical Treatment for Colposcopy

• **Loop excision is preferable as whole of transformation zone has histological examination**
  

• Colposcopically directed punch biopsy: a potentially misleading investigation.

• **Buxton EJ**, **Luesley DM**, **Shafi MI**, **Rollason M**.

• In 132 (54%) of the 243 women the histology of the punch biopsy and loop excision specimen did not agree.

• In 62 (47%) of these 132 women a more severe lesion was found in the excised transformation zone, including three unsuspected adenocarcinoma in situ and one stage Ia1 cancer.

• 80% of loop specimens should be single exisions to facilitate pathology assessment
Treatment Failure after excisional treatment of CIN

- Clear margins: 5%
- Involved margins: 16-28%

Risk factors

- Age > 40
- Glandular involvement
- HPV satellite lesions
- Advanced age
- Endocervical extension
- High grade CIN
HOW DO YOU DETERMINE IF TREATMENT WAS CRYOTHERAPY ADEQUATELY DONE?
Risk of Invasive Cervical Cancer

- Risk x 4-5 times > general population
- Incidence of Cx Ca: SIMILAR between methods
- Risk for 20 years

Soutter, de Barros Lopes, Fletcher, Monaghan, Dunkan, Paraskevaidis, Kitchener. *Lancet, 1997*

Kalliala I, Anttila A, Pukkala E, Nieminen P. *BMJ, 2005*

Soutter WP, Sasieni P, Panoskaltsis T. *Int J Cancer, 2006*
Risk of Invasive Cervical Cancer

- **Risk** x 4-5 times > general population
- **Incidence of Cx Ca:** ABLATION AND PARTICULARLY CRYOTHERAPY INCREASED RISK
- **Risk** for 20 years

Melnikow, McGahan, Sawaya, Ehlen, Coldman. *JNCI, 2009*

Rapiti, Usel, Neyroud-Caspar, Merglen, Verkooijen, Vlastos, Pache, Kumar, Bouchardy. *EJC, 2012*
Cervical Intraepithelial Neoplasia Outcomes After Treatment: Long-term Follow-up From the British Columbia Cohort Study

Joy Melnikow, Colleen McGahan, George F. Sawaya, Thomas Ehlen, Andrew Coldman

37 142 women treated for CIN 1, 2, or 3 from January 1, 1986, through December 31, 2000 (CIN cohort), British Columbia compared to 71 213 women with normal cytology and no previous CIN diagnosis.

Overall incidence of invasive cancer (per 100 000 woman-years) was higher in the CIN cohort (37 invasive cancers, 95% CI = 30.6 to 42.5 cancers) than in the comparison cohort (six cancers, 95% CI = 4.3 to 7.7 cancers)
### Estimated rates of CIN 2/3 per 1000 women in the initial 6-year period after treatment for CIN by index diagnosis, age group, and index treatment (cone biopsy, LEEP, laser excision or ablation, or cryotherapy)

<table>
<thead>
<tr>
<th>Index diagnosis</th>
<th>Age, y</th>
<th>Cone</th>
<th>LEEP</th>
<th>Laser</th>
<th>Cryotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIN 1</td>
<td>21–29</td>
<td>28.1 (20.2 to 36.1)</td>
<td>23.3 (16.4 to 30.1)</td>
<td>45.6 (39.0 to 52.1)</td>
<td>54.7 (48.6 to 60.9)</td>
</tr>
<tr>
<td></td>
<td>30–39</td>
<td>33.1 (23.9 to 42.3)</td>
<td>27.4 (19.4 to 35.3)</td>
<td>53.5 (45.1 to 61.8)</td>
<td>64.1 (56.2 to 72.0)</td>
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<tr>
<td></td>
<td>40–49</td>
<td>31.9 (22.8 to 41.0)</td>
<td>26.4 (18.5 to 34.3)</td>
<td>51.6 (42.0 to 61.3)</td>
<td>61.9 (52.3 to 71.6)</td>
</tr>
<tr>
<td></td>
<td>≥50</td>
<td>22.4 (14.7 to 30.0)</td>
<td>18.5 (11.5 to 25.5)</td>
<td>36.3 (25.1 to 47.5)</td>
<td>43.7 (31.1 to 56.2)</td>
</tr>
<tr>
<td>CIN 2</td>
<td>21–29</td>
<td>34.8 (28.2 to 41.5)</td>
<td>41.9 (34.8 to 49.0)</td>
<td>73.0 (66.6 to 79.4)</td>
<td>133.3 (124.5 to 142.2)</td>
</tr>
<tr>
<td></td>
<td>30–39</td>
<td>35.0 (28.3 to 41.7)</td>
<td>42.2 (34.9 to 49.5)</td>
<td>73.0 (66.6 to 79.4)</td>
<td>134.1 (123.3 to 144.9)</td>
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<tr>
<td></td>
<td>40–49</td>
<td>35.7 (28.4 to 43.0)</td>
<td>43.0 (34.6 to 51.4)</td>
<td>74.8 (64.4 to 85.3)</td>
<td>136.5 (119.2 to 153.8)</td>
</tr>
<tr>
<td></td>
<td>≥50</td>
<td>29.5 (21.4 to 37.5)</td>
<td>35.5 (25.3 to 45.8)</td>
<td>62.1 (45.9 to 78.3)</td>
<td>114.1 (85.3 to 142.9)</td>
</tr>
<tr>
<td>CIN 3</td>
<td>21–29</td>
<td>56.3 (52.0 to 60.6)</td>
<td>86.1 (78.3 to 94.0)</td>
<td>117.2 (109.6 to 124.8)</td>
<td>241.6 (228.7 to 254.5)</td>
</tr>
<tr>
<td></td>
<td>30–39</td>
<td>62.9 (58.1 to 67.6)</td>
<td>95.8 (87.0 to 104.7)</td>
<td>130.1 (121.3 to 138.9)</td>
<td>265.1 (249.3 to 281.0)</td>
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<tr>
<td></td>
<td>40–49</td>
<td>85.3 (77.5 to 93.2)</td>
<td>129.0 (114.7 to 143.4)</td>
<td>173.6 (156.9 to 190.2)</td>
<td>340.0 (309.3 to 370.8)</td>
</tr>
<tr>
<td></td>
<td>≥50</td>
<td>90.4 (77.3 to 103.4)</td>
<td>136.4 (113.7 to 159.0)</td>
<td>183.0 (154.1 to 212.0)</td>
<td>355.4 (300.1 to 410.7)</td>
</tr>
</tbody>
</table>
Association between risk factors and risk of invasive cancer after treatment for CIN over the first 10 years of follow-up (n = 37 142)

<table>
<thead>
<tr>
<th>Factor (comparison)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial treatment (cryotherapy vs other)</td>
<td>2.98 (2.09 to 4.26)</td>
</tr>
<tr>
<td>Initial diagnosis (CIN 3 vs CIN 1 and 2)</td>
<td>4.10 (2.70 to 6.22)</td>
</tr>
<tr>
<td>Age (≥40 vs &lt;40 y)</td>
<td>1.75 (1.12 to 2.74)</td>
</tr>
</tbody>
</table>
Omission of excisional therapy is associated with an increased risk of invasive cervical cancer after cervical intra-epithelial neoplasia III.

EUROPEAN JOURNAL OF CANCER 48 (2012) 845-852

All women diagnosed with CIS/CIN III in Geneva (Switzerland) between 1970 to 2002 (n = 2658) and followed for invasive cervical cancer recurrence until 31st December 2008

2307 women had excision 7 cancers Incidence Rate 2.4 95% CI (1-2.9)

108 women had ablation 2 cancers Incidence Rate 16.8 95% CI (2-16.8)
LEEP / LLETZ is safe, effective for treating HSIL and has no reproductive sequelae if done carefully in young women !!!!
Pregnancy Outcomes after Treatment for Cervical Cancer Precursor Lesions: An Observational Study
The Center for Health Research, Kaiser Permanente Northwest, Portland, Oregon, 2017
PLOS ONE

SIMILAR RESULTS TO UK DATA. CASTANON BMJ

- No difference in Preterm Delivery ablation or <10mm excisions; Majority of Excisions

- EXCISIONS >10mm
Treatment versus un-exposed: RR = 2.15, 95% CI 1.16±3.98
NO REASON TO DO CRYOTHERAPY IN ANY WOMAN IN US

EXCISION IS SUPERIOR IF DONE BY A COMPETENT COLPOSCOPISTS