

Topical Imiquimod is Highly Effective in the Treatment of High Grade Squamous Intraepithelial Dysplasia of the Lower Anogenital Tract: A Systematic Review and Meta-Analysis of Randomised Controlled Trials

Sanjaya Wijeyekoon FRCS¹, Andrei Ilczyszyn MRCS¹,
Tamzin Cuming FRCS¹, Anke De-Masi MRCP¹, Noreen
Chindawi RN¹, Mohamed Thaha FRCS², Mayura Nathan FRCP¹

1. *HANS, Homerton Anal Neoplasia Service, Homerton University Hospital NHS Foundation Trust*
2. *Academic Surgical Unit, Centre for Digestive Diseases, Blizard Institute, Barts and the London School of Medicine & Dentistry*

HANS

Homerton Anal Neoplasia Service

Pathogenesis

- High grade squamous intraepithelial dysplasia (HSIL) can affect any part of the lower anogenital tract (cervix/anus/vagina/perineum)
- HSIL is mediated by human papilloma virus (HPV)
- HSIL is a precursor to squamous cell carcinoma (SCC)

Darragh et al. 2013

Treatment Options

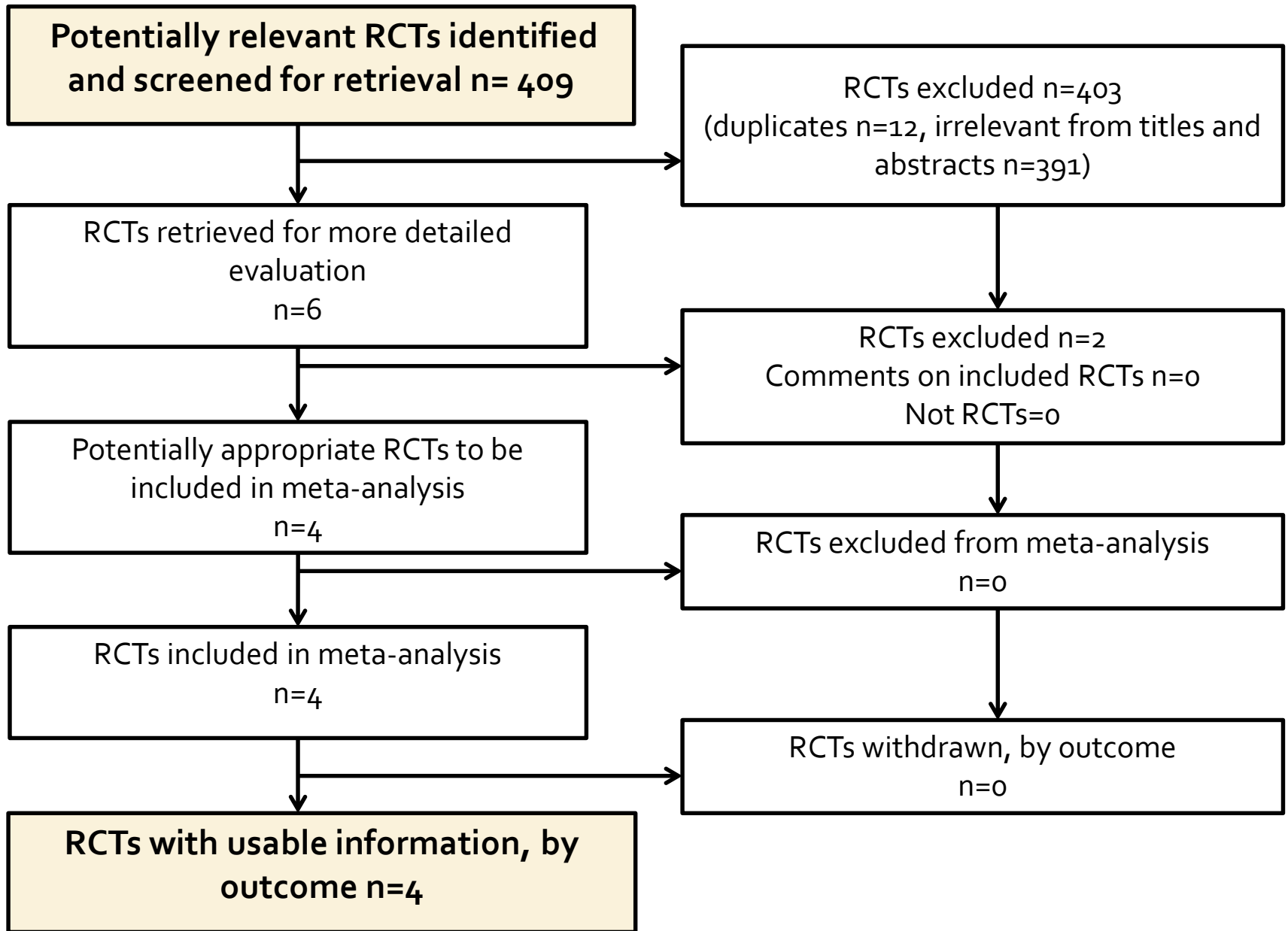
- Current ablative or surgical techniques are associated with significant morbidity
- Topical Imiquimod is an immunomodulatory agent and local application has been shown to be effective in downgrading HSIL within the anogenital tract
- We performed a meta-analysis assessing the effectiveness of topical imiquimod compared to placebo

Methods

- Meta-analysis was performed following recommendations of the Cochrane Collaboration
- Systematic keyword search within Medline, EMBASE and Science Citation Index Expanded
- Data independently extracted by two reviewers
- Statistical analysis utilised RevMan 5.0 using a random effects model
- Risk ratio (RR) was estimated with 95% confidence intervals (CI) based on an intention-to-treat analysis

Outcome Evaluation

- Biopsy proven HSIL
- 16 weeks of topical therapy
- Repeat high resolution anoscopy (HRA)/colposcopy assessment and biopsy
 - Primary outcome: Histological regression
 - Secondary outcome: Histological clearance
 - Treatment associated morbidity



Results

Baseline Characteristics

	Imiquimod	Placebo	p
N	113	93	NS
Age	29.2 - 46.6	31.8 - 50.3	NS
Gender (M:F)	36:77	28:65	NS
HIV +ve	36	28	NS

No significant differences in baseline characteristics

Results

Primary Outcome

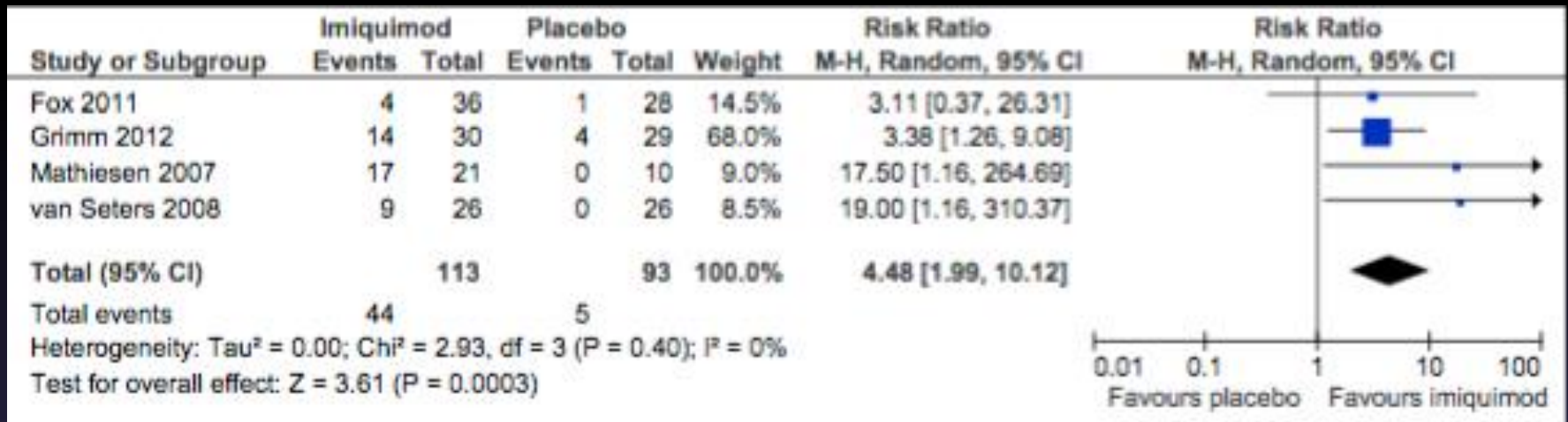


Histological regression of HSIL was significantly higher in the Imiquimod group versus placebo

62.8% vs. 14.0%; RR 7.49, 95% CI 1.26-44.50, P = 0.03

Results

Secondary Outcome



Complete histological clearance of HSIL was also significantly higher in the Imiquimod group versus the placebo group (38.9% vs. 5.4%; RR 4.48, 95% CI 1.99-10.12, $P < 0.05$)

Results

Morbidity

Two trials reported side effects (imiquimod n=56)

	N	%
Pain/Pruritus	52	93%
Flu-like symptoms	34	61%
Headache	32	57%
Myalgia	26	46%

No major side effects were reported

Conclusions

- Topical Imiquimod therapy is a highly effective treatment for HSIL of the lower anogenital tract
- Treatment is associated with mild side effects
- Topical Imiquimod may be a valuable treatment modality for HSIL particularly in cases of multifocal disease

Remaining Questions

- What is the optimal dose and duration of therapy?
- What is the relative effectiveness of Imiquimod versus destructive therapy?