
 **Banff March 2011**

DCRC Writing Group reports


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 **Why papers?**


- Visibility of the DCRC
- Academic advancement on the topic
- Guidance on study design & analysis (avoid the 'sins' of the past)
- Measureable output (metric) for future EASD (+/- ECCO funding)

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 **Principles of process**


- Ideas (currently limited to 4 - deliverable in next 12 mo.)
- Establish a writing group (typically 4 to 6)
- Draft documents
- Revisions among writing group
- Circulation to wider DCRC (minor ratifications)
- Submission

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 **4 concept papers**

1. A framework to evaluate the impact of diabetes on mortality in patients with cancer
Andrew Renehan, Jessica Hsin-Chieh (at John Hopkins), Johnson, Wild, Gale, Moller
Status – advanced draft circulated
2. Timing of Cancer Incidence and diabetes onset - including sections covered in Bendix's tabulation document, Copenhagen, June 2010
Bendix Carstensen, Jeff Johnson, Samantha Bowker, Daniel Witte
Status – work in progress
3. Diabetes, smoking and colorectal cancer: a meta-analysis
Andrew Renehan, Peter Campbell (at ACS) Edwin Gale, Sarah Wild, Iain Buchan
Status – advanced draft by 1st April
4. A common analytic framework for glucose-lowering therapies and cancer risk - including sections covered in Bendix's tabulation document, Copenhagen, June 2010
Bendix Carstensen, Jeff Johnson, Samantha Bowker, Daniel Witte
Status – work in progress


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 **Where are these papers going**

1. A framework to evaluate the impact of diabetes on mortality in patients with cancer
Target submission – Diabetologia
2. Timing of Cancer Incidence and diabetes onset - including sections covered in Bendix's tabulation document, Copenhagen, June 2010
Target submission – Diabetologia
3. Diabetes, smoking and colorectal cancer: a meta-analysis
Target submission – Diabetologia (stand alone 'Original manuscript')
4. A common analytic framework for glucose-lowering therapies and cancer risk - including sections covered in Bendix's tabulation document, Copenhagen, June 2010
Post as a report on website

} Plan: to submit simultaneously

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 **Paper 1**

The impact of pre-existing diabetes on mortality in patients with cancer: a framework for evaluation

Andrew G Renehan,¹ Hsin-Chieh Yeh,² Jeff Johnson,³ Sarah H Wild,⁴ Edwin Gale,⁵ Henrik Møller,⁶ on behalf of the Diabetes and Cancer Research Consortium*

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Research questions for DCRC

The following research questions are central to the work of this consortium:

1. What is the temporal relationship between cancer incidence and onset of diabetes?
2. Why does cancer have a worse prognosis in people with diabetes?
3. To what extent is cancer risk (incidence and prognosis) modified by diabetes treatments?

Prognostic versus predictive 'biomarker'

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Paper 1: framework

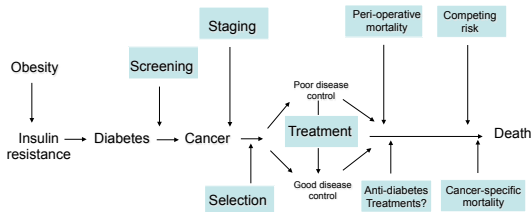
1. Differential utilization of cancer screening
2. Advanced stage at diagnosis
3. Selection bias for initial and adjuvant cancer treatment
4. Complications of initial treatment/treatment failures
5. Peri-treatment mortality (short-term mortality)
6. Competing risks for death for long-term mortality
7. Interactions with therapies
8. Effects of anti-diabetes treatments
9. Differences in tumour biology

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Paper 1: framework (graphical)



Work in progress

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Paper 2 & 4

Jeff – do you want to verbally update?

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Paper 3

Diabetes, smoking and incident colorectal cancer risk: a meta-analysis

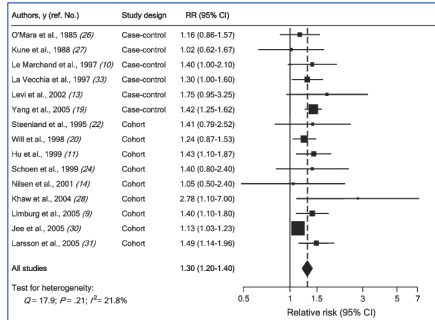
Andrew G Renehan,¹ Peter Campbell,² Susanna Larsson,³ Sarah Wild,⁴ Edwin Gale,⁵ on behalf of the Diabetes and Cancer Research Consortium*

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We have updated Larsson meta-analysis



Journal of the National Cancer Institute, Vol. 97, No. 22, November 16, 2005

BMI & cancer: sex-specific associations

	Studies		Cases		Risk ratio in men*	Risk ratio in women*	p value†
	Men	Women	Men	Women			
Colon cancer							
All studies	22	19	22,440	20,975	1.24 (1.21-1.28)	1.08 (1.05-1.14)	<0.0001
Studies with both sexes	13	13	17,495	19,256	1.24 (1.18-1.31)	1.08 (1.02-1.14)	0.001
All but one study**	21	18	8635	4337	1.26 (1.21-1.30)	1.10 (1.06-1.15)	<0.0001
Rectal cancer							
All studies	18	14	14,894	9,052	1.09 (1.05-1.12)	1.02 (0.99-1.04)	0.001
Studies with both sexes	11	11	11,035	8,644	1.08 (1.05-1.11)	1.01 (0.98-1.04)	0.003
All but one study**	17	13	5712	1,560	1.09 (1.05-1.15)	1.05 (0.99-1.12)	0.32

*Risk ratio per 5 kg/m² increase in BMI (95% CI). †Meta-regression analysis with univariable model of sex. ‡Meta-regression analysis with multivariable models including the method of BMI determination (measured or self-reported)-the extent of cancer site specific, risk factor adjustment and geographic region. We analyzed only cancer sites with more than 30 studies that included both sexes.

Table 2: Comparisons of risk ratios in men and women

Renehan et al. *Lancet* 371: 569-578, 2008

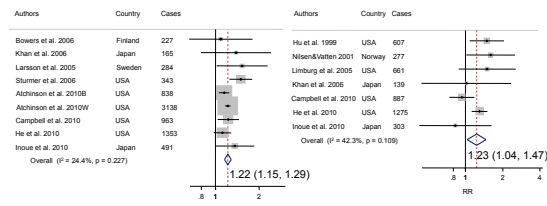
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Demographics: sex – colon cancer

Colon Cancer men
Diabetes - Yes/No

Colon Cancer Women
Diabetes - Yes/No



Meta-regression for gender difference: $p = 0.801$

Renehan et al. *Update of Larsson Meta-analysis*

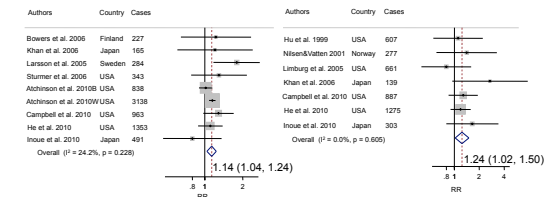
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Demographics: sex – rectal cancer

Rectal Cancer men
Diabetes - Yes/No

Rectal Cancer Women
Diabetes - Yes/No



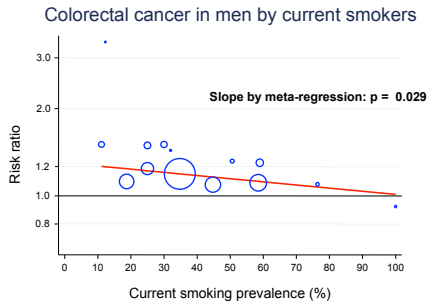
Meta-regression for gender difference: $p = 0.527$

Renehan et al. *Update of Larsson Meta-analysis*

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Diabetes, smoking & colorectal cancer

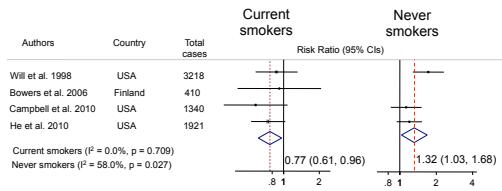


Renehan et al. manuscript in preparation

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Diabetes, smoking & colorectal cancer

Colorectal Cancer men



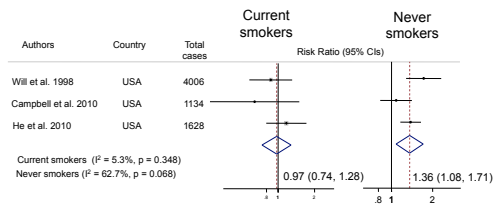
Difference: $p = 0.024$

Renehan et al. manuscript in preparation

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Diabetes, smoking & colorectal cancer

Colorectal Cancer women



Difference: $p = 0.156$

Renehan et al. manuscript in preparation

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Summary

- Diabetes associated with risk of colon & rectal cancers
- (No gender differences; no population differences)
- Patterns differ for diabetes compared with BMI
- Smoking is an effect-modifier (in men)
- (Modest residual risk for min. v max. adjusted estimates – suggesting that 'confounding' of treatment likely to be modest)
