Embracing Heterogeneity in Evidence Synthesis to Inform Intervention Development

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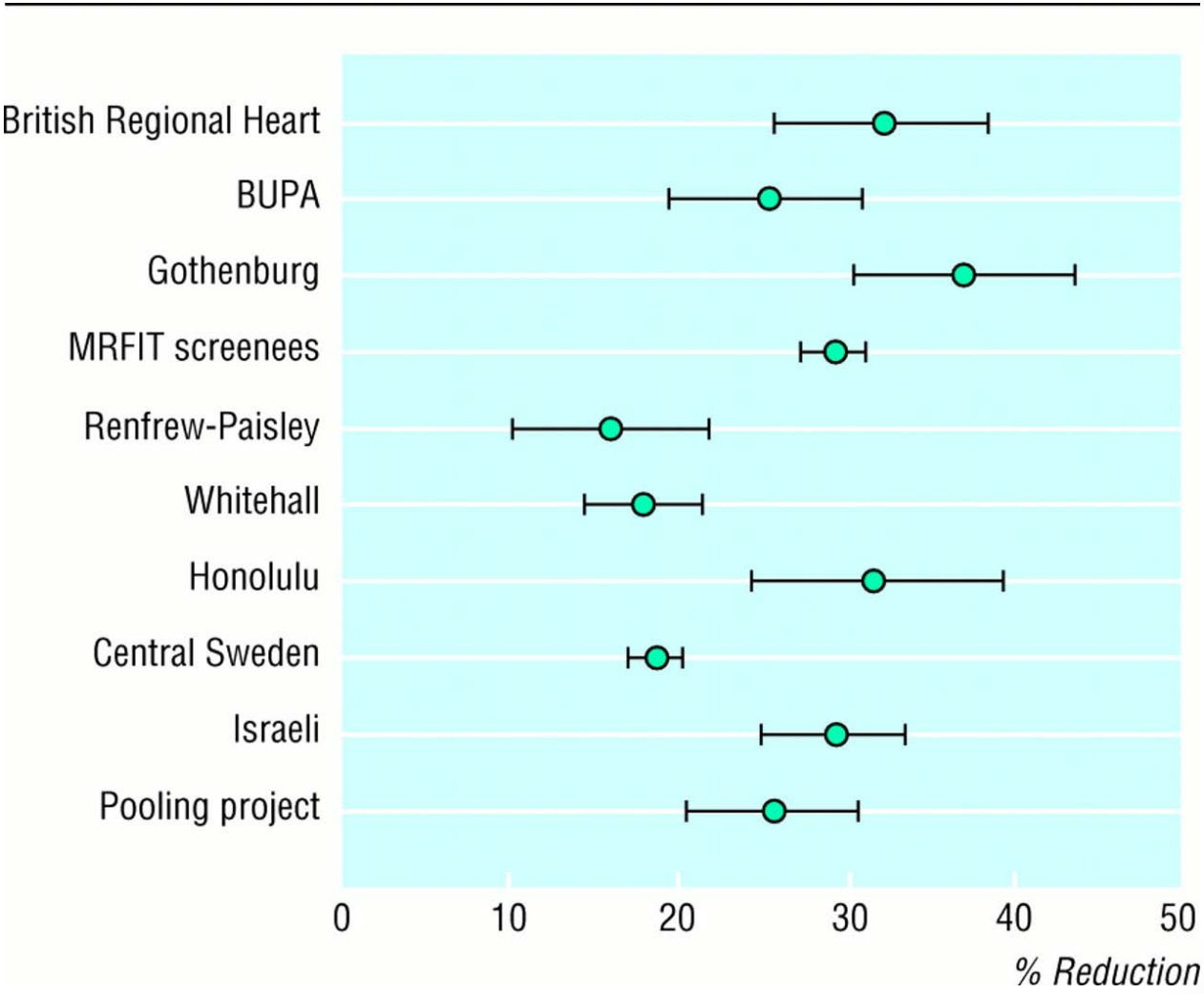
Reduction in risk of heart disease by strategies for lowering cholesterol.

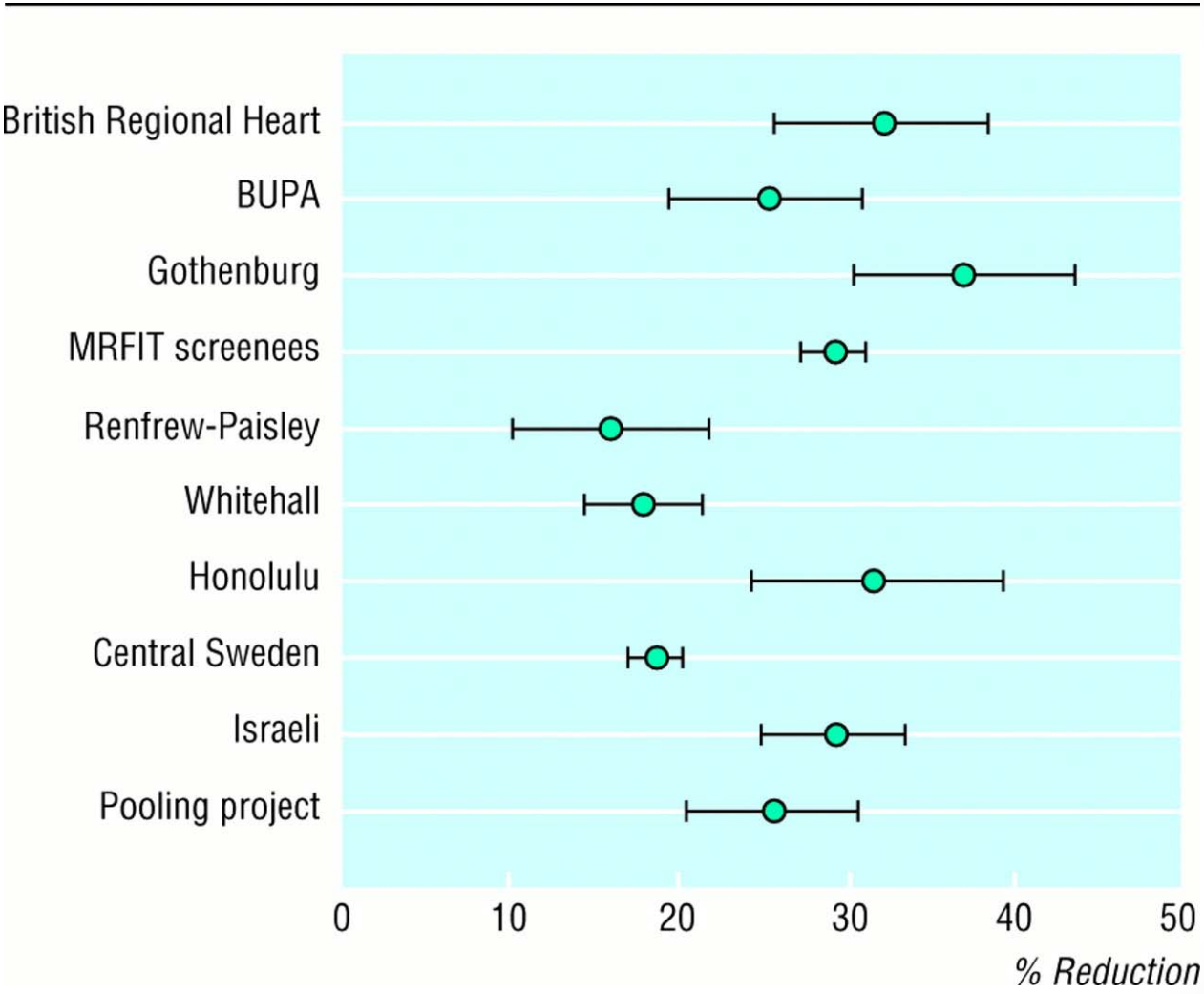


Greenhalgh T BMJ 1997;315:672-675

Some Practical Questions

- Does it work?
- What is “it”?
- What do I need to replicate it here? (how does it work? What will it cost etc)
- If I replicate it here will I get the same results?

Reduction in risk of heart disease by strategies for lowering cholesterol.



Greenhalgh T BMJ 1997;315:672-675

Working after cancer: a systematic review, meta-regression and explanatory meta-synthesis of the qualitative evidence

Dr Mary Wells, Brian Williams, Thilo Kroll

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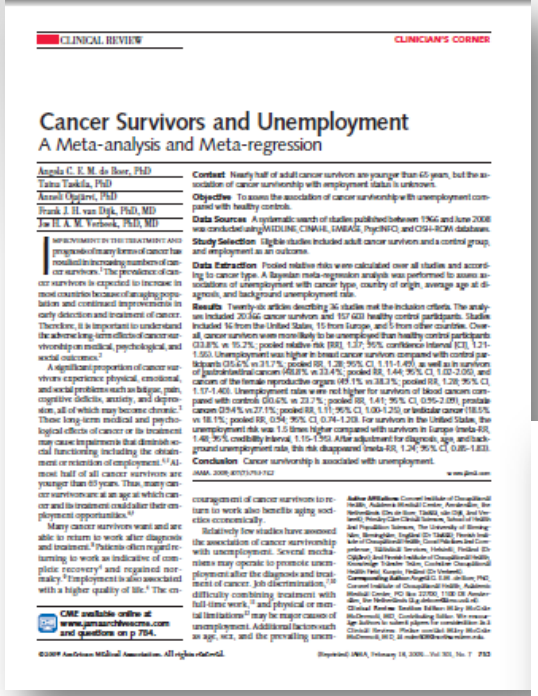

CLINICAL REVIEW

CLINICIAN'S CORNER

Cancer Survivors and Unemployment

A Meta-analysis and Meta-regression

Angela G. E. M. de Boer, PhD
Taina Taskila, PhD
Annali Ojajärvi, PhD
Frank J. H. van Dijk, PhD, MD
Jac H. A. M. Verbeek, PhD, MD

Context Nearly half of adult cancer survivors are younger than 65 years, but the association of cancer survivorship with employment status is unknown.

Objective To assess the association of cancer survivorship with unemployment compared with healthy controls.

Data Sources A systematic search of studies published between 1966 and June 2008 was conducted using MEDLINE, CINAHL, EMBASE, PsycINFO, and OSH-ROM databases.

Study Selection Eligible studies included adult cancer survivors and a control group, and employment as an outcome.

Data Extraction Pooled relative risks were calculated over all studies and according to cancer type. A Bayesian meta-regression analysis was performed to assess associations of unemployment with cancer type, country of origin, average age at diagnosis, and background unemployment rate.

Results Twenty-six articles describing 36 studies met the inclusion criteria. The analysis included 20 366 cancer survivors and 157 603 healthy control participants. Studies included 16 from the United States, 15 from Europe, and 5 from other countries. Overall, cancer survivors were more likely to be unemployed than healthy control participants (33.8% vs 15.2%; pooled relative risk [RR], 1.37; 95% confidence interval [CI], 1.21-1.55). Unemployment was higher in breast cancer survivors compared with control participants (35.6% vs 31.7%; pooled RR, 1.28; 95% CI, 1.15-1.49) as well as in survivors of gastrointestinal cancers (48.8% vs 33.4%; pooled RR, 1.44; 95% CI, 1.03-2.09), and cancers of the female reproductive organs (49.1% vs 38.3%; pooled RR, 1.28; 95% CI, 1.17-1.40). Unemployment rates were not higher for survivors of blood cancers compared with controls (30.6% vs 23.7%; pooled RR, 1.41; 95% CI, 0.95-2.09), prostate cancer (29.4% vs 27.1%; pooled RR, 1.11; 95% CI, 1.00-1.21), or testicular cancer (18.5% vs 18.1%; pooled RR, 0.94; 95% CI, 0.74-1.20). For survivors in the United States, the unemployment risk was 1.5 times higher compared with survivors in Europe (meta-RR, 1.48; 95% credibility interval, 1.15-1.95). After adjustment for diagnosis, age, and background unemployment rate, this risk disappeared (meta-RR, 1.24; 95% CI, 0.85-1.83).

Conclusion Cancer survivorship is associated with unemployment.

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www.jama.com

CME available online at www.jamaarchivescme.com and questions on p 754.

(Reprinted) JAMA, February 18, 2009—Vol 301, No. 7 753

courangement of cancer survivors to return to work also benefits aging societies economically.

Relatively few studies have assessed the association of cancer survivorship with unemployment. Several mechanisms may operate to promote unemployment after the diagnosis and treatment of cancer. Job discrimination,[10] difficulty combining treatment with full-time work,[11] and physical or mental limitations[12] may be major causes of unemployment. Additional factors such as age, sex, and the prevailing unem-

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Clinical Review Section Editor: Mary McCabe, MD. Contributing Editor: We encourage authors to submit papers for consideration to the Clinical Review Section. Please contact Mary McCabe, MD, at mdmccabe@earthlink.net.

Table 4. Results of Univariate and Multivariate Bayesian Meta-regression Models With Crude and Adjusted Meta-relative Risks for Prognostic Factors

Factor	No. of Studies	All Studies (n = 36)		High-Quality Studies[a]	
		Crude Meta-RR (95% CrI) Univariate	Adjusted Meta-RR (95% CrI) Multivariate[b]	No.	Adjusted Meta-RR (95% CrI) Multivariate (n = 25)[b]
Country					
Europe	16	1 [Reference]	1 [Reference]	15	1 [Reference]
United States	15	1.48 (1.15-1.95)	1.24 (0.85-1.83)	7	0.98 (0.66-1.56)
Other	5	1.47 (1.03-2.12)	1.16 (0.68-1.96)	3	1.34 (0.85-2.27)
Cancer diagnosis					
Testicular	3	1 [Reference]	1 [Reference]	3	1 [Reference]
Breast	10	1.35 (0.76-2.37)	1.20 (0.65-2.22)	6	1.15 (0.67-1.85)
Prostate	3	1.21 (0.62-2.39)	1.17 (0.55-2.47)	3	1.28 (0.67-2.31)
Blood	7	1.42 (0.77-2.64)	1.38 (0.79-2.50)	6	1.27 (0.74-2.04)
Other or mixed	13	1.58 (0.90-2.75)	1.48 (0.87-2.56)	7	1.35 (0.84-2.09)
Patient age					
18-50 y	23	1 [Reference]	1 [Reference]	15	1 [Reference]
>50 y	8	0.99 (0.70-1.40)	1.08 (0.70-1.69)	6	1.03 (0.72-1.46)
Not reported	5	1.19 (0.81-1.77)	1.10 (0.70-1.77)	4	1.09 (0.69-1.65)
Background unemployment rate	36	0.24 (0.11-0.54)	0.38 (0.11-1.27)	25	0.63 (0.21-1.99)

Abbreviations: CrI, credibility interval; RR, relative risk.
[a] High quality denotes 16 points or greater on the MINORS test.
[b] Adjusted for all the other variables in the model.

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Through a meta-synthesis of qualitative studies:

Is there evidence to explain the likely mechanisms by which these variables impact on return to work?

Are there variables which have not been included in meta-regression that might predict?

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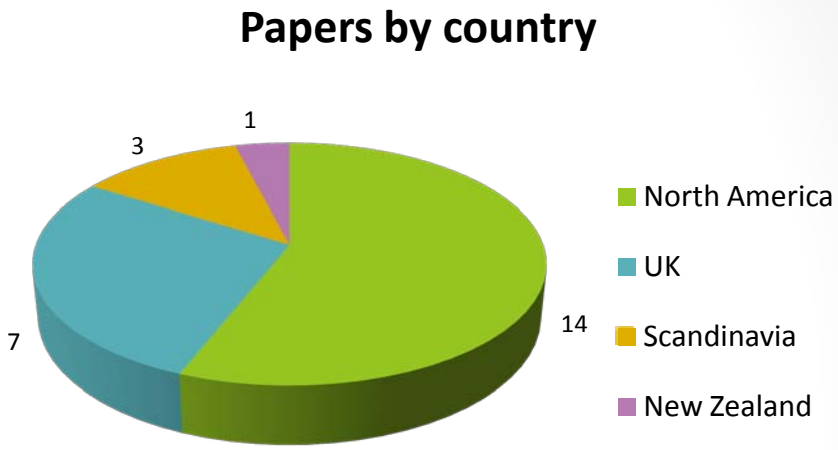
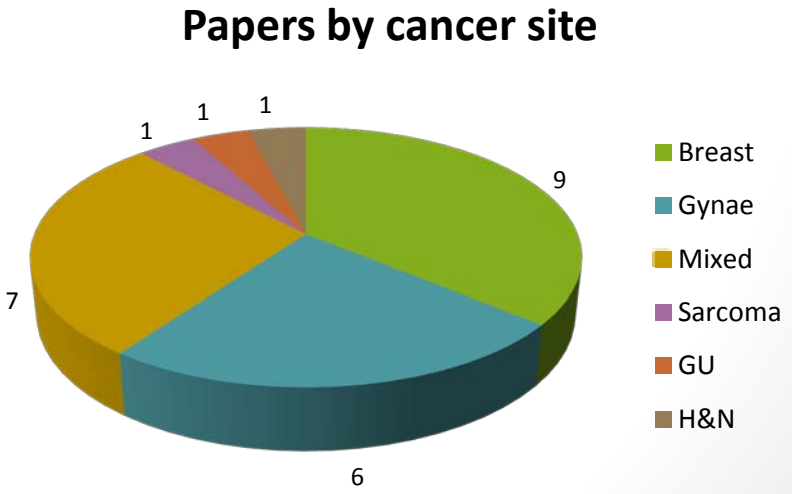
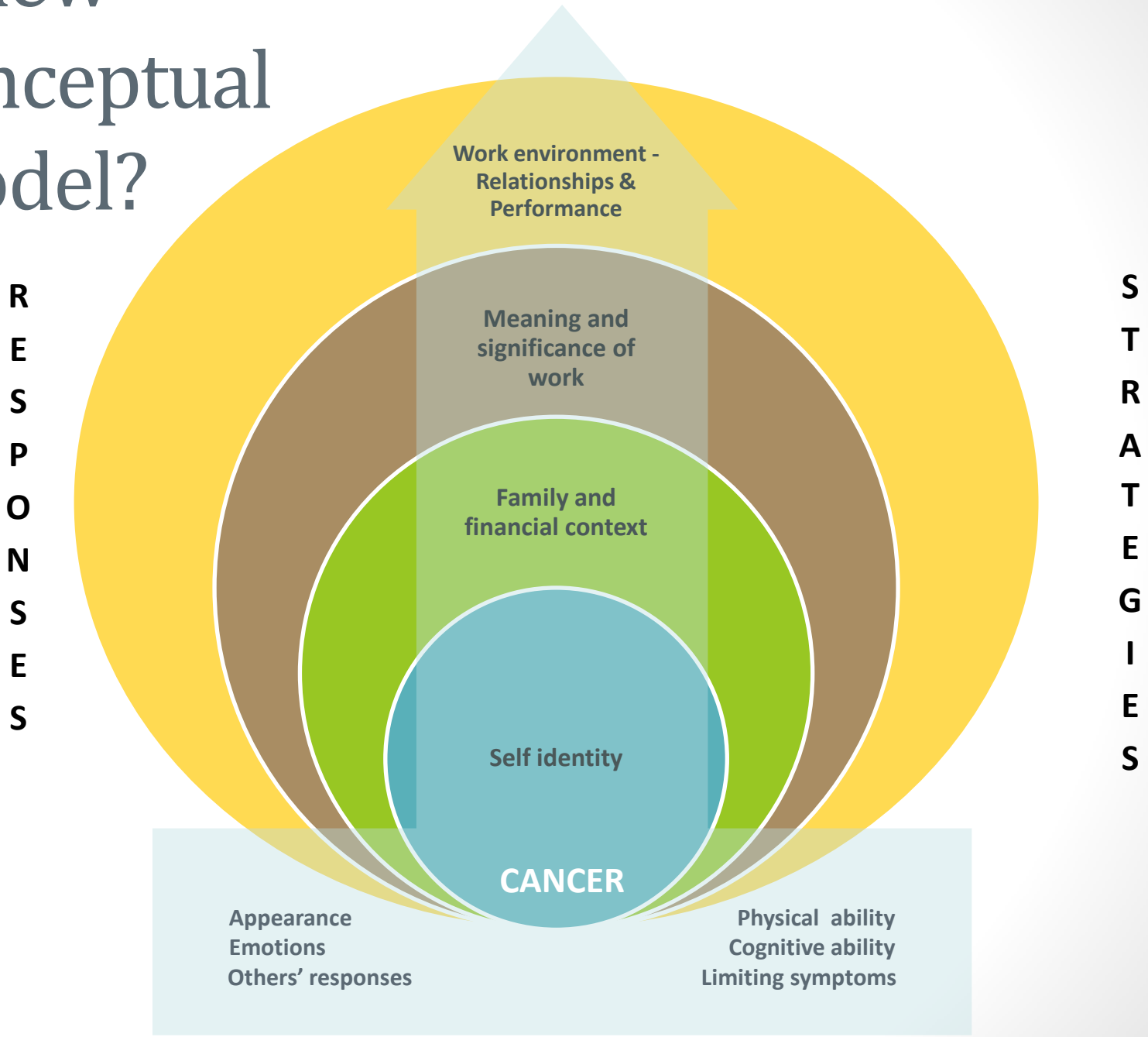
Inclusion of papers

- 13,233 titles & abstracts screened for relevance
- 69 full papers obtained
- 48 excluded – not qualitative, no relevant data
- 21 quality appraised
- 2 located via experts
- 2 located from journals ‘in press’
- 19 ‘full’ papers, 6 ‘partial’





A new conceptual model?



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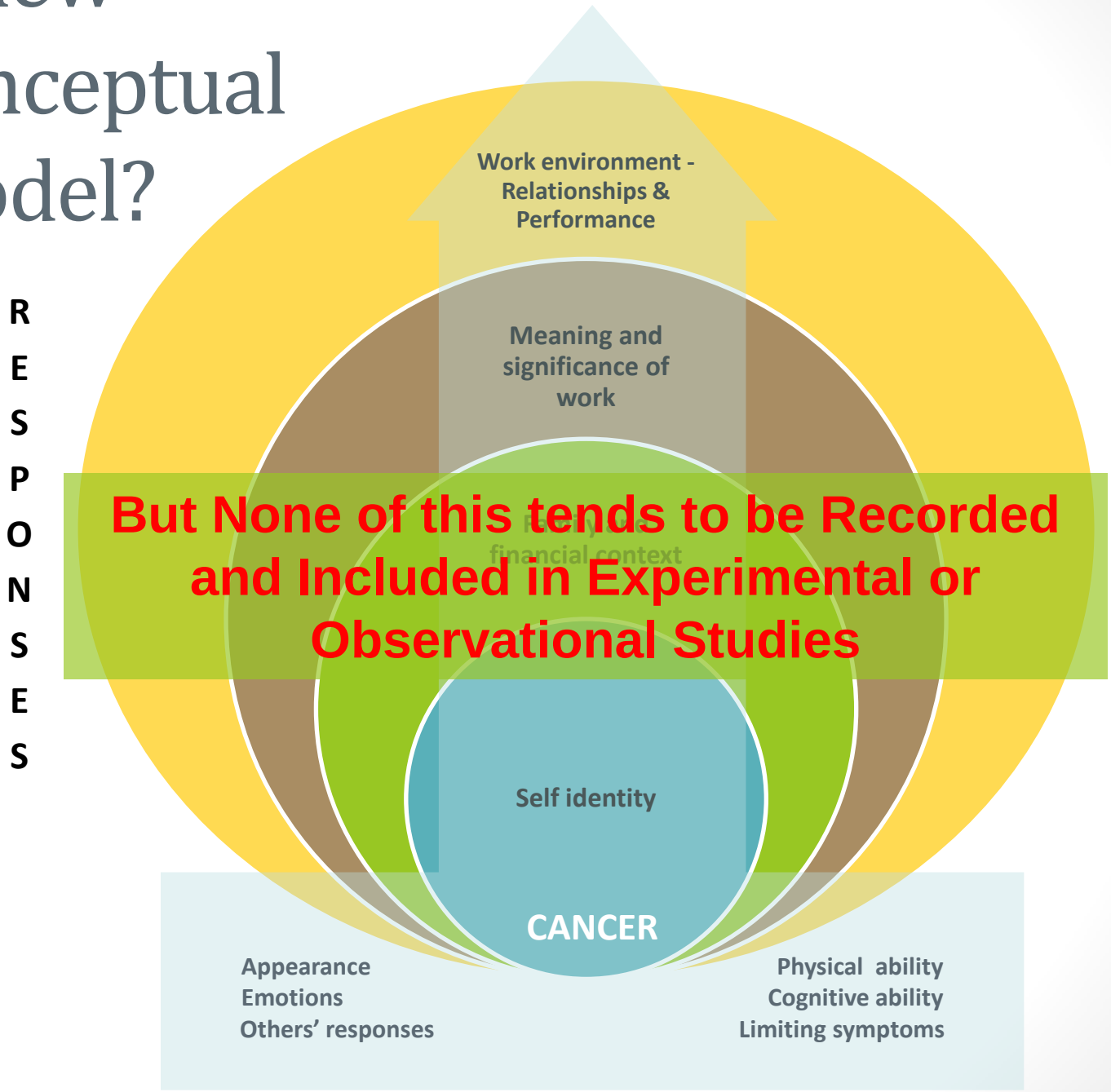

Intervention description is not enough: evidence from an in-depth multiple case-study on the untold role and impact of context in RCTs of 7 Complex Interventions.

Mary Wells, Shaun Treweek, Julie Taylor, Brian Williams

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	Number and nature of participants / documents	Total number of data sources (interviews, focus groups & documents)
Phase 1: Single Exploratory Case		
Interviews	13 longitudinal interviews with 4 Breast care nurse: Three interviewed 3 times. One interviewed 4 times. Plus: One interview with a research nurse And one interview with a charge nurse	15
Documents	Protocol, Ethics application, Monitoring reports x 2, Final report, Minutes of meetings x 15, Field notes of PI and researcher	22
Phase 2: Multiple Explanatory Case Study		
Interviews	7 Principal Investigators and 1 research assistant	8
Documents	7 trial protocols / proposals 6 ethics forms 5 monitoring reports 7 final reports 5 published papers	30
Focus groups	1 group with 3 Research nurses 1 group with 2 Nurse members of the Ethics committee 1 group with 4 PIs	9
Total		84

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- **Personal, organisational, trial and problem context are crucial to understanding how a complex intervention works**
- **The ways in which context challenged trial operation was often complex, idiosyncratic, and subtle; often falling outside of current trial reporting formats.**
- **Information on such issues appeared to be available via first hand "insider accounts" of each trial suggesting that improved reporting on the role of context is possible.**

"We have a habit of writing articles published in scientific journals to make the work as finished as possible, to cover up all the tracks, to not worry about the blind alleys or describe how you had the wrong idea first, and so on. So there isn't any place to publish, in a dignified manner, what you actually did in order to get to do the work"

Richard Feynman 1965

A Meta-Regression and Multiple Case Study to Inform the Development of an Improved Ante and Postnatal Weight Management Intervention: Learned the Lessons from Existing RCTs.

Maggie Styles, Helen Cheyne, Jon Godwin, Annie Anderson, Brian Williams

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Some concluding thoughts:

- Heterogeneity can be helpful
- Analysis of past RCTs may help to identify parameters that predict success i.e. mechanisms that define the intervention.
- But……..we need more honest and open reporting of trials. For the moment we may obtain information from in-depth qualitative analysis of documents and interviews with PIs.
- Embedding qualitative data collection in trials is important ……but could we standardise some common coding categories to facilitate meta-analysis/regression.