Inspired by research. Driven by compassion. Inspiré par la recherche. Guidé par la compassion.

# SEEING THE FOREST AND THE TREES – GETTING MORE VALUE OUT OF SYSTEMATIC REVIEWS OF COMPLEX INTERVENTIONS

**Danko KJ***, Dahabreh IJ, Ivers NM, Trikalinos TA, **Grimshaw JM**

JEREMY GRIMSHAW
SENIOR SCIENTIST, OTTAWA HOSPITAL RESEARCH INSTITUTE
PROFESSOR, DEPARTMENT OF MEDICINE, UNIVERSITY OF OTTAWA
CANADA RESEARCH CHAIR IN HEALTH KNOWLEDGE TRANSFER AND UPTAKE

5TH FEBRUARY 2018
@GRIMSHAWJEREMY

The Ottawa Hospital RESEARCH INSTITUTE | L'Hôpital d'Ottawa INSTITUT DE RECHERCHE

www.ohri.ca | Affiliated with • Affilié à uOttawa

# FUNDING


DIABETES CANADA

# ACKNOWLEDGEMENTS

Kristin Danko

Noah Ivers

Issa Dahabreh

Tom Trikalinos

- John Lavis
- Braden Manns
- David Moher
- Justin Presseau
- Tim Ramsay
- Kaveh Shojania
- Sharon Straus
- Cello Tonelli
- Andrea Tricco

- Alun Edwards
- Michael Hilmer
- Peter Sargious
- Cat Yu
- Caroline Gall Casey

---

- Katrina Sullivan
- Johananie Lepine
- Sathya Karunananthan

# COMPLEX INTERVENTIONS

Complex interventions contain several interacting components

**Box 2** What makes an intervention complex?

Some dimensions of complexity

- Number of and interactions between components within the experimental and control interventions
- Number and difficulty of behaviours required by those delivering or receiving the intervention
- Number of groups or organisational levels targeted by the intervention
- Number and variability of outcomes
- Degree of flexibility or tailoring of the intervention permitted

Implications for development and evaluation

- A good theoretical understanding is needed of how the intervention causes change, so that weak links in the causal chain can be identified and strengthened
- Lack of impact may reflect implementation failure (or teething problems) rather than genuine ineffectiveness; a thorough process evaluation is needed to identify implementation problems.
- Variability in individual level outcomes may reflect higher level processes; sample sizes may need to be larger to take account of the extra variability, and cluster- rather than individually-randomized designs considered.
- Identifying a single primary outcome may not make best use of the data; a range of measures will be needed, and unintended consequences picked up where possible.
- Ensuring strict fidelity to a protocol may be inappropriate; the intervention may work better if adaptation to local setting is allowed.

UK MRC (2006)

# SYSTEMATIC REVIEW OF DIABETES QI STRATEGIES

REVIEW

Articles

## Effects of Quality for Type 2 Diabete
### A Meta-Regression Ana


Kaveh G. Shojania, MD
Sumant R. Ranji, MD
Kathryn M. McDonald, MM
Jeremy M. Grimshaw, MBChB, PhD
Vandana Sundaram, MPH
Robert J. Rushakoff, MD
Douglas K. Owens, MD, MS



**Contex** the care clear.

**Object** ity impr

**Data S** rane Co covers r random interver reporte

**Data E** a meta- vention

**Data S** 13 cont vention 0.29%- than th larger t with me effects ( of QI st team ch (0.52% egies co volving than th ues by ( agemen cation a (95% C terventi


DIABETES MELLITUS HAS reached epidemic proportions in the United States.[1,2] Despite well-established processes of care to reduce morbidity associated with diabetes, widespread quality problems exist.[3-5] The literature contains numerous reports of interventions designed to remedy these problems, but their effectiveness remains unclear.[6]

Previous systematic reviews of quality improvement (QI) strategies for diabetes have provided only qualitative analysis[7] or have focused on single types of interventions,[8-15] leaving the relative effectiveness of different strategies unknown. This is particularly problematic, since many interventions include components of multiple QI strategies. Thus, some of the same trials[16-21] may appear in reviews of pa-

## Effectiveness of quality improvement strategies on the management of diabetes: a systematic review and meta-analysis


Andrea C Tricco, Noah M Ivers, Jeremy M Grimshaw, David Moher, Lucy Turner, James Galipeau, Ilana Halperin, Brigitte Vachon, Tim Ramsay, Braden Manns, Marcello Tonelli, Kaveh Shojania



### Summary

**Background** The effectiveness of quality improvement (QI) strategies on diabetes care remains unclear. We aimed to assess the effects of QI strategies on glycated haemoglobin ($HbA_{1c}$), vascular risk management, microvascular complication monitoring, and smoking cessation in patients with diabetes.

**Methods** We identified studies through Medline, the Cochrane Effective Practice and Organisation of Care database (from inception to July 2010), and references of included randomised clinical trials. We included trials assessing 11 predefined QI strategies or financial incentives targeting health systems, health-care professionals, or patients to improve management of adult outpatients with diabetes. Two reviewers independently abstracted data and appraised risk of bias.

**Findings** We reviewed 48 cluster randomised controlled trials, including 2538 clusters and 84 865 patients, and 94 patient randomised controlled trials, including 38 664 patients. In random effects meta-analysis, the QI strategies reduced $HbA_{1c}$ by a mean difference of 0·37% (95% CI 0·28–0·45; 120 trials), LDL cholesterol by 0·10 mmol/L (0·05–0·14; 47 trials), systolic blood pressure by 3·13 mm Hg (2·19–4·06, 65 trials), and diastolic blood pressure by 1·55 mm Hg (0·95–2·15, 61 trials) versus usual care. We noted larger effects when baseline concentrations were greater than 8·0% for $HbA_{1c}$, 2·59 mmol/L for LDL cholesterol, and 80 mm Hg for diastolic and 140 mm Hg for systolic blood pressure. The effectiveness of QI strategies varied depending on baseline $HbA_{1c}$ control. QI strategies increased the likelihood that patients received aspirin (11 trials; relative risk [RR] 1·33, 95% CI 1·21–1·45), antihypertensive drugs (ten trials; RR 1·17, 1·01–1·37), and screening for retinopathy (23 trials; RR 1·22, 1·13–1·32), renal function (14 trials; RR 128, 1·13–1·44), and foot abnormalities (22 trials; RR 1·27, 1·16–1·39). However, statin use (ten trials; RR 1·12, 0·99–1·28), hypertension control (18 trials; RR 1·01, 0·96–1·07), and smoking cessation (13 trials; RR 1·13, 0·99–1·29) were not significantly increased.



Published Online June 9, 2012 DOI:10.1016/S0140-6736(12)60480-2

See Online/Comment DOI:10.1016/S0140-6736(12)60637-0



Li Ka Shing Knowledge Institute of St Michael's Hospital, Toronto, ON, Canada (A C Tricco PhD); Women's College Hospital and Department of Family and Community Medicine (N M Ivers M D) and Division of Endocrinology, Department of Medicine (I Halperin M D), University of Toronto, Toronto, ON, Canada; Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, ON, Canada (Prof J M Grimshaw PhD, D Moher PhD, L Turner M Sc, J Galipeau PhD, B Vachon PhD, T Ramsay PhD); Department of Medicine (Prof J M Grimshaw)

# INCLUSION CRITERIA – TYPES OF INTERVENTIONS

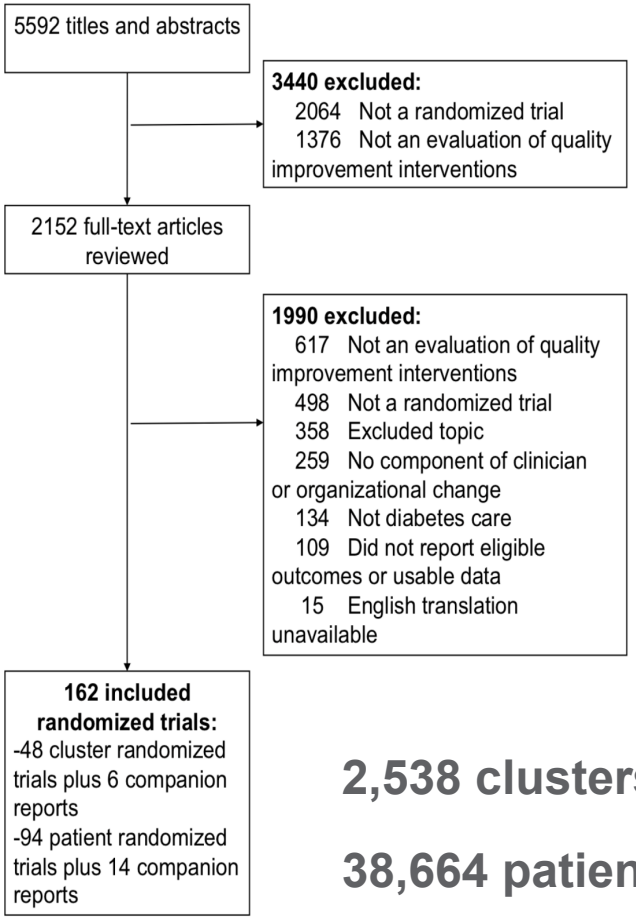
- Audit and feedback
- Case management
- Team changes (provider role changes)
- Electronic patient registry
- Clinician education
- Clinician reminders
- Facilitated relay of information to clinicians
- Patient education*
- Promotion of self-management*
- Patient reminder systems
- Continuous quality improvement
- Financial incentives

(* Only included if part of a multifaceted intervention including professional targeted interventions)

# INCLUSION CRITERIA – OUTCOMES OF INTEREST

| Domain | Process measure | Intermediate outcome |
|---|---|---|
| Glycemic control | HbA1c measurement | HbA1c levels |
| Vascular risk factor management | Patients on ASA, statins, anti hypertensives | Lipid levels<br>BP |
| Retinopathy screening | Patients screened | |
| Foot screening | Patients screened | |
| Renal function | Patients monitored | |
| Smoking cessation | Patients on NRT | Patients successfully quitting |

# RESULTS: STUDY FLOW

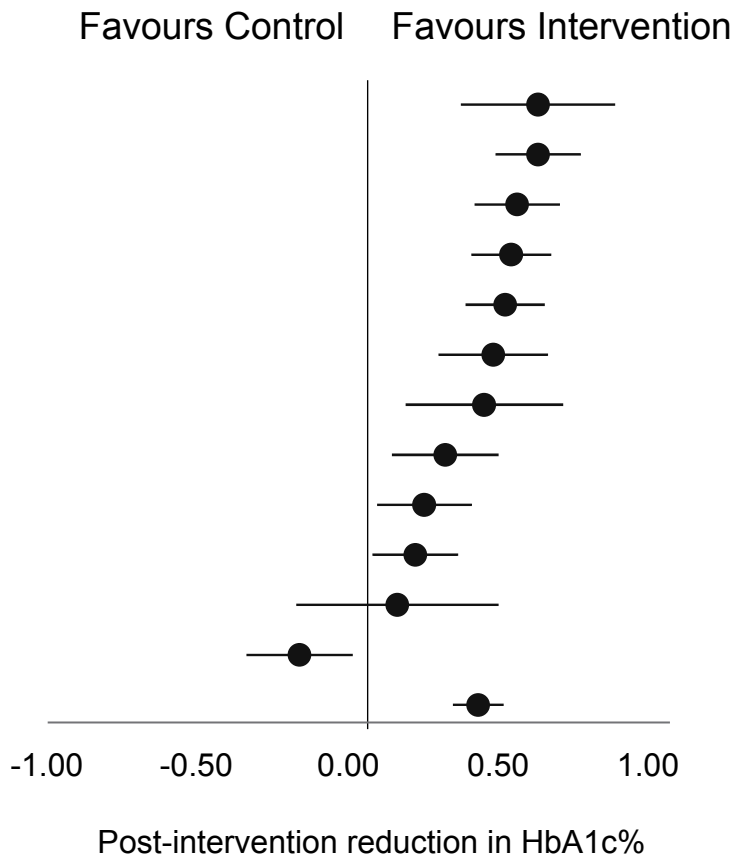



**2,538 clusters and 84,865 patients**

**38,664 patients**

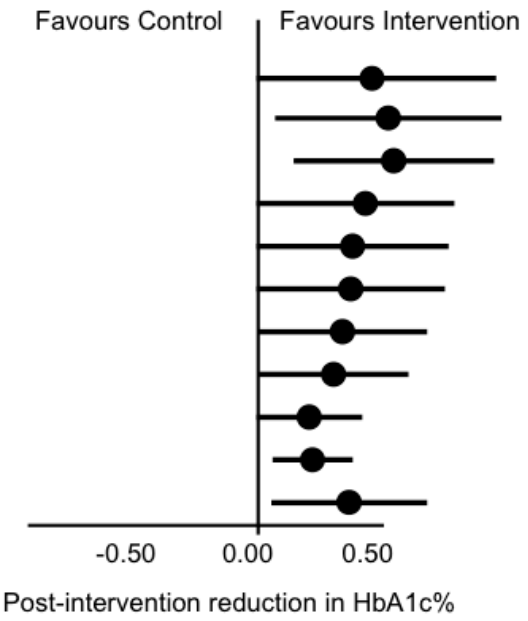
# RESULTS: HBA1C META-ANALYSIS

| Quality Improvement Strategy | # RCTs | MD | 95% CI | |
|---|---|---|---|---|
| Promotion of Self-management | 60 | 0.57 | 0.31 | 0.83 |
| Team Changes | 48 | 0.57 | 0.42 | 0.71 |
| Case Management | 57 | 0.50 | 0.36 | 0.65 |
| Patient Education | 52 | 0.48 | 0.34 | 0.61 |
| Facilitated Relay | 32 | 0.46 | 0.33 | 0.60 |
| Electronic Patient Register | 27 | 0.42 | 0.24 | 0.61 |
| Patient Reminders | 21 | 0.39 | 0.12 | 0.65 |
| Audit and Feedback | 8 | 0.26 | 0.08 | 0.44 |
| Clinician Education | 15 | 0.19 | 0.03 | 0.35 |
| Clincian Reminders | 18 | 0.16 | 0.02 | 0.31 |
| Financial Incentives | 1 | 0.10 | -0.24 | 0.44 |
| Continuous Quality Improvements | 2 | -0.23 | -0.41 | -0.05 |
| **All Interventions** | **120** | **0.37** | **0.28** | **0.45** |



# RESULTS: HBA1C META-REGRESSION

| Quality Improvement Strategy | # RCTs | MD | 95% CI |
|---|---|---|---|
| Team Changes | 47 | 0.52 | 0.00, 1.04 |
| Facilitated Relay | 31 | 0.49 | 0.02, 0.96 |
| Promotion of Self-management | 57 | 0.45 | 0.04, 0.87 |
| Case Management | 52 | 0.41 | 0.00, 0.82 |
| Patient Education | 52 | 0.40 | 0.00, 0.80 |
| Electronic Patient Register | 28 | 0.39 | 0.00, 0.78 |
| Clinician Reminders | 16 | 0.35 | 0.00, 0.70 |
| Patient Reminders | 20 | 0.31 | 0.00, 0.62 |
| Audit and Feedback | 9 | 0.22 | 0.00, 0.44 |
| Clinician Education | 12 | 0.16 | 0.01, 0.33 |
| **All Interventions** | **117** | **0.33** | **0.01, 0.65** |



# META-ANALYSIS STRATIFIED BY BASELINE CONTROL

| | All studies | | | Glycated haemoglobin >8·0% | | | Glycated haemoglobin ≤8·0% | | |
|---|---|---|---|---|---|---|---|---|---|
| | Rank | Number of trials | Mean difference (95% CI) | Rank | Number of trials | Mean difference (95% CI) | Rank | Number of trials | Mean difference (95% CI) |
| Promotion of self management | 1 | 60 | −0·57 (−0·83 to −0·31) | 4 | 37 | −0·56 (−0·70 to −0·42) | 6 | 23 | −0·29 (−0·47 to −0·12) |
| Team changes | 2 | 47 | −0·57 (−0·71 to −0·42) | 1 | 31 | −0·62 (−0·79 to −0·46) | 2 | 17 | −0·46 (−0·71 to −0·21) |
| Case management | 3 | 57 | −0·50 (−0·65 to −0·36) | 2 | 37 | −0·61 (−0·80 to −0·42) | 7 | 17 | −0·25 (−0·44 to −0·07) |
| Patient education | 4 | 52 | −0·48 (−0·61 to −0·34) | 3 | 39 | −0·59 (−0·74 to −0·43) | 5 | 13 | −0·39 (−0·71 to −0·06) |
| Facilitated relay | 5 | 32 | −0·46 (−0·60 to −0·33) | 6 | 19 | −0·42 (−0·56 to −0·29) | 1 | 13 | −0·54 (−0·79 to −0·30) |
| Electronic patient register | 6 | 27 | −0·42 (−0·61 to −0·24) | 5 | 9 | −0·47 (−0·79 to −0·14) | 4 | 18 | −0·41 (−0·60 to −0·22) |
| Patient reminders | 7 | 21 | −0·39 (−0·65 to −0·12) | 8 | 10 | −0·39 (−0·77 to −0·00) | 3 | 11 | −0·42 (−0·70 to −0·15) |
| Audit and feedback | 8 | 8 | −0·26 (−0·44 to −0·08) | 7 | 5 | −0·40 (−0·77 to −0·03) | 9 | 3 | −0·06 (−0·16 to 0·06) |
| Clinician education | 9 | 15 | −0·19 (−0·35 to 0·03) | 10 | 10 | −0·33 (−0·57 to −0·10) | 10 | 5 | 0·03 (−0·18 to 0·25) |
| Clinician reminders | 10 | 18 | −0·16 (−0·31 to −0·02) | 9 | 9 | −0·35 (−0·56 to −0·13) | 8 | 9 | −0·06 (−0·15 to 0·04) |
| All interventions | | 120 | −0·37 (−0·45 to −0·28) | | 70 | −0·46 (−0·58 to −0·35) | | 46 | −0·23 (−0·34 to −0·13) |

***Table 4:*** **Ranking of quality improvement strategies across glycated haemoglobin primary and secondary meta-analyses**

# DISCUSSION – GLYCEMIC CONTROL

- QI interventions led to 0.33% reduction in HbA1c, larger effects with poorer baseline control
- All categories of QI interventions appeared effective but larger effects observed for
  - Team changes
  - Facilitated relay
  - Promotion of self management
  - Case management
  - Patient education
  - Electronic patient register
  - Patient reminders
- Difficult to disentangle optimal combination of interventions

# A CASE STUDY IN COMPLEXITY



## Effectiveness of quality improvement strategies on the management of diabetes: a systematic review and meta-analysis

Andrea C Tricco, Noah M Ivers, Jeremy M Grimshaw, David Moher, Lucy Turner, James Galipeau, Ilana Halperin, Brigitte Vachon, Tim Ramsay, Braden Manns, Marcello Tonelli, Kaveh Shojania

**Summary**

**Background** The effectiveness of quality improvement (QI) strategies on diabetes care remains unclear. We aimed to assess the effects of QI strategies on glycated haemoglobin ($HbA_{1c}$), vascular risk management, microvascular complication monitoring, and smoking cessation in patients with diabetes.

**Methods** We identified studies through Medline, the Cochrane Effective Practice and Organisation of Care database (from inception to July 2010), and references of included randomised clinical trials. We included trials assessing 11 predefined QI strategies or financial incentives targeting health systems, health-care professionals, or patients to improve management of adult outpatients with diabetes. Two reviewers independently abstracted data and appraised risk of bias.

**Findings** We reviewed 48 cluster randomised controlled trials, including 2538 clusters and 84 865 patients, and 94 patient randomised controlled trials, including 38 664 patients. In random effects meta-analysis, the QI strategies reduced $HbA_{1c}$ by a mean difference of 0·37% (95% CI 0·28–0·45; 120 trials), LDL cholesterol by 0·10 mmol/L (0·05–0.14; 47 trials), systolic blood pressure by 3·13 mm Hg (2·19–4·06, 65 trials), and diastolic blood pressure by 1·55 mm Hg (0·95–2·15, 61 trials) versus usual care. We noted larger effects when baseline concentrations were greater than 8·0% for $HbA_{1c}$, 2·59 mmol/L for LDL cholesterol, and 80 mm Hg for diastolic and 140 mm Hg for systolic blood pressure. The effectiveness of QI strategies varied depending on baseline $HbA_{1c}$ control. QI strategies increased the likelihood that patients received aspirin (11 trials; relative risk [RR] 1·33, 95% CI 1·21–1·45), antihypertensive drugs (ten trials; RR 1·17, 1·01–1·37), and screening for retinopathy (23 trials; RR 1·22, 1·13–1·32), renal function (14 trials; RR 128, 1·13–1·44), and foot abnormalities (22 trials; RR 1·27, 1·16–1·39). However, statin use (ten trials; RR 1·12, 0·99–1·28), hypertension control (18 trials; RR 1·01, 0·96–1·07), and smoking cessation (13 trials; RR 1·13, 0·99–1·29) were not significantly increased.

Published Online
June 9, 2012
DOI:10.1016/S0140-6736(12)60480-2

See Online/Comment
DOI:10.1016/S0140-6736(12)60637-0

Li Ka Shing Knowledge Institute of St Michael's Hospital, Toronto, ON, Canada (A C Tricco PhD); Women's College Hospital and Department of Family and Community Medicine (N M Ivers MD) and Division of Endocrinology, Department of Medicine (I Halperin MD), University of Toronto, Toronto, ON, Canada; Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, ON, Canada (Prof J M Grimshaw PhD, D Moher PhD, L Turner M Sc, J Galipeau PhD, B Vachon PhD, T Ramsay PhD); Department of Medicine (Prof J M Grimshaw)

# A CASE STUDY IN COMPLEXITY

## Challenges

- Firstly, programs are usually complex, involving multifaceted approaches that may contain a mix of effective and ineffective (or even harmful) component KT/QI interventions that may (or may not) be interdependent and that may (or may not) interact synergistically (or antagonistically).
- Identifying the effective (and ineffective) components within programs is necessary to ensure sustainability and to facilitate replication.

# A CASE STUDY IN COMPLEXITY

## Challenges

- Secondly, the effects of complex KT/QI programs are likely modified by poorly recognised and ill-defined contextual factors making judgements about the applicability of the effects of interventions in different contexts more challenging.
- Traditional meta-analyses estimate the ‘average’ effect across studies, ignoring effect modification by contextual factors, which is of vital importance to health system decision makers trying to assess the applicability of the results of a systematic review to their context.

# A CASE STUDY IN COMPLEXITY

## Challenges

- Thirdly, the mechanisms of action of KT/QI programs (and component interventions) are poorly understood, resulting in lack of consensus about terminology
- Authors of syntheses often develop pragmatic (somewhat arbitrary) definitions of programs and interventions of interest.
- However that misclassification of interventions may lead to “noise” in a meta-analysis by artificially increasing the observed heterogeneity of comparisons by including studies testing different programs and/or reducing precision by artificially excluding studies that evaluate the same program from a comparison.

# A CASE STUDY IN COMPLEXITY

## Challenges

- Fourthly, these issues are exacerbated by poor reporting of interventions and contextual factors in primary studies.

# A CASE STUDY IN COMPLEXITY

- As a result of these four key challenges, systematic review authors expect substantial heterogeneity within syntheses of KT/QI programs.
- In such cases estimating the 'average' effect of interventions is often inadequate; where we are interested in understanding the sources of complexity and how they modify the effects of the intervention of interest
- **Key question: Can we do better?**

# SEEING THE FOREST AND THE TREES

Ivers *et al. Systematic Reviews* 2014, **3**:88
http://www.systematicreviewsjournal.com/content/3/1/88

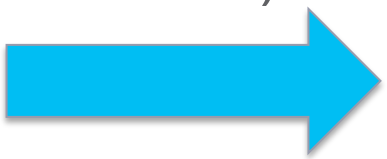

PROTOCOL Open Access

## Seeing the forests *and* the trees—innovative approaches to exploring heterogeneity in systematic reviews of complex interventions to enhance health system decision-making: a protocol

Noah Ivers[1], Andrea C Tricco[2], Thomas A Trikalinos[3], Issa J Dahabreh[3], Kristin J Danko[4], David Moher[4,5], Sharon E Straus[2], John N Lavis[6], Catherine H Yu[2], Kaveh Shojania[7], Braden Manns[8,9], Marcello Tonelli[10], Timothy Ramsay[4,5], Alun Edwards[9], Peter Sargious[9], Alison Paprica[11], Michael Hillmer[11,12] and Jeremy M Grimshaw[4,5*]

# SEEING THE FOREST AND THE TREES

- Challenge 1 (better specification of effects of components) and challenge 2 (better specification of effect modifiers)



Synthesis with hierarchical regression

- Challenge 4 (poor reporting)

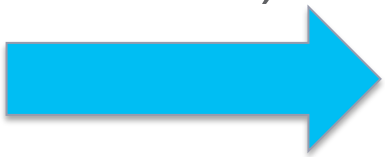
Author survey

- Challenge 3 (intervention description)

Author survey, alternative taxonomies

# SEEING THE FOREST AND THE TREES

- Challenge 1 (better specification of effects of components) and challenge 2 (better specification of effect modifiers)



Synthesis with
hierarchical regression

# STANDARD META-ANALYSIS METHODS LIMITATIONS

- Given K components of interest, $2^K$ possible interventions
  - K=10 → ~1000 interventions
  - K=12 → ~4000 interventions
- Standard meta-analysis approaches pose three challenges to learning about such vast number of combinations

## Challenge #1: Data sparsity

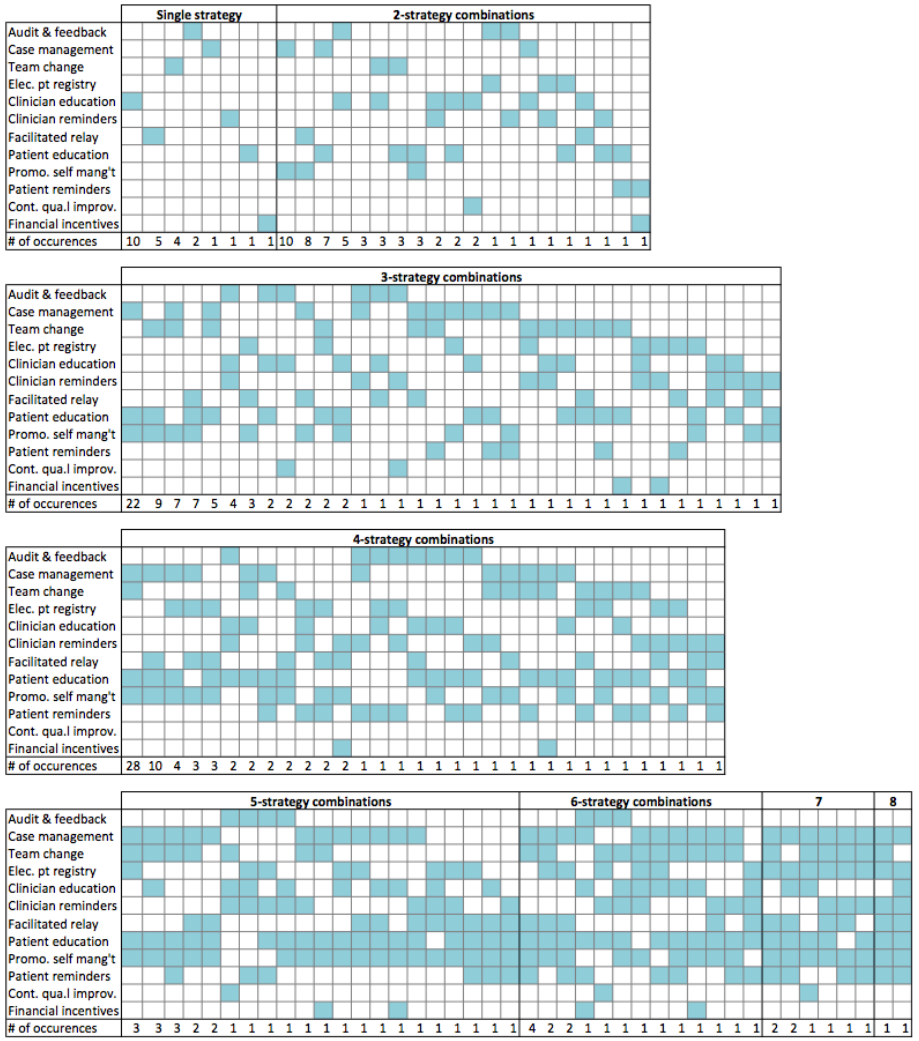
- Standard meta-analysis approaches learn across studies that have 'similar' interventions and comparator → rare

## Challenge #2: Confounding

- Several applied works focus on the presence/absence of components → ignore co-occurring components

## Challenge #3: Information loss

- To support pairwise synthesis structure, often data reductions (multi-arm → 2 arm; all components → difference of components)



# STANDARD META-ANALYSIS METHODS

- Control arm effects are “removed” by differencing
- Sampling variances are considered known
- Unexplained variability of the treatment effect is accounted for (between-study variance component)

$$d_i = y_{2,i} - y_{1,i}$$
$$d_i \sim N(\delta_i, SE_i^2)$$
$$\delta_i \sim N(\Delta, \tau^2)$$

# STANDARD META-ANALYSIS METHODS

- One row per study
- Two arms included (most intensive vs least intensive in multi arm trials)
- Differencing approach
  - Consider trial a+b+c vs c
  - In standard model, this is considered as a trial a+b vs control

# SYNTHESIS WITH HIERARCHICAL META-REGRESSION

- Instead we impose some structure by modeling each component separately. We do this with a hierarchical meta-regression analysis
- Typically two parts:
  - Observational part

$$Y_{ij} \sim N(\mu_{ij}, \sigma^2{}_{ij}), \quad i = 1,\ldots,N_{studies}; j = 1,\ldots,N_{arms};$$

  - Structural part

$$\mu_{ij} = \beta_{0i} + \sum_{k=1}^{K} \beta_{ki} X_{kij}$$

$$\beta_{0i} \sim N(\tilde{\beta}_0, \tilde{\tau}_0{}^2)$$

$$\beta_{ki} \sim N(\tilde{\beta}_k, \tilde{\tau}_k{}^2), \quad k = 1,\ldots\mathrm{K}$$

# SYNTHESIS WITH HIERARCHICAL META-REGRESSION

- One row per study arm (linked to study)
- All arms included
- All intervention (and control) components considered

# SYNTHESIS WITH HIERARCHICAL META-REGRESSION

- Treating the problem as a meta-regression allows:
  - Inclusion of all relevant data (arms, components)
  - Estimation of individual component effects
- Models can be extended to assess:
  - Interactions between components
  - Effect modification by population, setting, and contextual factors
- Convenient structure to account for data limitations in a principled way (e.g., missing data from cluster trials)

# CASE STUDY APPLIED TO LANCET DATASET

- Using data from HbA1c outcome with complete baseline and follow-up data (n=111 studies, 241 arms)
- Implemented a series of hierarchical models to isolate the effects of the QI strategies and compared to standard approach
  - Analysis 1: standard meta-analysis, pairwise data
  - Analysis 2: hierarchical meta-regression, pairwise data
  - Analysis 3: hierarchical meta-regression, complete data
- Ranking
- Model extensions

# CASE STUDY APPLIED TO LANCET DATASET

| QI component | ANALYSIS 1 Standard model, pairwise data | ANALYSIS 2 Hierarchical model, pairwise data | ANALYSIS 3 Hierarchical model, complete data |
|---|---|---|---|
| | n=111 studies; 41,475 patients | | n=241 arms; ` 45,629 patients |
| CM | -0.42 (-0.55, -0.29) | 0.03 (-0.14, 0.17) | 0.04 (-0.12, 0.17) |
| TC | -0.53 (-0.69, -0.37) | -0.38 (-0.55, -0.19) | -0.37 (-0.53, -0.19) |
| EPR | -0.37 (-0.53, -0.22) | -0.17 (-0.41, 0.10) | -0.16 (-0.45, 0.06) |
| CE | -0.23 (-0.37, -0.09) | -0.20 (-0.51, 0.04) | -0.19 (-0.48, 0.06) |
| FR | -0.40 (-0.54, -0.26) | -0.23 (-0.44, -0.06) | -0.22 (-0.44, -0.02) |
| PE | -0.44 (-0.56, -0.32) | -0.08 (-0.24, 0.16) | -0.07 (-0.25, 0.11) |
| PSM | -0.41 (-0.52, -0.30) | -0.20 (-0.38, -0.01) | -0.19 (-0.38, -0.03) |
| PR | -0.33 (-0.53, -0.14) | 0.05 (-0.23, 0.30) | -0.01 (-0.24, 0.19) |
| Other | -0.19 (-0.31, -0.06) | 0.00 (-0.26, 0.26) | 0.00 (-0.22, 0.17) |

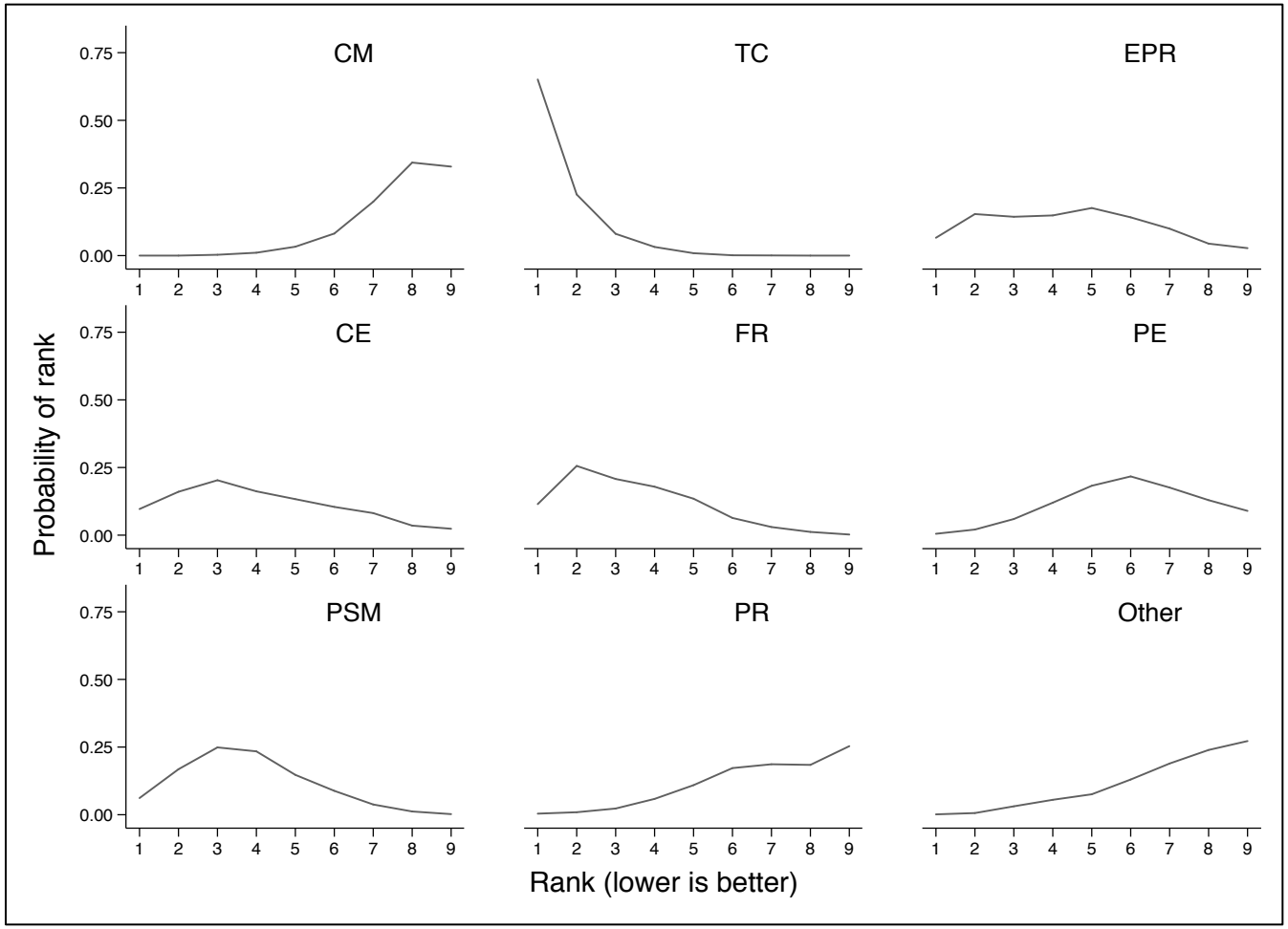
# CASE STUDY APPLIED TO LANCET DATASET

| QI component | ANALYSIS 1 Standard model, pairwise data | ANALYSIS 2 Hierarchical model, pairwise data | ANALYSIS 3 Hierarchical model, complete data |
|---|---|---|---|
| | n=111 studies; 41,475 patients | | n=241 arms; ` 45,629 patients |
| CM | -0.42 (-0.55, -0.29) | 0.03 (-0.14, 0.17) | 0.04 (-0.12, 0.17) |
| TC | -0.53 (-0.69, -0.37) | -0.38 (-0.55, -0.19) | -0.37 (-0.53, -0.19) |
| EPR | -0.37 (-0.53, -0.22) | -0.17 (-0.41, 0.10) | -0.16 (-0.45, 0.06) |
| CE | -0.23 (-0.37, -0.09) | -0.20 (-0.51, 0.04) | -0.19 (-0.48, 0.06) |
| FR | -0.40 (-0.54, -0.26) | -0.23 (-0.44, -0.06) | -0.22 (-0.44, -0.02) |
| PE | -0.44 (-0.56, -0.32) | -0.08 (-0.24, 0.16) | -0.07 (-0.25, 0.11) |
| PSM | | | |
| PR | | | |
| Other | | | |

- Fewer effective components
- Effects are smaller due to isolation of individual components
- Rankings are altered
- Estimates are more precise with more data

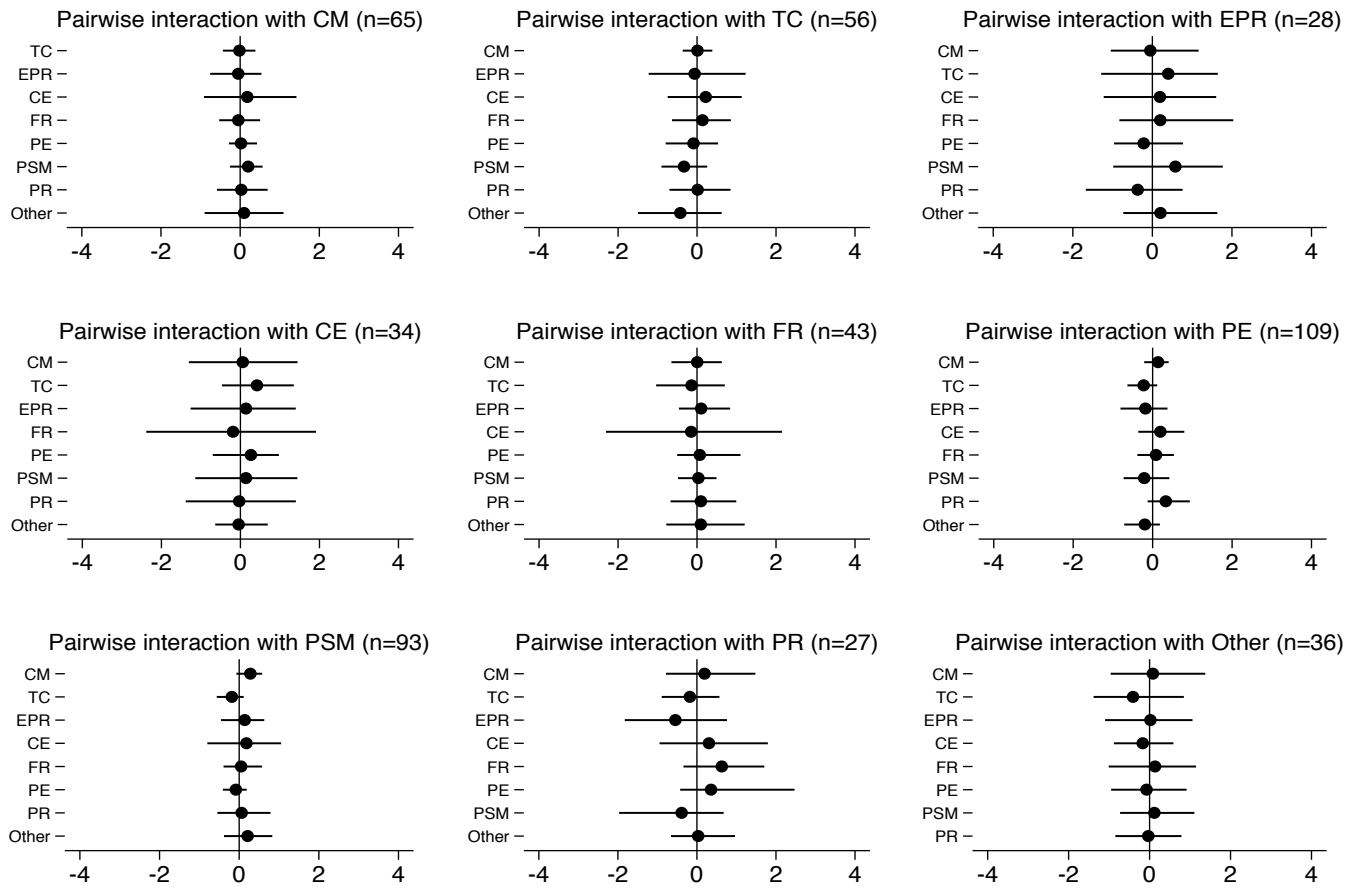
# CASE STUDY APPLIED TO LANCET DATASET

Ranking



# CASE STUDY APPLIED TO LANCET DATASET

## Pairwise interactions



# CASE STUDY APPLIED TO LANCET DATASET

Effect modification – Baseline risk (treated as a binary variable)

| QI | Controlled | Uncontrolled | Difference | Interpretation |
|---|---|---|---|---|
| CM | 0.17 (-0.05, 0.41) | -0.20 | -0.37 (-0.72, 0.04) | More effective in uncontrolled |
| TC | -0.24 (-0.56, 0.05) | -0.34 | -0.10 (-0.48, 0.37) | More effective in uncontrolled |
| EPR | -0.11 (-0.44, 0.24) | 0.02 | 0.13 (-0.64, 0.91) | More effective in controlled |
| CE | -0.14 (-0.41, 0.16) | -0.12 | 0.02 (-0.68, 0.78) | Almost no difference |
| FR | -0.23 (-0.68, 0.10) | -0.20 | 0.03 (-0.38, 0.57) | Almost no difference |
| PE | 0.01 (-0.25, 0.30) | -0.07 | -0.08 (-0.50, 0.36) | Almost no difference |
| PSM | -0.31 (-0.61, 0.07) | -0.19 | 0.12 (-0.48, 0.80) | More effective in controlled |
| PR | -0.20 (-0.64, 0.21) | 0.13 | 0.33 (-0.40, 0.96) | More effective in controlled |
| Other | 0.05 (-0.24, 0.24) | -0.23 | -0.28 (-0.96, 0.51) | No interpretation |

# SYNTHESIS WITH HIERARCHICAL META-REGRESSION

**Benefits**

- Models the statistical distribution of data in each study arm
- Can use of all data from all studies
- Allows for identification of average component effects
- Allows for between-study heterogeneity
- Allows modeling of effect modifiers
- Can be extended to incorporate approaches that impute missing data
- Can predict effects of yet unrealized combinations

All of these are an augmentation over traditional approach

# SYNTHESIS WITH HIERARCHICAL META-REGRESSION

## Limitations

- Instead of nearly 4,000 main effects, is uses only 12, assuming interactions are negligible
- No free lunch. All results are conditional on the model
  - The organization into components is extra-evidentiary (e.g., 93 components with other framework)
- Inherits all the challenges of traditional meta-analysis
  - Publication bias
  - Reporting bias
  - Missing information

# SUMMARY

- Significant body of evidence about QI strategies
- Traditional approaches to MA and MR provide limited information insufficient to needs of decision makers
- Opportunities to maximise learning from existing body of evidence (before planning new trials):
  - Alternative classification approaches
  - Enriching dataset by author contact
  - Novel analytical approaches

# CONTACT DETAILS


- Jeremy Grimshaw

  jgrimshaw@ohri.ca

  @GrimshawJeremy

- Kristin Danko

  kdanko@ohri.ca

- Centre for Implementation Research

  @TOH_CIR

  http://www.ohri.ca/cir/