A Snapshot of Rapid Reviews at
the Ottawa Hospital Research
Institute (OHRI)

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OTTAWA METHODS CENTRE

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Seoul, Korea
OMC was launched in 2006 to enable and enhance research at OHRI, Ottawa Hospital, uOttawa & beyond

OMC is based within the Clinical Epidemiology Program (CEP) based at OHRI

Provides an umbrella of services to support clinical researchers at all stages of a research project from inception to dissemination

Comprised of 9 Scientists; 40 Research Staff; 6 affiliated OHRI Scientists

Nine key service areas
Ottawa
Methods
Centre:
9 Service
Areas

- Research Design & Methodology
- Data Management
- Statistical Consultation
- Knowledge Syntheses
- Health Economics
- Health Technology Assessment
- Big Data Analytics
- Journalology
- KT: Evidence Implementation
Knowledge Synthesis Group

• Academic group engaged exclusively in knowledge syntheses and related methods research (n=25)

• Home to several initiatives:
  • Reporting guideline initiatives for protocols, trials and systematic reviews (e.g., SPIRIT, CONSORT, PRISMA, PRISMA-P, PRISMA-NMA)
  • Network Meta-analysis Collaborating Centre for CIHR Drug Safety and Evaluation Network (DSEN)
  • Evidence-Synthesis Review Centre, Canadian Task Force on Preventive Health Care (new)
  • Cochrane Rapid Reviews Methods Group (new)
  • AHRQ-designated EPC (2002-2012)

• A cornerstone of our work is devoted to developing various methodologies related to the conduct of SRs – including RRs
For the last 7 years, our group has explored the:
- methods
- execution; and
- teaching of rapid reviews across various healthcare topics

Started in 2009 with a local partnership with the Champlain Local Health Integrated Network (LHIN), which is 1 of 14 LHINs in the province of Ontario responsible for planning, coordinating and funding health services in the region

Aided by funding through a 2-year CIHR Knowledge to Action (KTA) grant
Our RR Story

- LHIN wanted evidence-based answers to help direct policy, implementation, and practice decisions
- Our team set up a ‘knowledge intelligence service’
- Resulted in our team developing a series of rapid evidence summaries (n=18) each produced in 4-6 weeks in response questions posed by the LHIN
- Funding has since ended
Initially lost at sea....

- At the outset -- very uncomfortable straying off course from traditional SR methods
- Limited in terms of published literature on ‘rapid reviews’ to guide our process.
- What did come across confirmed ‘no’ universally accepted definition of RR
- Variance in nomenclature, methods, timeframes, formats etc.
Essentially, borrowed from widely accepted SR standards (Cochrane and non-Cochrane methods)

Made certain concessions compared to a traditional SR to accommodate an expedited turnaround time

Out of which emerged a staged RR process developed iteratively (trial and error) across the ‘Evidence Summaries’ conducted over a 24-month span
Based on this grant, we published our RR approach in 2012 (Khangura et al., Systematic Reviews Journal 2012)

Key turning point for us in continuing our RR involvement

We continue to refine and expand upon our RR methods (stay tuned)
General Rapid Review Stages

Stage 1. Needs Assessment  (Request Intake)

Stage 2. Topic Refinement  (PICO Framework)

Stage 3. Protocol Development

Stage 4. Literature Search

Stage 5. Screening & Study Selection

Stage 6. Data Extraction  (includes quality assessment/ ROB)

Stage 7. Synthesis  (Narrative &/or Quantitative)

Stage 8. Report Production

Stage 9. Follow up with clients (end-users)
Key Audiences:

- Policymakers - people who make important decisions that impact healthcare that affects everyone
- Use of RR by decision-makers is happening within various sectors related to healthcare
- Important to incorporate decision-maker needs into the RR process
- Ensures a tailored product, ‘fit for purpose’
Involving Decision-makers

Stage 1. Needs Assessment (Request Intake)

Stage 2. Topic Refinement (PICO Framework)

Stage 3. Protocol Development

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Stage 9. Follow up with clients (end-users)

- Key periods of engagement
- Input sought but to a lesser degree
• Education & training session with client upfront so there is a clear understanding of what our process is and to manage expectations & limitations of RRs (1-2 hr session)

• Build in an internal assessment as to suitability of RR approach for each question under consideration
  • What is the reason for the request, type of decision-maker, and intended audience? Why is the RR so important?

• Condensed timeframe (4 to 16 weeks);

• During ‘topic refinement’ development of the question (using PICOTS framework) focused on manageability as first priority (due to time/volume) much more so than for SRs

• A brief protocol (2-4 pages) is developed
Highlights of how we approach RRs

Protocol Development (con’t), Searching

- Open to tackling different types of research questions
  - harms and benefits of treatments, health service configurations; accuracy of diagnostic tests; experiences of patients undergoing treatments; prevalence of conditions etc.

- RRs various types of interventions
  (pharmacological, non-pharmacological, behavioural, health systems etc.)

- Searching is limited:
  - key databases only
  - usually staged with a focus on SRs, then if needed primary studies

- Common restrictions:
  - by language, years, publication status, region
  - Grey literature may or may not be searched (topic dependent)

- Aim to peer review (PRESS) searches if feasible

- Point of possible post-hoc adjustments
Screening and selection of studies (done in duplicate)

- Emphasis on high quality SRs
- Then cautious inclusion of primary studies (e.g., high quality RCTS, non-RCTs, and/or observational studies)
- Screening staged by study design to capture higher level evidence first using search filters (allows us to put in stop rules if higher level of evidence exist)
- Point of possible post-hoc adjustments

Data extraction (1 reviewer + 1 verification)

- Aim to keep to a minimum (only most relevant information as related to study characteristics, interventions, populations, and outcomes of interest) vs. comprehensive extraction done for full SRs across all
- Once our pool of included studies is clear, only then do we pull out effect estimates
- Quality assessment/risk of bias – using validated tools
Highlights of how we approach RRs

Synthesis

- Designed to provide a sense of the volume and direction of the available evidence
  - at times that is all we can do due to time or the nature of the evidence
- Present summary of search findings (include PRISMA flow diagram)
- First, use a simple classification scheme by outcome to get an overview of results
  - Conclusive (favours treatment);
  - Conclusive (favours control); or
  - Inconclusive with counts (n studies) provided
  - No available evidence
- Followed by a formal narrative synthesis
- Formal quantitative synthesis (e.g., meta-analysis) not usual practice but may be considered if time/funds permit
- GRADE (takes time); not always feasible
Highlights of how we approach RRs

- Acutely aware of the reader who may not read past the first page
- All have taken on an ‘executive summary’ style which is very brief with key messages upfront
- Use shorter sentences, more reliance on tables, bullet points, call out boxes, and compelling images/graphics – less reliance for lots of text
Rapid Review Format

Primary research question as the title

Brief context, objectives

Informative sidebar outlines the program; PICOTS framework; and our group as the producer

“Key messages” section aims to summarize overall findings

Reference to the disclaimer

Effects of Performing Complex Pediatric Intracavitary (IC) Surgical Procedures in Specialized versus Non-specialized Centers in High Risk Children: Cochrane Response Rapid Review

Context

This review is being conducted as part of Cochrane Innovations Rapid Response program. The Children’s Hospital Association (CHA) has undertaken an initiative to develop a system of care for infants, children, adolescents and their families with surgical needs. The aim is to optimize outcomes by matching patient needs prospectively defined with appropriate resources, and by improving the coordination of care for surgical patients within a given region. As such, the CHA has requested a rapid review to assist in informing pediatric surgical initiatives. Findings from this exercise will inform the U.S. Task Force for Children’s Surgical Care discussions.

Objectives

CHA is interested in development of a rapid review that addresses the effects of performing certain pediatric surgical procedures in specialized centers. The population of interest would be children who are at high risk because of their age or co-morbidities. primary condition requiring surgery, or because the procedure they require is rarely performed or highly complex.

Key Messages

- From this rapid review of observational studies, the identified evidence signals that specialization compared with non-specialization may be generally effective for reducing mortality after pediatric cardiac surgery.
- For other outcomes and surgeries findings are ambiguous because: i. Results were inconsistent across studies (i.e., a mix of positive, negative, or non-significant findings); or ii. There was lack of clarity as to whether the results favoured specialization, non-specialization, or showed equivalence of surgical services (i.e., the majority of studies were statistically non-significant).
- Given the potential shortcomings of the rapid review process, and the limitations of analyses from observational studies, conducting a full systematic review in order to confirm our findings may be warranted.

Policy Implications

- Given the findings with cardiac surgery, policy decision-makers need to determine whether to generalize these findings to other complex, high risk (non-cardiac) conditions in the pediatric population.
- Further investigation may be needed to determine if other ‘lower acuity’ conditions (e.g., appendicitis) require surgical specialty care.

Disclaimer: While every effort has been made to reflect all scientific research available, this document may not fully do so. Please refer to the full disclaimer on pg. 12 for more information.
**Specifics of PICOTS elements (in detail)**

**Population:** We included children aged 0-18 yrs considered to be high risk meeting the following criteria: i) requiring surgery as a neonate (newborn infant <28 days of age) or infant up to 1 year (based on age alone); ii) pre-existing or co-morbid condition(s) that would put them at increased risk for adverse surgical outcome; ii) undergoing intracavitary (IC) procedures that are rarely performed and/or other specific IC surgeries of a complex nature.

Surgical procedures were limited to procedures of the abdomen, pelvis, chest (thoracic), and intracavitary surgeries (non-traumatic), and could be either open, and/or minimally invasive (i.e., laparoscopy). We excluded ‘trauma’ related procedures, common surgeries including appendectomies, hernias, and other soft tissue-related surgeries; tubing and scoping procedures (e.g. chest tube, endoscopy).

**Intervention/Exposure:** Undergoing surgery in a specialized center, or volume-based regionalization programs as reported and where feasible categorized according to the US Task Force for Children's Surgical Care "Optimal Resources for Children's Surgical Care in the United States." Comparators: Surgeries performed in a non-specialized center, or other specialized centers which are different from centers in the intervention group. As per the classification of centers, 'basic children's surgical centers' are considered 'non-specialized.'

**Outcomes:** The following outcomes were evaluated: mortality, length of stay (LOS), postoperative morbidity (i.e., aggregate or surgical site infection (SSI) or cardiac or respiratory events), cost (resource utilization/economic impact), patient/family experience (i.e., patient travel burden, other reported measures of patient/family experience).

**Timing:** na

**Setting:** Was restricted to studies conducted in Canada, France, Germany, United States, Japan, Italy, Russia, United Kingdom, Austria, Belgium, Denmark, Finland, Greece, Iceland, Ireland, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, Australia, and New Zealand.

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**Key Question(s)**

In children considered high-risk, do outcomes vary when performing intracavitary procedures in specialized centers versus non-specialized centers?

**Snapshot of the Evidence**

- A total of 8,291 citations were screened, of which 62 were found to be of relevance (Figure 1).
- The primary evidence base is comprised of 62 cohorts. Most were retrospective in design.
- Most studies were from the United States (n=44) followed by Canada, the United Kingdom, and Japan each with 4 studies. In addition, studies were identified from The Netherlands (n=2), the US/Canada combined (n=2) with single studies identified from Australia, Norway, Finland, France, and Germany. Two studies were conducted across multiple European countries.
- Although all studies were published after 2000, study periods ranged from 1991 to 2010 with sample sizes ranging from 64 to 55,164 (operations). It is noted that these studies did not report study period while six studies did not report sample sizes.
- Most studies were related to cardiac surgical procedures (n=25; 38%, majority were congenital heart surgeries), general surgeries (n=21; 31%), and neurosurgical procedures (n=7; 10%) (Figure 2).
- Five key types of exposure comparisons were identified (i.e., hospital volume; surgeon volume; children’s versus general hospitals; comprehensive pediatric versus general hospitals; and specialized pediatric surgeons versus general surgeons) with several studies reporting on multiple comparisons (Figure 3).
- The risk of bias scores were generally between 7-9 (higher score indicates lower risk of bias). Heterogeneity in effect estimates by risk of bias could not be assessed given the similarities in scores.
- See Appendix A tables for details about individual studies by outcome.

**Abbreviations**

- CHA = Children’s Hospital Association
- CI = confidence interval
- HV = high volume
- IC = intracavitary
- LOS = length of stay
- MD = mean difference
- NS = non-significant
- RCT = randomized controlled trial
- RR = relative risk
- SSI = surgical site infection
  +ve = positive
  -ve = negative
PRISMA Flow diagram (anchors the report)
Aim is to limit text

RESULTS

- Utilize bullet points, tables, boxes to highlight messages

ANALYSIS

For each outcome, we initially examined the exposure categories (i.e., hospital volume, comprehensive centre, etc) collectively as proxies of hospital specialization across all surgical domains. In studies that presented more than one analysis, we avoided double-counting of subjects by eliminating subgroup analyses that overlapped with the primary study population and by selecting one exposure to analyze, according to the following hierarchy: (1) Comprehensive, (2) Children hospital, (3) Hospital volume; and (4) Surgeon volume. We narratively synthesized the data by tabulating the number of studies that found either positive results in favour of exposure (designated as +ve), positive results in favour of comparator (designated as -ve), or statistically non-significant results (designated as NS).

We proceeded with subsequent analyses according to a framework developed by the Cochrane Handbook for Systematic Reviews of Interventions. 19 (See Appendix 8)

- If 0% of studies favoured exposure, we indicated that specialization has no effect.
- If 1-33% of studies favoured exposure, we indicated that no conclusion favoring the exposure could be made. We further analyzed the data by cardiac vs. other surgical categories.
- If 54-66% of studies favoured exposure, we indicated that the effect of specialization was unclear. We then conducted subgroup analyses by individual exposure categories. We also analyzed data by cardiac vs. other surgical categories.
- If 57% of studies favoured exposure, we indicated that specialization is generally effective. We investigated if studies accounted for within-hospital clustering of patient data as one indicator of confidence in the results. We also analyzed data by cardiac vs. other surgical categories.

SUMMARY OF FINDINGS

MORTALITY

We found 31 unique studies with 31 analyses that reported mortality. All were cohorts and the majority were multicenter.

More than half of the studies were conducted in the United States (n=25). The remaining studies were conducted in Australia (n=1), two in Japan, 1,10 two in Canada, 111 two across both Ireland/United Kingdom, 111 two across both Canada/United States, and seven in Europe. One set of two studies and a separate set of three studies derived their analyses from the same database sources, which likely represents some overlap in the analyses. 1,11,10

Surgical category:
- Cardiac: 23 studies
- General: 8 studies
- Neurosurgery: 4 studies
- Respiratory: 4 studies
- Transplant: 2
- Urology: 2 studies

Bottom line - Mortality: Overall, the effect of specialization on mortality is unclear. This is based on approximately 276,071 children that were assessed in over 50 analyses from 41 cohort studies primarily from the United States, and based mostly on hospital volume and cardiac procedures. For cardiac surgeries, specialization may be generally effective in reducing mortality but those results are uncertain due to general limitations with analyses from observational studies. For all other surgeries combined, the effect upon mortality is unclear.

Table 1. Mortality

<table>
<thead>
<tr>
<th>Overall analysis</th>
<th>N</th>
<th>Results</th>
<th>Risk of Bias score</th>
<th>Interpretation</th>
<th>Applicability</th>
</tr>
</thead>
<tbody>
<tr>
<td>All analyses* (56 studies, &gt;276,071 children)</td>
<td>-ve: 20 (54%)</td>
<td>-ve: 0</td>
<td>N1: 20 (45%)</td>
<td>Unclear (nearly evenly distributed within range)</td>
<td>Unclear (mainly hospital volume studies; half cardiac surgeries; wide age range; majority inhospital mortality or time not defined (range 30 to 10y))</td>
</tr>
</tbody>
</table>

Cardiac: 18 analyses* (>240,164 children)
-ve: 19 (60%) | -ve: 0 | N1: 8 (29%) | Unclear: 1 (4%) | Range 0-9 (half of analyses scored 0) | Generally effective for reduction in mortality, with uncertain confidence | Mainly hospital volume wide age range; about half in-hospital mortality |

Other surgery: 20 analyses (n=895 children)
-ve: 7 (33%) | -ve: 0 | N1: 12 (60%) | Unclear: 1 (5%) | Range 0-9 (nearly evenly distributed within range) | Unclear (mainly hospital volume wide age range; majority inhospital mortality or time not defined (range 30 to 10y)) |

Abbreviations: -ve = statistically significant results favour specialization, +ve = statistically significant results favour comparison group; d-day = number of days, mon: month, year: year. *More than half of analyses adjusted for confounding factors. **More than half of analyses adjusted for within hospital clustering of patient data. Less than half of analyses adjusted for confounding factors.

Overall analysis

Of the 51 analyses, 48 were amenable to an aggregate descriptive analysis, while the three remaining studies conducted a different type of analysis. 1,11,10 Analyses were mainly assessing...
Methods

Search strategies were developed and peer reviewed by trained information retrieval specialists. Searches were run in Ovid Medline, Embase, and The Cochrane Library (Jan. 1, 2000 to March 1, 2013). Retrieved records were systematically screened in duplicate at two levels using DistillerSR. We included comparative experimental and observational study designs and systematic reviews. Only those studies published between 2000 - present were considered for inclusion. Studies were included if they presented data separately for the eligible intravascular surgical interventions across high risk pediatric populations as described by our PICOTS framework. We used the Newcastle-Ottawa scale (score out of 9) to assess observational cohort studies. We conducted a narrative synthesis by first assessing outcomes across all exposure categories and surgical domains and then by individual exposure categories as described in our analysis. We conducted a subgroup analyses by surgical category (i.e., cardiac versus all others). We summarize results as to whether studies were non-significant, significant in favour of exposure, or significant in favour of comparator. This report was conducted over 10 weeks (Feb.-Apr 2013).

Report citation: (Authors in alphabetical order)

CHA Collaborators: Drs. Oldham, Moss, Rangel, Goldin, and Keuser.

Cochrane Innovations: Dr. Lorne Becker

Acknowledgements: The authors thank Michelle Flander (Information Specialist) for developing the test searches; Beddy Skidmore (Information Specialist) for search refinements; Katrina Campbell (Information Specialist) for PRESS Peer Review of the final searches; Dr. Russell Gruen for external content and Cochrane Review expertise; and Raymond Daniel for database management.

Conflicts of Interest: none declared

Additional Materials Available Upon Request:
- Level 1 screening form
- Level 2 screening form
- Search strategies
- List of excluded studies
- List of possibly relevant non-English citations

Disclaimer: The information in this report is a summary of available material and is designed to give readers (health systems stakeholders, policy and decision makers) a starting point in considering currently available research evidence. Other relevant scientific findings may have been reported since completion of the review. This report is current to the date of publication and may be superseded by an updated publication on the same topic. You should consult other sources in order to confirm the currency, accuracy and completeness of the information contained in this publication and, in the event that medical treatment is required you should take professional expert advice from a legally qualified and appropriately experienced medical practitioner.

Report – 12 pages in length (not including references)
# Appendices – Brief Evidence Tables

## Table 1: Studies that report mortality

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Surgery</th>
<th>Country</th>
<th>Data Source</th>
<th>Study Period</th>
<th>Number of Centers</th>
<th>Sample size</th>
<th>Population Summary</th>
<th>Risk of Bias Total Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bennett, T. D., (2010)</td>
<td>Cardiac lesions ductal dependent with a cardiac procedure</td>
<td>United States</td>
<td>Washington State Comprehensive Hospital Abstract Reporting System (CHARS)</td>
<td>1987-2006</td>
<td>NR</td>
<td>623</td>
<td>Infants diagnosed with a cardiac lesion likely to be ductal dependent and who underwent a cardiac procedure within 30 days after birth</td>
<td>9</td>
</tr>
</tbody>
</table>
Spectrum of Rapid Review Products

<table>
<thead>
<tr>
<th>Types</th>
<th>Evidence brief</th>
<th>Rapid evidence map (SRs plus primary studies)</th>
<th>Rapid evidence map (SRs only)</th>
<th>Rapid review (Primary studies only)</th>
<th>Rapid review (SRs plus primary studies)</th>
<th>Rapid review (SRs only)</th>
<th>Traditional systematic review conducted rapidly</th>
</tr>
</thead>
</table>

Key features of each rapid review product

<table>
<thead>
<tr>
<th>Timeframe</th>
<th>24 hours – 3 weeks</th>
<th>4 -16 weeks</th>
<th>12 – 16 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>May include abbreviated literature search limits; limited number of sources searched; targeted grey literature sources; limited number of outcomes; study design restrictions. Limits will vary by topic.</td>
<td>Only report format abbreviated</td>
<td></td>
</tr>
<tr>
<td>Integration of the evidence</td>
<td>Annotated bib. or reference list</td>
<td>Various approaches to synthesis</td>
<td>Narrative +/- meta-analysis</td>
</tr>
<tr>
<td>Risk of Bias of Individual Studies</td>
<td>Not applicable</td>
<td>Yes (using validated instruments when available)</td>
<td></td>
</tr>
</tbody>
</table>

Cursory to more complex
Each RR requires at a minimum:

- At least 2 reviewers working in parallel, one of whom should be experienced with SRs (total of 1.15 – 1.30 FTE over duration of the RR)
- 1 Medical Librarian/Information Specialist (experienced) (15-37.5 hours to develop searches etc.)
- 1 Information Specialist Assistant content expertise, and the necessary input of the client (37.5-75 hours)
- Methodological expertise to guide protocol development and conduct (37.5 hours)
- Clinical expertise as required (variable)
- On-call point person representing the client/commissioner (variable)
Other Expenses

- Interlibrary loan costs; special orders (rush delivery of key articles) if required and funds allow
- Online collaborative systematic review software (facilitates our work)
- Conference call expenses (a lot of dialoguing with client/experts/team)
- Publication costs (open access)
- Additional staffing required to meet a tight timeline in proportion to volume of information to screen/include (shorter duration doesn’t necessarily mean cheaper)
- Additional costs to do GRADE; partake in follow up meetings on behalf of the client etc.
- Our goad is to cost recover
Portfolio & Funding

Primarily service-based agreements funds the RRs we carry out

- CIHR-KTA Grant – Evidence Summaries (2009-2011)
- IQ@TOH - Hospital-based HTA
- UK Public Health Screening Program (designation)
- Ontario's Better Outcomes Registry & Network (BORN)
- Accelerated Guideline Development (WHO; KCE-Belgium)
- Health Quality Ontario (Ontario Health Technology Advisory Committee – OHTAC)
- General services contracts (variety of topics/fields)
  - Approximately, $15,000 to $75,000 USD – price informed by scoping in advance of protocol
Collaborators and/or other groups with an interest in RRs
Dissemination

- KTA projects publically available at [www.ohri.ca/kta](http://www.ohri.ca/kta)
- Aim to publish our RRs
- Various external service contracts (unpublished reports)
  - To date we’ve completed 35+ RRs (completed) – on a spectrum on topics
- Training/education - requests (20+)
• **CIHR Operating Grant on RRs**
  CIHR FRN 142310-2015
  1: Descriptive analysis of RRs (format, reporting, conduct, etc.)
  2: Developing RR definition
  3: RR Process Map to guide conduct
  4: PRISMA-RR reporting guideline
  5: Examining use of RRs by funding agencies

• **Update of the OHRI RR methods**

• **Collaborating on the following:**
  • SPARKS Trial (CIHR funded) (Dr. Andrea Tricco – PI)
  • Searching project; Decision-maker uncertainty (Cochrane Austria)
Rapid review methods for Rapid Advice Guidelines
CIHR FRN 142310-2015

• In 2014, we assisted WHO with establishing guidance on how to produce evidence-informed RAGs in the context of a public health emergency
• Focus was on accelerating guideline development including conducting rapid evidence reviews to both inform and formulate recommendations
• We contributed a new chapter in the WHO Handbook (2nd edition)
• Related article – JCE publication (doi: 10.1016/j.jclinepi.2016.08.010)
Thank you!

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