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The Value of Synthesizing Evidence to Inform Cancer Nursing

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Jane Noyes

The value of synthesising evidence to inform cancer nursing

Making best use of evidence to inform cancer nursing practice is a global priority. Synthesising evidence is an efficient way of maximising use of existing evidence and preventing research wastage by commissioning unwarranted new research. The importance of the systematic review to informing clinical decisions is signified by the establishment of global clinical guideline developers such as the World Health Organisation (<https://www.who.int/publications/guidelines/en/>), United States Agency for Healthcare Research and Quality (<https://www.ahrq.gov/>), National Health and Medical Research Council of Australia (<https://www.nhmrc.gov.au/>), and the National Institute for Health and Care Excellence in the UK (<https://www.nice.org.uk/>). The entire clinical guideline development process is predicated on the systematic review of evidence from which recommendations for practice can be made. The field of cancer has also benefitted from national and international consensus statements on treatments and interventions drawing on systematic reviews in combination with clinical expertise and patient preferences.

Cancer was one of the first clinical specialities to embrace quantitative systematic reviews of the effects of drugs and other types of treatments. The Cochrane library for example, has more intervention effect reviews on cancer than any other topic. The large number of systematic reviews on cancer topics have subsequently been used to underpin clinical guideline development to transform the treatment options, associated nursing care, and improved outcomes for patients. Of specific interest, recent developments include a review to establish the effectiveness and value of European cancer nursing, which is one of the first of its type.¹

Whilst the Cochrane-type of quantitative intervention effect review has achieved a state of supremacy, over the last 20 years there has been prolific development of other review methodologies to address different types of questions with diverse types of evidence (such as qualitative and mixed-method). Interestingly, nurses have been highly influential in the methodological development of diverse review types that are more likely to be useful in developing new theory and new insights into patient experience and nursing care. The new Cochrane Handbook, for example, includes a chapter on qualitative evidence synthesis², and Cochrane has an Effective Practice and Organisation of Care review group (<https://epoc.cochrane.org/about-us>). In a more general context (see Figure 1), it is now possible to use diverse evidence synthesis methods for a much wider set of purposes, such as to:

- Determine the pool of known evidence on a topic
- Formulate review questions/determine outcomes and clarify review parameters
- Clarify concepts and synthesise theory
- Synthesise policy intentions and outcomes
- Synthesise system wide policy outcomes
- Develop theory to inform a primary study
- Develop theory as a primary purpose
- Understand illness experiences
- Determine how promising practices work
- Understand patient, carer and key stakeholder experiences, values and preferences concerning interventions
- Determine factors that impact on intervention implementation, fidelity, reach, acceptability, feasibility, and to identify benefits and harms
- Estimate the cost and effectiveness of interventions

- Determine prognosis
- Determine diagnostic test accuracy
- Determine the psychometric properties of instruments
- Determine the effects and impacts of complex, health system wide interventions
- Integrate quantitative and qualitative evidence

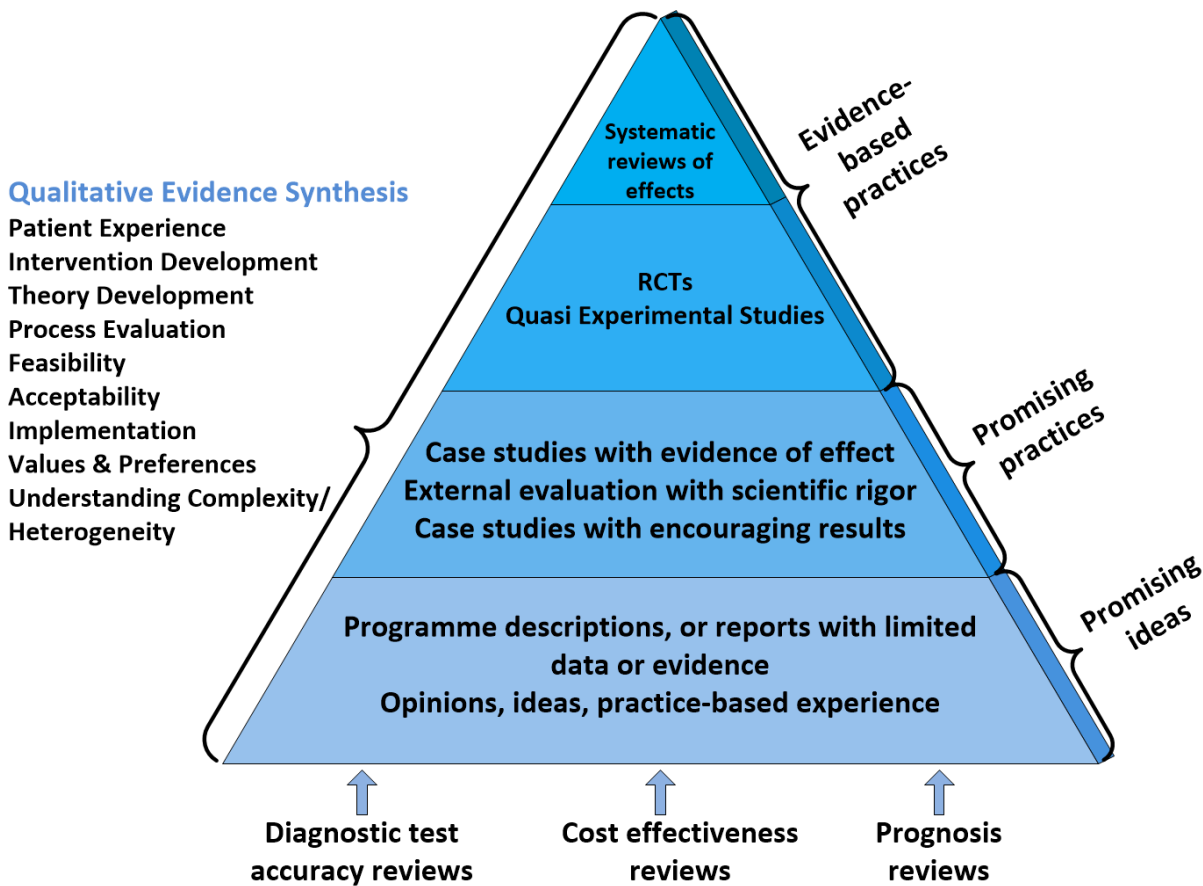


Figure 1. New hierarchy of evidence that responds to user requirements for the inclusion of diverse evidence for decision-making and timely reviews. Adapted from

https://www.homelesshub.ca/sites/default/files/attachments/PPFramework_Part1.pdf

Guideline developers and decision makers increasingly require qualitative and mixed method syntheses as well as reviews of intervention effects, diagnostic test accuracy and prognosis to populate specific aspects of the ‘evidence to decision’ framework³, such as patient values, preferences and experiences, feasibility, implementation and resource considerations, and equity implications (see Figures 1 and 2). It is these specific phenomena that can be addressed by newer review types and methods to better inform cancer nursing and underpin guideline development.

Evidence to recommendation framework - Health system and public health recommendations

Should collaborative care be implemented for the treatment of moderate and severe depression in (elderly) adults?

Problem: Moderate and severe depression in adults
Option: Collaborative care to augment primary care
Comparison: Usual care
Setting: Primary care
Perspective: Health system

Background: Depression is common and causes a greater decrease in health state than some chronic diseases.¹ It results in high treatment costs as well as a significant personal, family and wider social impact.¹ Studies suggest that treatment of depression often does not adhere to recommendations in practice guidelines.² There is evidence that collaborative care is effective in improving short-term (6 month) and longer-term (12+ months) outcomes for patients with depression.³ Collaborative care may include clinical interventions ranging from simple interventions, such as telephone contact, to more complex interventions such as intensive psychosocial follow-up, but should always comprise structured care involving a case manager working together with the primary care physician and with access to mental health specialist input.⁴

Criteria:

Problem

Values

Desirable effects

Undesirable effects

Certainty of the evidence

Balance of effects

Resources required

Certainty of evidence of required resources

Cost-effectiveness

Equity

Acceptability

Feasibility

Summary of judgments

Criteria Judgments Research evidence Additional considerations

CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
PROBLEM Is the problem a priority?	No <input type="checkbox"/> Probably no <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably yes <input type="checkbox"/> Yes <input type="checkbox"/>	Depression is the fourth highest cause of disability worldwide. ¹ In Norway it reduces the capacity for work, or is the reason for sickness pay in up to 10% of adults. ¹ In the UK it is the third most common reason for primary care consultation. ¹ International data suggest that management is often below evidence-based standards. ² The overall lifetime prevalence of depression in adulthood in Norway is 15.6%. ¹	

CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL INFORMATION																														
VALUES Is there important uncertainty about how much people value the main outcomes?	No <input type="checkbox"/> Probably no <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably yes <input type="checkbox"/> Yes <input type="checkbox"/>	Relative importance or value of the main outcomes of interest: <table border="1"> <tr> <th>Outcome</th> <th>Relative importance</th> <th>Certainty of the evidence</th> </tr> <tr> <td>Non-response to treatment</td> <td>No studies</td> <td>No studies</td> </tr> <tr> <td>Non-adherence at 12 months</td> <td>No studies</td> <td>No studies</td> </tr> <tr> <td>Relapse prevention at 12 months</td> <td>No studies</td> <td>No studies</td> </tr> <tr> <td>Non-adherence to medication</td> <td>No studies</td> <td>No studies</td> </tr> <tr> <td>Undesired effects</td> <td>No studies</td> <td>No studies</td> </tr> </table>	Outcome	Relative importance	Certainty of the evidence	Non-response to treatment	No studies	No studies	Non-adherence at 12 months	No studies	No studies	Relapse prevention at 12 months	No studies	No studies	Non-adherence to medication	No studies	No studies	Undesired effects	No studies	No studies													
Outcome	Relative importance	Certainty of the evidence																															
Non-response to treatment	No studies	No studies																															
Non-adherence at 12 months	No studies	No studies																															
Relapse prevention at 12 months	No studies	No studies																															
Non-adherence to medication	No studies	No studies																															
Undesired effects	No studies	No studies																															
DESIRABLE EFFECTS What is the overall certainty of the evidence of effectiveness?	No <input type="checkbox"/> Probably no <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably yes <input type="checkbox"/> Yes <input type="checkbox"/>	Summary of findings: Standard care vs collaborative care for depression (Final) (RoBmeta.net defined) <table border="1"> <tr> <th>Outcome</th> <th>Standard care (n)</th> <th>Collaborative care (n)</th> <th>Difference (95% CI)</th> <th>Certainty of the evidence (GRADE)</th> </tr> <tr> <td>Non-response to treatment</td> <td>56.9</td> <td>49.7</td> <td>7.1 lower (5 to 15 lower)</td> <td>High</td> </tr> <tr> <td>Non-adherence at 12 months</td> <td>47</td> <td>49.4</td> <td>2.4 more (5 lower to 0.1 more)</td> <td>Moderate</td> </tr> <tr> <td>Relapse prevention at 12 months</td> <td>17</td> <td>11.3</td> <td>5.7 lower (3.1 lower to 8.3 lower)</td> <td>Low</td> </tr> <tr> <td>Non-adherence to medication</td> <td>51.8</td> <td>30.8</td> <td>21.0 lower (17.4 lower to 24.6 lower)</td> <td>Moderate</td> </tr> <tr> <td>Undesired effects</td> <td>No information</td> <td></td> <td></td> <td></td> </tr> </table>	Outcome	Standard care (n)	Collaborative care (n)	Difference (95% CI)	Certainty of the evidence (GRADE)	Non-response to treatment	56.9	49.7	7.1 lower (5 to 15 lower)	High	Non-adherence at 12 months	47	49.4	2.4 more (5 lower to 0.1 more)	Moderate	Relapse prevention at 12 months	17	11.3	5.7 lower (3.1 lower to 8.3 lower)	Low	Non-adherence to medication	51.8	30.8	21.0 lower (17.4 lower to 24.6 lower)	Moderate	Undesired effects	No information				Collaborative care has been shown to be most effective in trials carried out in the US. Similar results would be expected in well-funded European healthcare systems although there may be big differences in the standard care used as the comparator in different studies, and the intensity and length of the collaborative care varied between studies. The strategy of the intervention affects the outcome. ³
Outcome	Standard care (n)	Collaborative care (n)	Difference (95% CI)	Certainty of the evidence (GRADE)																													
Non-response to treatment	56.9	49.7	7.1 lower (5 to 15 lower)	High																													
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Non-adherence to medication	51.8	30.8	21.0 lower (17.4 lower to 24.6 lower)	Moderate																													
Undesired effects	No information																																
UNDESIRABLE EFFECTS Are the desirable anticipated effects large?	No <input type="checkbox"/> Probably no <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably yes <input type="checkbox"/> Yes <input type="checkbox"/>	Based on The NICE guideline on the treatment and management of depression in adults 2010 Link to interactive Summary of Findings table Link to evidence profile																															
UNDESIRABLE EFFECTS Are the undesirable anticipated effects small?	No <input type="checkbox"/> Probably no <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably yes <input type="checkbox"/> Yes <input type="checkbox"/>																																
UNDESIRABLE EFFECTS Are the desirable effects large relative to undesirable effects?	No <input type="checkbox"/> Probably no <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably yes <input type="checkbox"/> Yes <input type="checkbox"/>																																

CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL INFORMATION
RESOURCES REQUIRED Are the resources required small?	No <input type="checkbox"/> Probably no <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably yes <input type="checkbox"/> Yes <input type="checkbox"/>	Main anticipated resource requirements Resource Case managers Specialist support Acknowledgements Psychological treatments Follow up In a review of economic evaluations of enhanced primary care for depression collaborative case management resulted in increased outcomes but were also associated with greater costs. When considering primary care depression treatment costs alone (ICER estimate ranged from \$13 to \$24 per additional course on the day). In a series of cost-effectiveness ratio acceptability analyses using cost-effectiveness acceptability thresholds, for a nurse-delivered case management approach there was a 65% probability that the cost-effectiveness of the intervention was less than \$20,000 per QALY and a 91% probability that it was less than \$50,000 per QALY.	Patient and family costs are likely small. Municipality costs may depend on how collaborative care is implemented, e.g. the qualifications of case managers. Healthcare costs (including the cost of antidepressant and psychological treatment) may be large.
COST-EFFECTIVENESS Is the incremental cost small relative to the net benefits?	No <input type="checkbox"/> Probably no <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably yes <input type="checkbox"/> Yes <input type="checkbox"/>		
EQUITY What would be the impact on health inequalities?	Unsure <input type="checkbox"/> Probably unsure <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably reduced <input type="checkbox"/> Reduced <input type="checkbox"/> None <input type="checkbox"/>	No evidence	Patients with less resources, social support and access to care may benefit more than resource strong patients, thereby reducing inequities.
ACCEPTABILITY Is the option acceptable to key stakeholders?	No <input type="checkbox"/> Probably no <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably yes <input type="checkbox"/> Yes <input type="checkbox"/>	No evidence	Fewer patients seeking collaborative care left the trials, for any reason (including being lost to follow-up) than patients receiving usual care. Part of this may be explained by a higher level of acceptability, but this is non-specific and the difference was small and non-significant.
FEASIBILITY Is the option feasible to implement?	No <input type="checkbox"/> Probably no <input type="checkbox"/> Uncertain <input type="checkbox"/> Probably yes <input type="checkbox"/> Yes <input type="checkbox"/>	No evidence	There may not be sufficient mental health professionals to provide the enhanced input and care coordination for all primary care patients with depression. ⁴

Balance of consequences	Undesirable consequences clearly outweigh desirable consequences in most settings	Undesirable consequences probably outweigh desirable consequences in most settings	The balance between desirable and undesirable consequences is closely balanced or uncertain	Desirable consequences probably outweigh undesirable consequences in most settings	Desirable consequences clearly outweigh undesirable consequences in most settings
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Type of recommendation	We recommend against the option	We suggest not offering this option	We suggest offering this option	We recommend the option
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Recommendation (text) Each municipality should create and implement a collaborative plan of care for patients with moderate to severe depression. The plan should define the responsibilities and communication between the various professional groups who have contact with patients, both in community health services and between, local and specialist healthcare, and appoint health professionals with special responsibility for follow-up of patients. The plan should include procedures for referral to specialist services.

Strong recommendation, moderate quality of the evidence. The plan may include organizational, educational and other measures that have evidence of moderate to high quality that they can lead to better outcomes for patients with depression.

Justification There is high quality evidence of improved care, adherence and patient outcomes. There is no evidence of adverse effects. The cost is uncertain, but is likely small for patients and their families, moderate for municipalities and moderate for the health services. The cost-effectiveness is similar to or less than many clinical interventions that are considered cost-effective.

Implementation considerations Implementation strategies should be tailored to municipalities (e.g. qualifications and location of case managers, communication and referrals) and may be helped by model plans, clarification of options and support to select appropriate options.

Monitoring and evaluation Monitoring of indicators of the quality of care and patient outcomes is warranted and should be incorporated in collaborative care plans.

Research priorities Ongoing and future research should clarify the importance of various components of collaborative care and the applicability of alternative models in different settings.

QUESTION

CRITERIA

CONCLUSION

Figure 2. The DECIDE Framework. Courtesy of Simon Lewin.

The majority of published contemporary reviews in cancer nursing however use very few of the many available newer methods, especially those qualitative evidence synthesis methods that are designed to advance new theory and theoretical insights that go beyond the primary studies.⁴ There are currently, for example, around 18 different and sometimes overlapping qualitative evidence synthesis methods that vary in complexity.⁵⁻⁷ Reviewers commonly find it difficult to select an appropriate synthesis methodology for their specific context. Reviewers also tend to stick to the same methodology that they are familiar with, rather than consider the best methodology for the type of available evidence. To support reviewers to make the best choice, Booth and colleagues have produced the RETREAT checklist of things to consider when selecting a methodology.⁵⁻⁶

Box 1. The RETREAT Framework for selecting an appropriate methodology. Reproduced from Booth et al.⁵⁻⁶

R	Review question
E	Epistemology
T	Time/time frame
R	Resources
E	Expertise
A	Audience and purpose
T	Type of data

Many cancer interventions that involve nursing also tend to be ‘complex interventions’ and there is less (although growing) experience of undertaking mixed-method reviews of complex interventions that focus on complexity and involve health systems level change.⁴⁻⁸ The use of theory to design reviews and interpret evidence is also increasingly used to help review authors to produce a more theory informed and useful product for decision-making. Theory in the form of logic models and social theories can help structure and focus a systematic review of any design and can be used as an integrative or interpretive lens. Cochrane has produced detailed guidance on the choice of theory for use in systematic reviews.⁹

Those reviewers that do apply newer and more novel methods frequently find it challenging to interpret and apply the evidence synthesis methods and tools as intended by the originators.¹⁰⁻¹¹ Whilst acknowledging that funded reviews often need to be undertaken rapidly, there appears to be a lot of confusion about synthesis methods and designs, blurring of different methods, short cuts being taken and missing out of important stages and processes when it is not appropriate to do so. Reviewers have also found it challenging to report their review in a way that has maximum utility for decision-makers.¹⁰ In recent years methodologists have recognised that too many qualitative evidence syntheses were poorly reported and thus could not be used to make decisions, and responded by developing detailed reporting guidelines to support both the better conduct and reporting of generic qualitative evidence syntheses and meta-ethnographies.¹²⁻¹³ Likewise many reports of meta-analyses do not meet the PRISMA reporting requirements, and reports of quantitative syntheses without meta-analysis have been particularly poor,

leading to the new (SWiM) reporting guidance which is an extension of PRISMA.¹⁴⁻¹⁵ There is at present no specific reporting guideline for mixed-method reviews, but Flemming and colleagues outline some principles to follow.¹⁶ Other recent developments include GRADE CERQual to assess the confidence in synthesised qualitative findings.¹⁷ This latter development is important as decision makers have got used to the similar GRADE method (<https://www.gradeworkinggroup.org/>) for assessing the certainty of evidence of intervention effects and were keen to have a similar system for qualitative evidence syntheses. Syntheses of qualitative evidence are of more value to decision makers if they have confidence in the quality of the review and the strength of the evidence.

Of particular concern, with some notable exceptions, patient and public involvement has been much slower to be fully integrated into the conduct of evidence syntheses, especially those reviews that are not funded. Many reviews are conducted without any patient and public involvement, whereas for most funded reviews their input is expected because the review product is likely to be more patient-centred and of greater value to decision makers if they are co-produced. Cochrane for example has a huge consumer network of people to draw on. Many local not for profit organisations and individuals are however more than willing to contribute to non funded reviews because they want to see improved treatments and services for people with cancer. There is also a big evidence gap in the conduct of reviews at the interface between health and social cancer care, and reviews focused purely on social care and cancer. People living with cancer experience a myriad of psychological, social and domestic problems that impact on their life and wellbeing. Cancer nurses are well placed to fill this known evidence gap to benefit patients.

It is however positive to see a mixture of different review types and designs in the current themed issue on evidence synthesis. Selected reviews include a scoping review, priority setting review, meta-analyses and qualitative evidence syntheses addressing various questions of importance to cancer nursing. Of particular interest, Bernier Carney et al¹⁸ use meta-ethnography to transform the findings of primary qualitative studies to better understand the experiences during childhood cancer survivorship. Meta-ethnography is one of the more complex qualitative evidence synthesis methods and requires experience of conducting primary qualitative research to fully utilise the power of the methodology to develop new theory and interpretations that move beyond the primary study findings. Cadarin et al¹⁹ undertook a mixed-method review and published their protocol in PROSPERO (International prospective register of systematic reviews <https://www.crd.york.ac.uk/PROSPERO/>). It is a marker of best practice to make publicly available the review protocol prior to conducting the review. Although the summary of findings is articulated very briefly and not in a way that was originally intended, it is good to see that Diaw et al²⁰ applied GRADE CERQual to assess the confidence in their synthesised qualitative findings. Presenting a summary of findings table with associated assessments of confidence can be exceptionally helpful for decision-makers. It was also encouraging to see Han et al²¹ use a symptom management theory as the theoretical framework to inform the design and interpretation of their quantitative review and meta-analysis.

In summing up the current state of the art of evidence synthesis in the first two decades of the 21st century, the best one can say is that it is a mixed-picture of great progress and unfulfilled potential. There are different evidence synthesis methods for varying purposes that are continuing to evolve. Global evidence synthesis producers, guideline producers and decision makers are now much more aware of the value of syntheses of diverse evidence types. There is further potential for cancer nurses to embrace the full range of synthesis methods available in order to make best use of the available evidence in health and social care. But, they need to apply evidence synthesis methods carefully and rigorously to produce higher quality reviews that are valued and used by decision-makers. There is now much better methodological

guidance to support the conduct and reporting of reviews to further improve their quality and utility for decision-making.

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