Cochrane Library

**Cochrane** Database of Systematic Reviews

# Patient navigator programmes for children and adolescents with chronic diseases (Protocol)

Lalji R, Francis A, Khalid R, Guha C, Johnson DW, Wong G

Lalji R, Francis A, Khalid R, Guha C, Johnson DW, Wong G.
Patient navigator programmes for children and adolescents with chronic diseases (Protocol).
*Cochrane Database of Systematic Reviews* 2021, Issue 7. Art. No.: CD014688.
DOI: 10.1002/14651858.CD014688.

**www.cochranelibrary.com**




WILEY

# TABLE OF CONTENTS

[Intervention Protocol]

# Patient navigator programmes for children and adolescents with chronic diseases

Rowena Lalji[1,2,3], Anna Francis[1,2,3], Rabia Khalid[4], Chandana Guha[4], David W Johnson[2], Germaine Wong[5]

[1]The Centre for Kidney Research, The University of Queensland, Brisbane, Australia. [2]Department of Nephrology, Princess Alexandra Hospital, Woolloongabba, Australia. [3]Department of Paediatric Nephrology, Queensland Children's Hospital, Brisbane, Australia. [4]School of Public Health, The University of Sydney, Sydney, Australia. [5]Centre for Kidney Research, The Children's Hospital at Westmead, Westmead, Australia

**Contact address:** Rowena Lalji, rowena.lalji@health.qld.gov.au.

**Editorial group:** Cochrane Effective Practice and Organisation of Care Group.
**Publication status and date:** New, published in Issue 7, 2021.

**Citation:** Lalji R, Francis A, Khalid R, Guha C, Johnson DW, Wong G. Patient navigator programmes for children and adolescents with chronic diseases (Protocol). *Cochrane Database of Systematic Reviews* 2021, Issue 7. Art. No.: CD014688. DOI: 10.1002/14651858.CD014688.



## ABSTRACT

### Objectives

This is a protocol for a Cochrane Review (intervention). The objectives are as follows:

To assess the effects of patient navigator programmes in children and adolescents with chronic diseases.

# BACKGROUND

## Description of the condition

Chronic diseases are broadly defined as persisting, non-communicable health conditions (physical or mental), which can impact upon a person's ability to function from a physical, cognitive, or social perspective. Although not immediate life-threatening, these conditions require long-term medical care or related services (Australian Institute of Health and Welfare 2020; CDC 2021).

Chronic disease represents a high cost, resource intensive subset of disease burden, which by 2020 is predicted to account for 73% of all deaths, and 60% of the worldwide burden of adult disease (WHO 2019). Mirroring the trend seen in adults, the prevalence of chronic disease within the paediatric population is increasing with time (Perrin 2014; Stoll 2010; Van Cleave 2010). An estimated one in four children is affected by at least one chronic disease, with some evidence to suggest this rate is even higher when accounting for both sex and ethnicity (Van Cleave 2010; Wiljaars 2016).

Children and adolescents represent a particularly vulnerable cohort, with unique healthcare requirements that are different from those of their adult counterparts (WHO 2018). Depending on the chronic disease, children have been shown to suffer from increased mortality (for example, up to 30 times that of their peers in the case of end-stage kidney disease (McDonald 2004)), and morbidity, including reduced self-reported quality of life, neurocognitive impairment, and appreciably higher rates of depression and anxiety (Bennett 1994; Bregnballe 2007; Francis 2019; Quittner 2008). Often, these burdens (and their health-related consequences) are carried into adulthood (Cohen 2018). Furthermore, the diagnosis and management of childhood chronic disease has significant financial, emotional, and psychological ramifications for the broader family unit (Lähteenmäki 2004; Medway 2015; Tsai 2006).

Social determinants of health (separate from biological factors) play a significant role in chronic disease outcomes for children, particularly within socially disadvantaged families and minority communities (Council on Community Pediatrics 2016; Marmot 2012; Wilson 2019). With continued gaps in chronic disease management, and persistent fragmentation in the healthcare system, medical professionals, policy makers, and relevant stakeholders, alike, are seeking new, cost-effective strategies to overcome modifiable barriers to accessing appropriate chronic disease care for children, and thus, improve their overall health outcomes.

## Description of the intervention

The intervention for this review will be patient navigators (PN). PN are trained medical or non-medical personnel (for example, lay health workers, community health workers, nurses, or care co-ordinators), who provide guidance for the children (and their primary caregivers, such as parents or guardians), as they move through the complex medical and social systems (Carter 2018; Kelly 2015). The navigator may deliver education, help to co-ordinate care, be an advocate (or a combination) for the child (and their primary caregivers), who are disadvantaged from a social, cultural, or economic perspective. Notably, there is variability and overlap with programmes of different names, within different health economies, when describing the PN role in the literature (Dohan 2005). It is generally accepted that the PN helps to navigate people through existing services, in contrast to case managers, who may also act as care providers (i.e. to provide psychosocial care (Kelly 2019)).

It has been shown that PNs improve health outcomes for adults with chronic diseases, particularly in the realm of cancer (Freeman 2005; Rodriguez-Torres 2019; Wells 2008), and diabetes (Spencer 2018; Thom 2013), by helping them overcome both individual and systemic barriers, and access timely and appropriate medical care. For young children specifically, the role of the PN is for the most part, to support and empower the family unit (rather than the children themselves), so that they can better understand the health requirements of their children, and how best to obtain this within the constraints of the health system that is available to them (Smith 2017). In adolescents, although the PN focus largely shifts to the young person's unmet healthcare needs, it is acknowledged that they, too, may be best served by addressing the needs of the family unit (Chu 2015).

## How the intervention might work

The fundamental role of the PN is to help guide, and proactively support people with a health problem (and their primary caregivers), to traverse the often bewildering, complex maze of the healthcare system, by enhancing the lines of communication, and providing a single point of contact (Kelly 2015). By identifying and matching a person's unmet needs to the appropriate health resources, the aim of the PN is to improve access to, and decrease the fragmentation of care to achieve optimal health outcomes for people with a health concern (Mackie 2018; Smith 2017). The PN can be of particular assistance to vulnerable and marginalized populations with chronic illness, to help them better understand their diagnoses, treatment options, and available resources (Natale-Pereira 2011; Pantell 2020). Distrust and fear of healthcare services, secondary to different cultural, language, or health beliefs, can also contribute to delays in seeking treatment, and high rates of non-adherence (Feinberg 2016; Natale-Pereira 2011; Petereit 2008). Patient navigators are ideally positioned to foster trust within these marginalized and minority communities (Rodriguez-Torres 2019).

Given the broad cognitive and development spectrum of the paediatric population (young children versus adolescents), the primary target of the PN role as an intervention will also differ. For young children (and adolescents with developmental delays), providing health guidance and support to the primary caregivers, is intended, in turn, to have a positive effect on the health outcomes of the family as a unit, rather than the young person as an individual. For adolescents, the PN focuses on supporting and empowering the young people themselves, in preparation for the inevitable transition to adult services, but they also support the family unit (Callahan 2001; Chu 2015). Ideally, early and appropriate health engagement for all children should improve their health outcomes, and reduce (if not prevent entirely) both the short- and long-term complications of their chronic diseases.

## Why it is important to do this review

Despite the growing worldwide popularity of this style of intervention, the evidence for the role of PN in the health care of young people is heterogeneous in the populations studied

(young children versus adolescents), the way PNs have been utilised (type and setting of intervention), and in the outcome measures reported (self-reported by young person versus reported by carer (Desveaux 2019; McBrien 2018). Whilst some studies have reported improvements in quality of life scores, reported by the young person and the carer (Gottlieb 2016; Krieger 2009), reduced presentations to the hospital or emergency department (Morgan 2013; Pantell 2020), and a health economic cost benefit (Jandorf 2013), other studies have found no difference in either clinical or self-reported outcomes (Caskey 2019; Resnick 2009; Simon 2017). There have also been reports of harm in adults, in the form of their discomfort with the gender or cultural mismatch of the PN and their intervention (Carroll 2010). It is currently unclear whether children and adolescents with chronic diseases, under the care of a patient navigator programme, have better or equivalent health outcomes compared with those receiving standard care.

## OBJECTIVES

To assess the effects of patient navigator programmes in children and adolescents with chronic diseases.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

We will include randomised trials of both individual and cluster design. If cross-over studies are available, we will use data from the first period of these studies. We will include full-text studies, conference abstracts, and unpublished data. We will include studies irrespective of their publication status and language of publication.

#### Types of participants

We will include all children and adolescents, diagnosed with any chronic diseases requiring ongoing medical care.

For the purpose of this review, we define children as those younger than 19 years of age, that is, aged 0 to 18 years, inclusive (WHO 2020).

We will include studies that include a subset of relevant participants (i.e. both adults and children), only if the study reports separate data for the eligible selection of the population (in which case, data from the eligible participants can be included in the review), or the majority of the participants in the study are < 19 years of age. We will document difficult decisions regarding inclusion or exclusion of specific studies in the review.

#### Types of interventions

We will use the following definition for a patient navigator (PN): "...a trained medical or non-medical person who assists people with chronic conditions to traverse complex health systems. PNs help people (particularly vulnerable and disadvantaged populations) to understand their diagnosis, treatment options, available resources, and provide a crucial link to overcome both individual and systemic barriers to healthcare access" (Natale-Pereira 2011).

The PN role is sometimes interchangeably referred to in the literature as that of a community health worker, navigator, health advocate, case manager, or care co-ordinator (Kelly 2019). We will consider studies that use these terms (or variations thereof) provided their role and function within the study fulfils the PN definition listed above.

##### *Inclusion criteria*

- We will include trials comparing a PN intervention with current standard of care (i.e. no PN), as well as trials with active comparison groups.
- PN programmes may be either hospital- or community-based.

##### *Exclusion criteria*

- Studies that focus on health coaches as the primary intervention of focus. The role of the PN is distinctly different from a health coach, who focuses specifically on the person's behaviour change, by encouraging the development of sustainable healthy behaviours and attitudes, in the people with whom they work, for chronic disease management and prevention (Conn 2019).

We will not exclude studies on the basis of outcomes reported, and we will include studies that do not contain any outcome data.

#### Types of outcome measures

##### *Primary outcomes*

1. Self-reported quality of life, or self-reported health status (assessed in any way. For young children, or children who have developmental delays, this is likely to be a proxy-report, given by the primary caregivers)
2. Caregiver health, functioning and quality of life (assessed in any way)
3. Abuse of any kind against the young person, the siblings, family, or the patient navigator (physical, emotional, mental, or sexual)

##### *Secondary outcomes*

1. Hospitalisation rates
2. Rates of emergency department attendance
3. Resource use, defined by the use of healthcare staff time, resource facilities, and consumables.
4. Days of school, college, daycare missed

### Search methods for identification of studies

#### Electronic searches

The EPOC Information Specialist will develop the search strategies in consultation with the review authors.

We will search the Cochrane Database of Systematic Reviews (CDSR) and Epistemonikos (www.epistemonikos.org) for related systematic reviews. We will search the following databases for primary studies, from inception to the date of search.

- Cochrane Central Register of Controlled Trials (CENTRAL; latest issue), in the Cochrane Library;
- MEDLINE Ovid (1946 to date of search);
- Embase Ovid (1974 to date of search);
- CINAHL EBSCO (Cumulative Index to Nursing and Allied Health Literature; 1982 to date of search).

Search strategies will comprise keywords and controlled vocabulary terms. We will not apply any limits on language, and we

will search all databases from inception to the date of search. We will use a methodology search filter to limit retrieval to appropriate study designs. See Appendix 1 for the MEDLINE search strategy, which we will adapt for other databases.

### Searching other resources

#### *Trial registries*

- WHO ICTRP (World Health Organization International Clinical Trials Registry Platform; www.who.int/ictrp; to date of search).
- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov; to date of search).

#### *Grey literature*

We will search the grey literature to identify studies not indexed in the databases listed above.

- UK National Institute for Health Research (NIHR; / www.nihr.ac.uk; to date of search);
- Health Research Board (HRB; www.hrb.ie; to date of search);
- National Institute for Health and Clinical Excellence (NICE; www.nice.org.uk; to date of search);

We will also review reference lists of all included studies and relevant systematic reviews for additional potentially eligible primary studies. We will contact authors of included studies and reviews to clarify reported published information, and to seek unpublished results and data. We will contact researchers with expertise relevant to the review topic and EPOC interventions. We will conduct cited reference searches for all included studies in ISI Web of Knowledge, and screen individual journals (e.g. handsearch JAMA Pediatrics, Archives of Disease in Childhood and Lancet Pediatrics).

We will provide appendices for all strategies used, including a list of sources screened and relevant reviews and primary studies reviewed.

## Data collection and analysis

### Selection of studies

We will download all titles and abstracts, retrieved by electronic searching, to a reference management database and remove duplicates. Two review authors (RL and RK) will independently screen titles and abstracts for inclusion. We will retrieve the full-text study reports or publication, and two review authors (RL and RK) will independently screen the full text, identify studies for inclusion, and identify and record reasons for exclusion of the ineligible studies. We will resolve any disagreement through discussion, or, if required, we will consult a third review author (CG).

We will list studies that initially appeared to meet the inclusion criteria, but that we later excluded, in the 'Characteristics of excluded studies' table. We will collate multiple reports of the same study, so that each study, rather than each report, is the unit of interest in the review. We will also provide any information we can obtain about ongoing studies. We will record the selection process in sufficient detail to complete a PRISMA flow diagram (Liberati 2009).

### Data extraction and management

We will use the EPOC standard data collection form, and adapt it for study characteristics and outcome data (EPOC 2017a); we will pilot the form on at least one study in the review. We will review the economic evidence (including reported resource use) reported in the trials and assess the efficacy of the interevention of interest based on the Johanna Briggs Evidence of Implementation reporting guidelines (Gomersall 2015). Two review authors (RL and RK) will independently extract the following study characteristics from the included studies, and enter the data into Review Manager 5 (Review Manager 2020).

1. Methods: study design, number of study centres and location, study setting, withdrawals, date of study, follow-up
2. Participants: number, mean age, age range, sex, ethnicity, chronic disease diagnosis, diagnostic criteria, inclusion criteria, exclusion criteria, other relevant characteristics
3. Interventions: intervention components, comparison, fidelity assessment
4. Outcomes: main and other outcomes specified and collected, time points reported
5. Notes: funding for trial, notable conflicts of interest of trial authors, ethical approval

Two review authors (RK and RK) will independently extract outcome data from included studies. We will note in the 'Characteristics of included studies' table if outcome data were reported in an unusable way. We will resolve disagreements by consensus, or by involving a third review author (CG).

### Assessment of risk of bias in included studies

Two review authors (RL and RK) will independently assess risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* Section 8. 5 (Higgins 2011), and guidance from the EPOC group (EPOC 2017b). We will resolve any disagreements by discussion, or by involving a third review author (CG). We will assess the risk of bias according to the following domains.

1. Random sequence generation
2. Allocation concealment
3. Blinding of participants and personnel
4. Blinding of outcome assessment
5. Incomplete outcome data
6. Selective outcome reporting
7. Baseline outcomes measurement
8. Baseline characteristics
9. Other bias, including contamination (e.g. participants from same family in different treatment arms), null bias due to poorly delivered intervention of too broad inclusion criteria, post hoc intensification of intervention.

We will judge each potential source of bias as high, low, or unclear, and provide a quote from the study report together with a justification for our judgement in the risk of bias table. We will summarise the risk of bias judgements across different studies for each of the domains listed. We will assign an overall risk of bias assessment (high, moderate, or low) for each of the included studies, using the approach suggested in Chapter 8 of the *Cochrane*

*Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will consider studies with low risk of bias for all key domains (namely, blinding of outcome assessment, incomplete outcome data, and selective reporting), or where it seems unlikely that bias might seriously alter the results, to have a low risk of bias. We will consider studies, in which the risk of bias in at least one domain was unclear, or judged to have some bias that could plausibly raise doubts about the conclusions, to have an unclear risk of bias. We will consider studies with a high risk of bias in at least one domain, or judged to have serious bias that decreases the certainty of the conclusions, to have a high risk of bias.

We will consider blinding separately for different key outcomes,when necessary (e.g. for unblinded outcome assessment, risk of bias for caregiver health may be very different than for a patient reported pain scale). When information on risk of bias relates to unpublished data or correspondence with a trialist, we will note this in the risk of bias table.

We will not exclude studies on the grounds of their risk of bias, but will clearly report the risk of bias when presenting the results of the studies.

When considering treatment effects, we will take into account the risk of bias for the studies that contribute to that outcome.

We will conduct the review according to this published protocol, and report any deviations form it in the 'Differences between protocol and review' section of the systematic review.

### Measures of treatment effect

We will estimate the effect of the intervention using risk ratio or risk difference for dichotomous data, together with the appropriate associated 95% confidence interval, and mean difference or standardised mean difference for continuous data, together with the 95% appropriate associated confidence interval (Higgins 2020). We will ensure that an increase in scores for continuous outcomes can be interpreted in the same way for each outcome, explain the direction to the reader, and report when we reversed the directions, if this was necessary.

### Unit of analysis issues

We will include studies with a cluster design (i.e. where groups of individuals, rather than individuals, are randomised to different interventions) where the unit of allocation is the cluster or group. If we include studies with a cluster design, we will attempt to determine if the authors of these studies appropriately controlled for clustering effects in their analysis, to avoid ‘unit of analysis error’ (Whiting-O'Keefe 1984). If there is doubt, we will contact the authors for clarification. If cluster studies have been appropriately analysed to account for clustering in the data, we will extract direct measures of effect, if available, and use them in the meta-analyses, using the generic inverse-variance method.

We will include the first period of data only from cross-over studies, if these are available.

### Dealing with missing data

We will contact investigators in order to verify key study characteristics, and obtain missing outcome data when possible (e.g. when a study is identified as abstract only). We will try to compute missing summary data from other reported statistics. Whenever it is not possible to obtain data, we will report the level of missingness, and consider how that might impact the certainty of the evidence.

### Assessment of heterogeneity

If we find a sufficient number of studies, for which we judge participants, interventions and comparisons, and outcomes to be sufficiently similar, we will conduct a meta-analysis (Borenstein 2009). In each analysis, we will use the $I^2$ statistic to measure heterogeneity among the trials. A rough guide to interpretation in the context of meta-analyses of randomized trials is as follows:

0-40%: might be important

30-60%: may represent moderate heterogeneity*

50-90%: may represent substantial heterogeneity*

75-100%: considerable heterogeneity*

*the importance of $I^2$ depends on (1) magnitude and direction of effects, and (2) strength of evidence of heterogeneity (e.g. P value from the $Chi^2$ test, or a confidence interval for $I^2$: uncertainty in the value of $I^2$ is substantial when the number of studies is small) (Higgins 2020). If we identify substantial heterogeneity (50-90%), we will explore it with prespecified subgroup analysis.

### Assessment of reporting biases

We will attempt to contact study authors, asking them to provide missing outcome data. When this is not possible, and the missing data are thought to introduce serious bias, we will explore the impact of including such studies in the overall assessment of results**.** If we are able to pool more than 10 trials, we will create and examine a funnel plot, to explore possible publication biases, interpreting the results with caution (Sterne 2011).

### Data synthesis

We will undertake meta-analyses only when this is meaningful, i.e. if the treatments, participants, and the underlying clinical question are similar enough for pooling to make sense (Borenstein 2009). A common way that trialists indicate they have skewed data, is by reporting medians and interquartile ranges. When we encounter this, we will note that the data are skewed and consider the implications of this. Where multiple trial arms are reported in a single trial, we will include only the relevant arms. If two comparisons (e.g. intervention A versus usual care and intervention B versus usual care) must be entered into the same meta-analysis, we will halve the control group to avoid double-counting.

If it is not possible to undertake a quantitative synthesis of the results, we will undertake non-quantitative synthesis using the most appropriate, acceptable alternative option (summarising effect estimates, combining P values, or vote counting based on direction of effect) suggested in Chapter 12 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2020).

### Subgroup analysis and investigation of heterogeneity

For this review, if there is heterogeneity in a sufficient number of studies that have similar outcomes and comparison groups, we will

perform a subgroup analysis for the following factors, which may potentially moderate the effect of the intervention:

1. Age: will divide into children (0 to 9 years, inclusive) and adolescents (10 to 18 years, inclusive (WHO 2020)). We hypothesise that PN effects will be more pronounced in young children, given that the intervention in this age group will more likely target the family as a unit (rather than the child as an individual).
2. Ethnicity: will divide into minority versus non-minority groups (minority groups will be defined as a minority group for the region or country in which the study was undertaken). Minority groups (including Indigenous Peoples) are a vulnerable cohort, who are more likely to belong to a lower socioeconomic group, have poorer health literacy, and experience language and cultural barriers, which affect their access to appropriate and timely health care (Natale-Pereira 2011). For this reason, we hypothesise that this subgroup may be more responsive to a PN intervention.
3. Cancer versus non-cancer diagnosis: we hypothesise that children and adolescents with a cancer diagnosis generally have significant healthcare burdens, which require multiple specialist medical reviews, and intensive in-hospital care. These young people may experience larger benefit from a PN than a young person with a non-cancer diagnosis.
4. Care setting for PN intervention (hospital versus community)
5. Traditional versus non-traditional family units (traditional refers to a nuclear family, and non-traditional incorporates all other variations)
6. Sex of the patient

We will apply a test for interaction to test for statistically significant differences between subgroups.

### Sensitivity analysis

We will conduct these sensitivity analyses to assess the robustness of our conclusions, and explore its impact on effect sizes.

1. Restricting the analysis to published studies
2. Restricting the analysis to studies with a low risk of bias

#### *Stakeholder consultation and involvement*

Chandana Guha (CG) is a consumer representative and research assistant at the Centre for Kidney Research (Westmead, Sydney) and is currently enrolled as a PhD student with the University of Sydney. CG is also the mother of a child with a serious chronic disease and has over twenty-five years of experience navigating complex health systems. She will provide firsthand insight into what families and consumers value. CG has been involved in the conception and drafting of this protocol and will be an active part of the systematic review (3rd author).

### Summary of findings and assessment of the certainty of the evidence

Two review authors will independently assess the certainty of the evidence (high, moderate, low, and very low), using the five GRADE considerations (risk of bias, consistency of effect, imprecision, indirectness, and publication bias (Guyatt 2008)). We will GRADE our top 7 outcomes of interests. We will assess blinding in accordance to the Cochrane risk of bias. We acknowledge some of our outcomes are likely to be 'subjective'. In that case, the lack of outcome assessment blinding will be consider as 'high risk of bias.

We will use methods and recommendations described in both Section 8.5 of the *Cochrane Handbook for Systematic Reviews of interventions* (Higgins 2011), Chapter 14 of the *Cochrane Handbook for Systematic Reviews of interventions* (Higgins 2020), the EPOC worksheets (EPOC 2017c), and GRADEpro GDT software (GRADEpro GDT). We will resolve disagreements on certainty ratings by discussion, provide justification for decisions to down- or upgrade the ratings using footnotes in the table, and provide comments to aid readers' understanding of the review, when necessary. We will use plain language statements to report these findings in the review (EPOC 2017c).

We will summarise the findings in a summary of findings table(s) for the main intervention comparison(s), and include the most important outcomes including:

1. Self-reported quality of life, or self-reported health status
2. Caregiver health, functioning, and quality of life
3. Abuse of any kind against the patient, the siblings, family, or the patient navigator (physical, emotional, mental or sexual)
4. Hospitalisation rates
5. Rates of emergency department attendance
6. Resource use, defined by the use of healthcare staff time, resource facilities, and consumables
7. Days of school, college, daycare missed

If during the review process, we become aware of an important outcome that we failed to list in our planned summary of findings table, we will include the relevant outcome in lieu of the outcome 'days of school/college/day-care missed' and explain the reasons for this in the section 'Differences between protocol and review'.

We will consider whether there is any additional outcome information that was not able to be incorporated into meta-analyses and note this in the comments and state if it supports or contradicts the information from the meta-analyses. If it is not possible to meta-analyse the data we will summarise the results in the text.

## ACKNOWLEDGEMENTS

We acknowledge the help and support of Cochrane Effective Practice and Organisation of Care (EPOC). The authors would also like to thank the following editors and peer referees who provided comments to improve the protocol: Noah Ivers (Contact editor), Christian Mansilla (Associate editor), JC Han (Managing editor), Paul Miller (Information specialist), Virginia Minogue (Consumer reviewer), Jennifer LaRosa (Consumer reviewer), Barbara Giambra (Context expert reviewer), Susan Samuel (Context expert reviewer) and Victoria Pennick, for copy-editing the protocol.

National Institute for Health Research (NIHR), via Cochrane Infrastructure funding to the Effective Practice and Organisation of Care (EPOC) Group. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, National Health Service (NHS), or the Department of Health.

The Australasian Satellite of the Cochrane EPOC Group is funded by Cochrane, and receives infrastructure support from Monash University, Monash Department of Clinical Epidemiology - Cabrini.

# REFERENCES

## Additional references


### Australian Institute of Health and Welfare 2020

Australian Institute of Health and Welfare, Australian Government. Chronic disease. www.aihw.gov.au/reports-data/health-conditions-disability-deaths/chronic-disease/overview September 2020.

### Bennett 1994

Bennett DS. Depression among children with chronic medical problems: a meta-analysis. *Journal of Pediatric Psychology* 1994;**19**(2):149-69.

### Borenstein 2009

Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. When does it make sense to perform a meta-analysis? In: Introduction to Meta-Analysis. Chichester, UK: John Wiley & Sons, Ltd, 2009.

### Bregnballe 2007

Bregnballe V, Thastum M, Schiotz PO. Psychosocial problems in children with cystic fibrosis. *Acta Paediatrica* 2007;**96**(1):58-61.

### Callahan 2001

Callahan ST, Winitzer RF, Keenan P. Transition from pediatric to adult-oriented health care: a challenge for patients with chronic disease. *Current Opinion in Pediatrics* 2001;**13**(4):310-6.

### Carroll 2010

Carroll J, Humiston S, Meldrum S, Salamone C, Jean-Pierre P, Epstein R, et al. Patients' experiences with navigation for cancer care. *Patient Education and Counselling* 2010;**80**(2):241-7. [DOI: 10.1016/j.pec.2009.10.024]

### Carter 2018

Carter N, Valaitis RK, Lam A, Feather J, Nicholl J, Cleghorn L. Navigation delivery models and roles of navigators in primary care: a scoping literature review. *BMC Health Services Research* 2018;**18**(1):1-3. [DOI: 10.1186/s12913-018-2889-0]

### Caskey 2019

Caskey R, Moran K, Touchette D, Martin M, Munoz G, Kanabar P, et al. Effect of comprehensive care coordination on medicaid expenditures compared with usual care among children and youth with chronic disease: a randomized clinical trial. *JAMA Network Open* 2019;**2**(10):e1912604.

### CDC 2021

Centers for Disease Control and Prevention. National Centre for Chronic Disease Prevention and Health Promotion - about chronic disease. www.cdc.gov/chronicdisease/about/index.htm (accessed 12 January 2021).

### Chu 2015

Chu PY, Maslow GR, von Isenburg M, Chung RJ. Systematic review of the impact of transition interventions for adolescents with chronic illness on transfer from pediatric to adult healthcare. *Journal of Pediatric Nursing* 2015;**30**(5):e19-27. [DOI: 10.1016/j.pedn.2015.05.022]

### Cohen 2018

Cohen S, Earing MG. Neurocognitive impairment and Its long-term impact on adults with congenital heart disease. *Progress in Cardiovascular Diseases* 2018;**61**(3-4):287-93.

### Conn 2019

Conn S, Curtain S. Health coaching as a lifestyle medicine process in primary care. *Australian Journal of General Practitioners* 2019;**48**(10):677-80.

### Council on Community Pediatrics 2016

Council on Community Pediatrics. Poverty and child health in the United States. Pediatrics 2016;**137**(4):e20160339. [DOI: https://doi.org/10.1542/peds.2016-0339]

### Desveaux 2019

Desveaux L, McBrien K, Barnieh L, Ivers N. Mapping variation in intervention design: a systematic review to develop a program theory for patient navigator programs. *Systematic Reviews* 2019;**8**(1):1-14. [DOI: https://doi.org/10.1186/s13643-018-0920-5]

### Dohan 2005

Dohan D, Schrag D. Using navigators to improve care of underserved patients: current practices and approaches. *Cancer* 2005;**104**(4):848-55. [DOI: 10.1002/cncr.21214]

### EPOC 2017a

Cochrane Effective Practice and Organisation of Care (EPOC). Data collection form. EPOC resources for review authors, 2017. Available from epoc.cochrane.org/epoc-specific-resources-review-authors (accessed 2 February 2021).

### EPOC 2017b

Cochrane Effective Practice and Organisation of Care (EPOC). Suggested risk of bias criteria for EPOC reviews. EPOC resources for review authors, 2017. Available from epoc.cochrane.org/epoc-specific-resources-review-authors (accessed 2 February 2021).

### EPOC 2017c

Cochrane Effective Practice and Organisation of Care (EPOC). EPOC worksheets for preparing a summary of findings table using GRADE. EPOC resources for review authors, 2017. Available from epoc.cochrane.org/epoc-specific-resources-review-authors (accessed 3 February 2021).

### Feinberg 2016

Feinberg E, Abufhele M, Sandler J, Augustyn M, Cabral H, Chen N, et al. Reducing disparities in timely autism diagnosis through family navigation: results from a randomized pilot trial. *Psychiatric Services* 2016;**67**(8):912-5. [DOI: 10.1176/appi.ps.201500162]

### Francis 2019

Francis A, Didsbury MS, van Zwieten A, Chen K, James LJ, Kim S, et al. Quality of life of children and adolescents with chronic kidney disease: a cross-sectional study. *Archives of Disease in Childhood* 2019;**104**:134-40. [10.1136/archdischild-2018-314934]

**Freeman 2005**

Freeman HP, Chu KC. Determinants of cancer disparities: barriers to cancer screening, diagnosis, and treatment. *Surgical Oncology Clinics of North America* 2005;**14**(4):655-9.

**Gomersall 2015**

Gomersall JS, Jadotte YT, Xue Y, Lockwood S, Riddle D, Preda A. Conducting systmatic reviews of economic evaluations. *International Journal of Evidence-Based Healthcare* Septmeber;**13**(3):170-8. [DOI: 10.1097/XEB.0000000000000063]

**Gottlieb 2016**

Gottlieb LM, Hessler D, Long D, Laves E, Burns AR, Amaya A, et al. Effects of social needs screening and in-person service navigation on child health: a randomized clinical trial. *JAMA Pediatrics* 2016;**170**(11):e162521.

**GRADEpro GDT [Computer program]**

McMaster University (developed by Evidence Prime) GRADEpro GDT. Version accessed 6 March 2020. Hamilton (ON): McMaster University (developed by Evidence Prime). Available at gradepro.org.

**Guyatt 2008**

Guyatt GH, Oxman AD, Vist G, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al, GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;**336**(7650):924-6.

**Higgins 2011**

Higgins JPT, Altman DG, Sterne JAC (editors). Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S, editor(s). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.handbook.cochrane.org.

**Higgins 2020**

Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al, editor(s). Cochrane Handbook for Systematic Reviews of Interventions version 6.1 (updated September 2020). Cochrane, 2020. Available from training.cochrane.org/handbook/archive/v6.1.

**Jandorf 2013**

Jandorf L, Stossel L, Cooperman L, Graff Zivin J, Ladabaum J, Hall U, et al. Cost analysis of a patient navigation system to increase screening colonoscopy adherence among urban minorities. *Cancer* 2013;**119**(3):612-20.

**Kelly 2015**

Kelly E, Ivers N, Zawi R, Barnieh L, Manns B, Lorenzetti DL, et al. Patient navigators for people with chronic disease: protocol for a systematic review and meta-analysis. *Systematic Reviews* 2015;**4**(1):1-6.

**Kelly 2019**

Kelly K, Doucet S, Luke A. Exploring the roles, functions, and background of patient navigators and case managers: a scoping review. *International Journal of Nursing Studies* 2019;**98**:27-47. [DOI: 10.1016/j.ijnurstu.2019.05.016]

**Krieger 2009**

Krieger J, Takaro T, Song L, Beaudet N, Edwards K. A randomized controlled trial of asthma self-management support comparing clinic-based nurses and in-home community health workers: the Seattle–King County healthy homes II project. *Archives of Pediatrics & Adolescent Medicine* 2009;**163**(2):141-9.

**Lähteenmäki 2004**

Lähteenmäki PM, Sjöblom J, Korhonen T, Salmi TT. The siblings of childhood cancer patients need early support: a follow up study over the first year. *Archives of Disease in Childhood* 2004;**89**(11):1008-13.

**Liberati 2009**

Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Medicine* 2009;**6**(7):e1000100.

**Mackie 2018**

Mackie AS, Rempel GR, Kovacs AH, Kaufman M, Rankin KN, Jelen A, et al. Transition intervention for adolescents with congenital heart disease. *Journal of the American College of Cardiology* 2018;**71**(16):1768-77. [DOI: 10.1016/j.jacc.2018.02.043]

**Marmot 2012**

Marmot M, Bell R. Fair society, healthy lives. *Public Health* 2012;**126**(Suppl 1):s4-10.

**McBrien 2018**

McBrien KA, Ivers N, Barnieh L, Bailey JJ, Lorenzetti DL, Nicholas D, et al. Patient navigators for people with chronic disease: a systematic review. *PLoS One* 2018;**13**(2):e0191980. [DOI: 10.1371/journal.pone.0191980]

**McDonald 2004**

McDonald SP, Craig JC, the Australian and New Zealand Paediatric Nephrology Association. Long-term survival of children with end-stage renal disease. *New England Journal of Medicine* 2004;**350**(26):2654-62. [DOI: 10.1056/NEJMoa031643]

**Medway 2015**

Medway M, Tong A, Craig JC, Kim S, Mackie F, McTaggart S, et al. Parental perspectives on the financial impact of caring for a child with CKD. *American Journal of Kidney Diseases* 2015;**65**(3):384-93.

**Morgan 2013**

Morgan S, Rahman C, Alqatari A, Pines M, Jesse M. Non-emergency department interventions to reduce ED utilization: a systematic review. *Academic Emergency Medicine* 2013;**20**(10):969-85.

**Natale-Pereira 2011**

Natale-Pereira A, Enard KR, Nevarez L, Jones LA. The role of patient navigators in eliminating health disparities. *Cancer* 2011;**117**(15):3543-52.

**Pantell 2020**

Pantell MS, Hessler D, Long D, Alqassari M, Schudel C, Laves E, et al. Effects of in-person navigation to address family social needs on child health care utilization: a randomized clinical trial. JAMA Network Open 2016 Nov 7 [Epub ahead of print];**3**(6):e206445. [DOI: 10.1001/jamanetworkopen.2020.6445]

**Perrin 2014**

Perrin J, Anderson E, Van Cleave J. The rise in chronic conditions among young infants, children and youth can be met with continued health system innovations. *Health Affairs* 2014;**33**(12):2099-2105. [DOI: 10.1377/hlthaff.2014.0832]

**Petereit 2008**

Petereit DG, Molloy K, Reiner ML, Helbig P, Cina K, Miner R, et al. Establishing a patient navigator program to reduce cancer disparities in the American Indian communities of Western South Dakota: initial observations and results. *Cancer Control* 2008;**15**(3):254-9.

**Quittner 2008**

Quittner AL, Barker DH, Snell C, Grimley ME, Marciel K, Cruz I. Prevalence and impact of depression in cystic fibrosis. *Current Opinion in Pulmonary Medicine* 2008;**14**(6):582-8.

**Resnick 2009**

Resnick E, Bishop M, O'Connell A, Hugo B, Isern G, Timm A, Ozonoff A, Geller A. The CHEER study to reduce BMI in elementary school students: a school-based, parent-directed study in Framingham, Massachusetts. *Journal of School Nursing* 2009;**25**(5):361-72.

**Review Manager 2020 [Computer program]**

The Cochrane Collaboration Review Manager 5 (RevMan 5). Version 5.4. The Cochrane Collaboration, 2020.

**Rodriguez-Torres 2019**

Rodriguez-Torres SA, McCarthy AM, He W, Ashburner JM, Percac-Lima S. Long-term impact of a culturally tailored patient navigation program on disparities in breast cancer screening in refugee women after the program's end. *Health Equity* 2019;**3**(1):205-10.

**Simon 2017**

Simon TD, Whitlock KB, Haaland W, Wright DR, Zhou C, Neff J, et al. Effectiveness of a comprehensive case management service for children with medical complexity. *Pediatrics* 2017;**140**(6):e20171641. [DOI: 10.1542/peds.2017-1641]

**Smith 2017**

Smith LR, Clayton ML, Woodell C, Mansfield C. The role of patient navigators in improving caregiver management of childhood asthma. Research Triangle Park (NC): RTI Press 2017. [DOI: 10.3768/ rtipress.2017.rr.0030.1704] [PMID: 30354041]

**Spencer 2018**

Spencer MS, Kieffer EC, Sinco B, Piatt G, Palmisano G, Hawkins J, et al. Outcomes at 18 months from a community health worker and peer leader diabetes self-management program for Latino adults. *Diabetes Care* 2018;**41**(7):1414-22. [DOI: 10.2337/dc17-0978]

**Sterne 2011**

Sterne JA, Sutton AJ, Ioannidis JP, Terrin N, Jones DR, Lau J, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ* 2011;**343**:d4002. [DOI: 10.1136/bmj.d4002]

**Stoll 2010**

Stoll BJ, Hansen NI, Bell EF. Neonatal outcomes of extremely preterm infants from the NICHD neonatal research network. *Pediatrics* 2010;**126**(3):443-56.

**Thom 2013**

Thom DH, Ghorob A, Hessler D, De Vore D, Chen E, Bodenheimer TA. Impact of peer health coaching on glycemic control in low-income patients with diabetes: a randomized controlled trial. *The Annals of Family Medicine* 2013;**11**(2):137-44.

**Tsai 2006**

Tsai TC, Liu SI, Tsai JD, Chou LH. Psychosocial effects on caregivers for children on chronic peritoneal dialysis. *Kidney International* 2006;**70**(11):1983-7.

**Van Cleave 2010**

Van Cleave J, Gortmaker SL, Perrin JM. Dynamics of obesity and chronic health conditions among children and youth. *JAMA* 2010;**303**(7):623-30. [DOI: 10.1001/jama.2010.104]

**Wells 2008**

Wells KJ, Battaglia TA, Dudley DJ, Garcia R, Greene A, Calhoun E, et al. Patient Navigation Research Program. Patient navigation: state of the art or is it science? *Cancer* 2008;**113**(8):1999-2010.

**Whiting-O'Keefe 1984**

Whiting-O'Keefe Q, Henke C, Simborg D. Choosing the correct unit of analysis in medical care experiments. *Medical Care* 1984;**22**(12):1101-14.

**WHO 2018**

World Health Organization. Standards for improving the quality of care for children and young adolescents in health facilities. available from www.who.int/maternal_child_adolescent/documents/quality-standards-child-adolescent/en/ 2018. [ISBN: 978 92 4 156555 4]

**WHO 2019**

World Health Organization. Integrated chronic disease prevention and control. available from www.who.int/chp/about/integrated_cd/en (accessed 3 January 2020).

**WHO 2020**

World Health Organization. Adolescent health. available from www.who.int/southeastasia/health-topics/adolescent-health (accessed 2 September 2020).

**Wiljaars 2016**

Wijlaars LPMM, Gilbert R, Hardelid P. Chronic conditions in children and young people: learning from administrative data. *Archives of Disease in Childhood* 2016;**101**(10):881-5.

**Wilson 2019**

Wilson T, Zhao Y, Condon J. Limited progress in closing the mortality gap for Aboriginal and Torres Strait Islander Australians of the Northern Territory. *Australian and New Zealand Journal of Public Health* 2019;**43**(4):340-5.

## APPENDICES

### Appendix 1. MEDLINE search strategy

Medline OVID, including Epub Ahead of Print, In-Process, & Other Non-Indexed Citations (1946 to present)

Search date: 5 May 2020

| No. | Search terms |
|---|---|
| 1 | chronic disease/ |
| 2 | health services for persons with disabilities/ |
| 3 | ((complex* or chronic* or rare or severe) adj2 (disease? or ill* or need? or problem? or condition?)).ti,ab,kf. |
| 4 | adolescent health services/ |
| 5 | transition to adult care/ |
| 6 | diabetes mellitus, type 1/ |
| 7 | diabet*.ti,ab,kf. |
| 8 | exp asthma/ |
| 9 | asthma*.ti,ab,kf. |
| 10 | exp cystic fibrosis/ |
| 11 | cystic fibrosis.ti,ab,kf. |
| 12 | pediatric obesity/ or obesity/ or overweight/ |
| 13 | (obese or obesit* or over weight or overweight).ti,ab,kf. |
| 14 | cerebral palsy.ti,ab,kf. |
| 15 | cerebral palsy/ |
| 16 | anemia, sickle cell/ |
| 17 | sickle cell.ti,ab,kf. |
| 18 | exp neoplasms/ |
| 19 | (neoplasm? or cancer?).ti,ab,kf. |
| 20 | or/1-19 |

*(Continued)*

| | |
|---|---|
| 21 | exp adolescent/ |
| 22 | exp child/ |
| 23 | exp infant/ |
| 24 | (adolescen* or babies or baby or boy? or boyhood or girlhood or child* or girl? or infan* or juvenil* or kid? or minors or minors* or neonat* or neo-nat* or newborn* or new-born* or paediatric* or peadiatric* or pediatric* or perinat* or preschool* or puber* or pubescen* or school* or teen* or toddler? or underage? or under-age? or youth*).ti,ab,kf. |
| 25 | (pediatric* or paediatric* or infan* or child* or adolescen* or young).jn,jw. |
| 26 | (parent? or mother? or father? or family or families or carer?).ti,ab,kf. |
| 27 | or/21-26 |
| 28 | case managers/ |
| 29 | case management/ |
| 30 | patient navigation/ |
| 31 | patient-centered care/ |
| 32 | transitional care/ |
| 33 | mentors/ |
| 34 | ((patient or care or healthcare or service? or communit* or system? or personal) adj3 navigat*).ti,ab,kf. |
| 35 | ((care or healthcare or management) adj2 (coordinat* or co-ordinat*)).ti,ab,kf. |
| 36 | (team* adj2 (care or healthcare or treat* or assess* or consult* or program* or intervention?)).ti,ab,kf. |
| 37 | ((phone or telephone) adj2 follow*).ti,ab,kf. |
| 38 | ((integrat* or coordinat* or co-ordinat* or collaborat* or cooperat* or co-operat*) adj2 (care or healthcare or intervention? or program* or service? or system?)).ti,ab,kf. |
| 39 | (communit* and navigat*).ti,ab,kf. |
| 40 | ((care or healthcare) adj2 ambassador?).ti,ab,kf. |
| 41 | ((parent? or healthcare or care or mother? or father?) adj3 mentor?).ti,ab,kf. |
| 42 | ((family or families) adj2 (care or healthcare or intervention? or program* or service? or system?)).ti,ab,kf. |
| 43 | (transition* adj2 (plan? or planning or planned or coordinat* or co-ordinat* or care or healthcare or program* or intervention?)).ti,ab,kf. |
| 44 | or/28-43 |

*(Continued)*

| | |
|---|---|
| 45 | exp randomized controlled trial/ |
| 46 | controlled clinical trial.pt. |
| 47 | randomi#ed.ti,ab. |
| 48 | placebo.ab. |
| 49 | randomly.ti,ab. |
| 50 | clinical trials as topic.sh. |
| 51 | trial.ti. |
| 52 | or/45-51 |
| 53 | exp animals/ not humans/ |
| 54 | 52 not 53 |
| 55 | 20 and 27 and 44 and 54 |

## CONTRIBUTIONS OF AUTHORS

Conceiving the protocol: (RL, AF, DJ, GW)

Designing the protocol: (RL, AF, CG, RK, DJ, GW)

Co-ordinating the protocol: (RL, AF, DJ, GW)

Designing search strategies: (RL, AF, DJ, GW)

Writing the protocol: (RL, AF, DJ, GW)

Providing general advice on the protocol: (CG, RK)

Securing funding for the protocol: (RL, DJ, GW)

## DECLARATIONS OF INTEREST

- Rowena Lalji: none known
- Anna Francis: none known
- Chandana Guha: none known
- Rabia Khalid: none known
- David Johnson: none known
- Germaine Wong: none known

## SOURCES OF SUPPORT

### Internal sources

- Centre for Kidney Research , Australia

  Infrastructure and practical support
- Metro South Integrative Nephrology and Transplant Services (MINTS), Princess Alexandra Hospital Brisbane, Australia

  Infrastructure support

**External sources**

- Monash University, Monash Department of Clinical Epidemiology - Cabrini, Australia

  Infrastructure support
- Beat-CKD, Australia

  Research scholarship 2019 for RL
- Royal Australasian College of Physicians, Australia

  Jacquot Scholarship 2020 & 2021 for RL
- Australian National Health and Medical Research Council (NHMRC), Australia

  DJ and GW both currently receive reserach grants from NHMRC
- Industry funding, Australia

  DJ has received funding from Astra-Zeneca, Ono, AWAK, Baxter and Amgen
- Royal Australasian College of Physicians, Australia

  Research grant 2021 for AF

## NOTES

This protocol is based on standard text and guidance provided by Cochrane Effective Practice and Organisation of Care (EPOC).