Medication support interventions and strategies for people with learning disabilities - a mixed methods evidence synthesis

Review protocols

Dr Julia Gauly, Iman Ghosh, Anna Brown, Danielle Adams, Daniel Sutherland, Dr Samantha Flynn, Kerry Martin, Stephen Patterson, David Mahon, Dr Peter Auguste, Dr Samuel Tromans, Prof Paramjit Gill, Prof Eddie Chaplin, Prof Peter Langdon, Prof Kate Seers, Dr Yen-Fu Chen

Version	2.1
Date	6 October 2024
Project duration	Start date 1 September 2022; End date 31 December 2024 (28 months)
Summary	This document contains the registered protocols for the four component reviews of the mixed methods evidence synthesis. The four component reviews are: • Issues related to medication usage experienced by people with a learning disability and their carers and interventions to address them: A scoping review Registration: Open Science Framework osf.io/frm6d • The challenges of using and managing medications: A meta-ethnography looking at the experiences and perceptions of people with a learning disability and their carers Registration: PROSPERO CRD42022362903 • The effectiveness and cost-effectiveness of interventions designed to support people with a learning disability and their carers to optimise their medication usage: A quantitative systematic review Registration: PROSPERO CRD42022363024 • The feasibility, acceptability, uptake and barriers and facilitators of implementation for interventions designed to optimise medication use for people with a learning disability: A mixed methods systematic review Registration: PROSPERO CRD42022362998
Changes from previous versions	Version 2.1 was an updated version from Version 2.0 with changes made to reflect the contract variation approved by the NIHR in September 2024 to further extend the project end date to 31 December 2024 and the corresponding changes in timelines for the expected completion of component reviews. Version 2.0 was an updated version from Version 1.0 with changes made to reflect: (1) the contract variation approved by the NIHR in February 2024 to extend the project end date to 30 June 2024 and corresponding changes in timelines for the expected completion of component reviews; (2) changes in project personnel and in the name of affiliated institution; (3) corrections to reference lists; (4) correction to the wording of project title and addition of project start and end dates.

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Issues related to medication usage experienced by people with a learning disability and their carers and interventions to address them: A scoping review

Dr Julia Gauly, Iman Ghosh, Anna Brown, Danielle Adams, Daniel Sutherland, Dr Samantha Flynn, Kerry Martin, Stephen Patterson, David Mahon, Dr Peter Auguste, Dr Samuel Tromans, Prof Paramjit Gill, Prof Eddie Chaplin, Prof Peter Langdon, Prof Kate Seers, Dr Yen-Fu Chen

Version & date

Version 2.1, 6 October 2024

Background

People with a learning disability might have some difficulty in understanding complicated information, learning certain skills, and/or looking after themselves or living alone (1). A learning disability is defined by three core criteria: lower intellectual ability (usually defined as an IQ of less than 70), significant impairment of social or adaptive functioning and onset in childhood (2). Terminology used to describe a learning disability varies over time and by geographical location. The term 'learning disability' is the preferred term used in the UK including governmental documents and official guidelines. For this project, we will adopt this preferred term and follow recommendations made by the NHS England for the choice of words to describe people with a learning disability (3). Internationally, the alternative term 'intellectual disability' has been widely used and is adopted in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-V) (4). The International Classification of Diseases 11th Revision (ICD-11) uses a slightly different term 'disorder of intellectual development'. Historically, the term 'mental retardation' was used in DSM-IV and ICD-10 and older literature (4).

People with a learning disability often require medications for their chronic conditions, mental health issues or challenging behaviour (5)(6). A large population-based study

indicated that the mean number of conditions is as high as 11 and the prevalence of multiple long-term chronic health conditions (MLTC) is 98.7% (6). Adhering to medication as prescribed can be challenging for various reasons related to their disability and a lack of support and reasonable adjustments. Likewise, being exposed to under- and overprescribing of medication can be a challenge experienced by people with a disability and their carers. A high proportion of people with learning disabilities further receive psychotropic medications (7). Many of these people receive them for behavioural issues, even though the medications have not been indicated for this use (7). Additionally, diagnostic overshadowing is increasingly recognised to contribute to health inequalities experienced by people with a learning disability (8). Diagnostic overshadowing refers to when symptoms arising from physical or mental health problems are wrongly attributed to learning disability, leading to delayed diagnosis and treatment (9). A recent scoping review further showed that people with a learning disability often lack understanding of their medication, including its name, purpose and when and how to take it (10). Lack of routine monitoring of prescribed medication and follow-up; and issue of administration and storage of prescribed medication are further potential problems that people with a learning disability may encounter.

This scoping review aims to explore what research has been conducted on issues related to medication usage experienced by people with a learning disability and their carers, and strategies and interventions that have been proposed or evaluated to address these issues. This scoping review is part of a larger mixed methods evidence synthesis project on interventions to promote the optimal use and management of medication for people with a learning disability. The findings of this scoping review will be fed into and subsequently integrated with the findings of the wider project (which includes a meta-ethnography of medication use issues; a quantitative review of intervention effectiveness and cost-effectiveness; and a mixed methods review of feasibility, acceptability, uptake, and facilitators and barriers of intervention implementation) using the Pillar Integration Process (11) or Metrices (12–14) in order to develop recommendations on what interventions have been shown to be effective and cost-effective, and how interventions need to be designed to support people with a learning disability and their carers to optimise their use of medications.

Patient and public involvement (PPI)

We aim to co-produce this study protocol and the protocols of the other components of the broader evidence synthesis (mixed methods review; meta-ethnography; quantitative review) with people with a learning disability, their family and carers and health and social care professionals working with them. We will therefore establish two PPI groups to facilitate the co-production process: a Learning Disability PPI Group which consists of members of people with a learning disability and a Stakeholder PPI Group which includes family members and health and social care professionals who care for or work with people with a learning disability. In addition, we will also establish a Project Advisory Group which includes two members of people with a learning disability and other stakeholders to advise on practical challenges and provide strategic guidance for this evidence synthesis.

Our PPI lead (DM) will work with the two PPI Groups to obtain their feedback on our project scope and terminologies used in the protocol. We will also share the protocols with our Project Advisory Group and ask for their feedback. Further inputs will be sought from the Project Advisory Group and the PPI Groups throughout the process of our project. These include verifying the comprehensiveness of our literature search in terms of type of literature and topic areas covered; helping with making sense of our initial review findings; formulating practice and research recommendations based on review findings; and creating materials to facilitate dissemination.

Review Question

- What research has been conducted in order to understand issues faced by people with a learning disability in relation to their medication usage, and what interventions have been proposed or evaluated to address these issues?

Aim and Objectives:

Aim:

- To gauge the volume and nature of research that has been conducted in order to understand what issues people with a learning disability face in relation to their medication used, and how the medication usage can be optimised

Objectives:

- To identify literature exploring issues related to medication usage for people with a learning disability and interventions to address these issues
- To explore the volume and nature of the body of literature by charting key characteristics of identified studies

Design of the review

This scoping review will follow the Joanna Briggs Institute's guidance (15) on undertaking a scoping review and will be reported in accordance with the PRISMA Extension for Scoping Reviews (PRISMA-ScR). (16) This protocol will be registered with the Open Science Framework (OSF).

Searches

The electronic databases MEDLINE All (via Ovid), Embase (Ovid), CINAHL (EbscoHost), Science, Social Science and Conference Proceedings Citation Indices (Web of Science), Cochrane Library (all databases, via Wiley) and PsycINFO (Ovid) will be searched, from database inception to the current issue. Grey literature will be identified via internet (Google) searches, ProQuest Dissertations & Theses database, proceedings of selected conferences of interest and websites of relevant organisations.

Search strategies will be developed by an information specialist (AB) in collaboration with other members of the project team, and will be informed by previous reviews in the field and guided by the approach described in the Cochrane handbook (17). Searches will combine keywords and, where appropriate, thesaurus (e.g., MeSH, EMTREE) terms, and will be based around the concepts of learning disabilities and medicines optimisation (to include (non-)adherence, compliance, persistence, usage, self-administration, self-management, medicines management, prescribing appropriateness, knowledge and understanding of medication). No language restrictions, date limits or study type filters (other than the exclusion of animal studies, where appropriate) will be applied. The search strategy will initially be developed in Ovid MEDLINE; a draft MEDLINE search strategy is

provided in Appendix 1. This will be peer reviewed by another information specialist not otherwise involved in the project, before being adapted for other databases/interfaces.

Reference lists of included studies and a selection of recent, relevant systematic reviews will be checked. Forwards citation tracking from key publications of included studies (to identify citing papers) will also be undertaken. Supplemental searches will be developed iteratively, as additional search terms, concepts and sources are identified; these may include specific projects, interventions, key authors, theories or organisations.

Types of study to be included

Inclusion Criteria:

- Qualitative, quantitative and/or mixed methods studies reporting empirical evidence
- Systematic reviews
- Studies published in English (or with available English translation). A record will be kept for potentially relevant studies published in non-English language to ensure that no important topics are neglected due to the language restriction
- Studies which give insight into issues hindering the optimisation of medication usage for people with a disability and/or interventions to address these issues
- Studies from Low- and middle-income countries (LMIC) will be included when considered applicable to the UK (this will be assessed by two researchers, and disputes resolved by third person, a senior researcher)

Exclusion:

- Studies which do not provide insight into issues related to the optimisation of medication usage for people with a learning disability and/or interventions to address these issues
- Studies exclusively focusing on individual conditions such as autism and epilepsy without referring to learning disability

- Studies from low- and middle-income countries (LMIC) will be excluded when considered not applicable to the UK (this will be assessed by two researchers, and disputes resolved by third person, a senior researcher)

Condition or domain being studied

- People with a learning disability and a physical long-term condition (e.g. diabetes, chronic obstructive pulmonary disease, arthritis, hypertension) for which there is currently no cure, and which are managed with drugs or other treatment
- People with a learning disability and mental health issues and/or challenging behaviour for which medication is prescribed

Participants/population

Children, adolescents and adults with a learning disability and carers of people with a learning disability. A learning disability is defined by three core criteria as mentioned earlier (2).

We will not include populations which have what is defined in the United Kingdom as learning difficulty (e.g., dyslexia, agraphia, dyscalculia). We will also not include populations which have autism or attention deficit hyperactivity disorder (ADHD) or epilepsy but no learning disability.

Intervention(s), exposure(s)

Issues faced by people with a learning disability in relation to medication usage; strategies/interventions that are developed to support people with a learning disability and their carers to optimise the usage of medications required for their chronic condition, mental health issues or challenging behaviour.

Comparator(s)/control

Studies that are comparing strategies to support people with a learning disability to use and manage their medications; but also studies with no comparator will be included.

Context

This scoping review will provide an overview of the research looking at issues hindering optimisation of medication usage for people with a learning disability and interventions to address these issues.

Main outcome

- Experiences and perceptions of people with a learning disability regarding issues hindering the optimal use and management of medications (e.g. non-adherence to medication for long-term conditions, mental health issues and challenging behaviour; under or over-prescribing of medications; issues related to storage and administration of medication, or review and monitoring of its use)
- Experiences and perceptions of people who support people with a learning disability to ensure optimal use and management of medication for chronic diseases, mental health issues and challenging behaviour.
- Intervention description
- Feasibility of interventions
- Acceptability of interventions
- Uptake of interventions
- Barriers and facilitators for the implementation of interventions
- Cost-effectiveness of interventions
- Effectiveness of interventions

Measures of effect:

NA

Additional outcome(s):

NA

Evidence mapping and data extraction (charting)

After search completion, all references will be imported into 'EndNote' and will be deduplicated. All references will be screened at title/abstract level against the inclusion criteria by at least two reviewers in 'Covidence'. Discrepancies will be resolved through discussion or a further reviewer. All papers which meet the inclusion criteria at abstract stage will then be screened at full text and exclusion will have to be justified. When no consensus can be reached between the reviewers, a further reviewer will be consulted. The study selection process will be described in a PRISMA flow chart. The reviewers will independently code the features of issues related to medication use or interventions. Features of interest will include:

- Author
- Title
- Year of publication
- Country
- Population description (number of study participants, severity of learning disability, age of participants, type of chronic disease(s)/ long-term condition(s)
- Study Design
- Type of intervention

Interventions, their components and the contexts in which they are deployed will be characterised according to the following attributes:

- ***Broad type of interventions***: e.g. patient and carer education, prompting and reminders, adherence monitoring (e.g. whether the medications have been taken according to doctor's or non-medical prescriber's instructions) and feedback, habit analysis, multicomponent approaches, dose simplification, special medication packaging,
- ***Stages of medication use process***: prescribing, dispensing, supply, storage & administration, review and monitoring, or generic interventions and

strategies affecting multiple stages (e.g. communication skills; designated supporters for people with learning disability)

- ***Targeted group(s) of people with learning disability***: by severity of learning disability or mental capacity; by conditions associated with learning disability; by age and sex; by ethnicity and cultural / religious background
- ***Targeted health conditions*** for which the medications are described / targeted medications
- ***Settings*** in which the interventions are to be implemented: e.g. at home (**living arrangement**: independent, supported), long-term care institutions, hospitals, schools
- ***Type of intervention evaluation***: e.g. process evaluation, effectiveness evaluation, economic evaluation (costs analysis, cost-consequence, cost-effectiveness, cost-utility, net benefit analysis). This will inform the contribution of individual studies to other sub-sections of the review.

Risk of bias (quality assessment)

This scoping review aims to give a descriptive overview of evidence on the optimisation of medication usage for people with a learning disability and their carers without critically appraising individual studies or synthesizing evidence from different studies (18,19), which will be undertaken in other parts of the broader evidence synthesis project.

Presentation of the results

A narrative summary and summary tables will be provided to highlight major characteristics of the identified literature and potential gaps in the evidence base.

Ethical approvals

Since a scoping review involves the presentation of available resources, no ethics approval is required.

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Dr Yen-Fu Chen. Associate Professor, Warwick Medical School, University of Warwick

Prof Kate Seers. Professor, Warwick Medical School, University of Warwick

Type and method of review

Mixed methods study, Systematic Review

Anticipated or actual start date

September 2022

Anticipated completion date

October 2024

Funding sources/ sponsors

National Institute for Health and Care Research (NIHR) Health Technology Assessment (HTA) Programme

Conflict of interest

None known

Language

English

Country

England

Stage of review

Writing up

References

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Appendix

Appendix 1: Draft Medline Search

Ovid MEDLINE(R) ALL <1946 to July 22, 2022>

Date searched: 25/07/22

1 Developmental Disabilities/ or exp Learning Disabilities/ or Persons with Mental Disabilities/ or exp Intellectual Disability/ 144901

2 Neurodevelopmental Disorders/ or exp Child Development Disorders, Pervasive/ 48270

3 ((learning or intellectual* or developmental* or neurodevelopmental*) adj (disabilit* or disabled or handicap* or impair* or retard* or deficien* or disorder* or

subnormal*)).kf,tw. 68799

4 (mental* adj (disabilit* or disabled or handicap* or impair* or retard* or deficien* or subnormal*)).kf,tw. 44722

5 (development* adj1 delay*).kf,tw. 21027

6 (down* syndrome or fragile x or william* syndrome or angelman or cri du chat or smith magenis or de lange syndrome or rubinstein taybi or prader willi or patau* syndrome or trisomy 13 syndrome or wagr syndrome* or wilms tumo?r aniridia).kf,tw. 41074

7 "profound intellectual and multiple disab*".kf,tw. 123

8 (PMLD or PIMD).kf,tw. 262

9 (autis* or asperger* or neurofibromatos* or hypothyroid* or phenylketonuria or digeorge or lesch nyhan or rett* syndrome or overgrowth syndrome* or pervasive development* disorder* or f?etal alcohol or prenatal alcohol exposure or fasd or velocardiofacial or velo cardio facial or velo cardiofacial or velocardio facial or klinefelter* or childhood disintegrative or static encephalopath*).kf,tw. 140549

10 (22q11?2 adj1 deletion).kf,tw. 1826

11 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 336013

12 exp Medication Adherence/ or Self-Management/ or Medication Review/ or Medication Therapy Management/ or Deprescriptions/ or Inappropriate Prescribing/ or Polypharmacy/ or Self Administration/ 53452

13 ((medication? or medicine?) adj support).kf,tw. 193

14 ((medication? or medicine? or drug?) adj4 (adheren* or nonadheren* or persisten* or complian* or noncomplian*)).kf,tw. 34530

15 ((medication? or medicine? or drug?) adj3 (understand* or knowledg*)).kf,tw. 14592

16 ((medicine? or medication?) adj management).kf,tw. 4989

17 ((medicine? or medication?) adj review?).kf,tw. 2839

18 (selfmanagement or self management).kf,tw. 24535

19 ((medication? or medicine?) adj3 (administ* or selfadminist*)).kf,tw. 13214

20 ((medication? or medicine? or drug? or prescri*) adj2 (optim* or appropriate* or inappropriate*)).kf,tw. 22997

21 ((medication? or medicine? or drug?) adj1 (discontinu* or taper* or withdraw* or reduc* or decreas*)).kf,tw. 23003

22 (deprescri* or de prescri*).kf,tw. 1768

23 (overprescri* or over prescri* or underprescri* or under prescri*).kf,tw. 2542

24 polypharmacy.kf,tw. 10065

25 ("medication? use" or "medication? usage" or "medicine? use" or "medicine? usage").kf,tw. 24225

26 ((medication? or medicine?) adj (reminder? or list? or information)).kf,tw. 3395

27 ((medication? or medicine? or drug?) adj3 decision making).kf,tw. 1468

28 Pharmacists/ or "pharmacist*".kf,tw. 44457

29 "Off-Label Use"/ or off label.kf,tw. 11336

30 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 238704

31 11 and 30 1961

32 exp animals/ not humans/ 5039010

33 31 not 32 1908

Search strategies and filters from the following studies were consulted in development of this search strategy:

Sheerin F, Eustace-Cook J, Wuytack F, Doyle C. Medication management in intellectual disability settings: a systematic review. Journal of Intellectual Disabilities 2019;25(2):242-76. http://dx.doi.org/10.1177/1744629519886184

Morel T, Nguyen-Soenen J, Thompson W, Fournier J-P. Development and validation of search filters to identify articles on deprescribing in Medline and Embase. BMC Med Res Methodol 2022;22:79. https://doi.org/10.1186/s12874-022-01515-x

Adams D, Hastings R, Maidment I, Shah C and Langdon P. Deprescribing psychotropic medicines for behaviours that challenge in people with intellectual disabilities: a systematic review. [unpublished; personal communication].

The following tools were used to identify search terms and refine the search strategy: Systematic Review Accelerator SearchRefinery.

https://sr-accelerator.com/#/searchrefinery

Scells H, Zuccon G. Searchrefiner: a query visualisation and understanding tool for systematic reviews. Proceedings of the 27th ACM International Conference on Information and Knowledge Management. 2018 Oct 17:1939–42.

Sinclair S, Rockwell G. Voyant Tools. 2016. http://voyant-tools.org/

The challenges of using and managing medications: A meta-ethnography looking at the experiences and perceptions of people with a learning disability and their carers

Dr Julia Gauly, Iman Ghosh, Anna Brown, Danielle Adams, Daniel Sutherland, Dr Samantha Flynn, Kerry Martin, Stephen Patterson, David Mahon, Dr Peter Auguste, Dr Samuel Tromans, Prof Paramjit Gill, Prof Eddie Chaplin, Prof Peter Langdon, Dr Yen-Fu Chen, Prof Kate Seers

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People with a learning disability might have some difficulty in understanding complicated information, learning certain skills, and/or looking after themselves or living alone (1). A learning disability is defined by three core criteria: lower intellectual ability (usually defined as an IQ of less than 70), significant impairment of social or adaptive functioning and onset in childhood (2). Terminology used to describe a learning disability varies over time and by geographical location. The term 'learning disability' is the preferred term used in the UK including governmental documents and official guidelines. For this project, we will adopt this preferred term and follow recommendations made by the NHS England for the choice of words to describe people with a learning disability (3). Internationally, the alternative term 'intellectual disability' has been widely used and is adopted in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-V) (4). The International Classification of Diseases 11th Revision (ICD-11) uses a slightly different term 'disorder of intellectual development'. Historically, the term 'mental retardation' was used in DSM-IV and ICD-10 and older literature (4).

People with a learning disability often require medications for their chronic conditions, mental health issues or challenging behaviour (5)(6). A large population-based study

indicated that the mean number of conditions is as high as 11 and the prevalence of multiple long-term chronic health conditions (MLTC) is 98.7% (6) . Adhering to medication as prescribed can be challenging for various reasons related to their disability and a lack of support and reasonable adjustments. Likewise, being exposed to under- and overprescribing of medication can be a challenge experienced by people with a disability and their carers. A high proportion of people with learning disabilities further receive psychotropic medications (7). Many of these people receive them for behavioural issues, even though the medications have not been indicated for this use (7). Additionally, diagnostic overshadowing is increasingly recognised to contribute to health inequalities experienced by people with a learning disability (8). Diagnostic overshadowing refers to when symptoms arising from physical or mental health problems are wrongly attributed to learning disability, leading to delayed diagnosis and treatment (9). A recent scoping review further showed that people with a learning disability often lack understanding of their medication, including its name, purpose and when and how to take it (10). Lack of routine monitoring of prescribed medication and follow-up; and issue of administration and storage of prescribed medication are further potential problems that people with a learning disability may encounter.

The aim of this meta-ethnography is to explore what challenges people with learning disabilities and their carers experience regarding the optimal use and management of medications. This review is part of a larger mixed methods evidence synthesis project on the optimal use and management of medication for people with a learning disability. The findings of this review will be integrated with the findings of the wider project (a scoping review of all relevant literature; a quantitative review of effectiveness and cost-effectiveness of medication support interventions; a mixed methods review of feasibility, acceptability and barriers and facilitators of the interventions) using the Pillar Integration Process (11) or Metrices (12–14) in order to develop recommendations on how interventions need to be designed to support people with a learning disability and their carers to use and manage their medication.

Patient and public involvement (PPI)

We aim to co-produce this meta-ethnography protocol and the protocols of the other study

components (scoping review; quantitative review; mixed methods review) with people with learning disabilities, their family and carers and health and social care professionals working with them. We will therefore establish two PPI groups to facilitate the co-production process: a Learning Disability PPI Group which consists of members of people with learning disabilities and a Stakeholder PPI Group which includes family members and health and social care professionals who care for or work with people with learning disabilities. In addition, we will also establish a Project Advisory Group which includes two members of people with learning disabilities and other stakeholders to advise on practical challenges and provide strategic guidance for this review.

Once the draft of all protocols for this project have been agreed by the research team, we our PPI lead (DM) will work with the two PPI Groups to obtain feedback on our project scope and terminologies used in the protocol. We will also share the protocols with our Project Advisory Group and ask for their feedback. Further inputs will be sought from the Project Advisory Group and the PPI Groups throughout the process of our project. These include verifying the comprehensiveness of our literature search in terms of type of literature and topic areas covered; helping with making sense of our initial review findings; formulating practice and research recommendations based on review findings; and creating materials to facilitate dissemination.

Review Question

- What challenges do people with learning disabilities and their carers experience regarding the optimal use and management of their medications?

Searches

The electronic databases MEDLINE All (via Ovid), Embase (Ovid), CINAHL (EbscoHost), Science, Social Science and Conference Proceedings Citation Indices (Web of Science), Cochrane Library (all databases, via Wiley) and PsycINFO (Ovid) will be searched, from database inception to the current issue. Grey literature will be identified via internet (Google) searches, ProQuest Dissertations & Theses database, proceedings of selected conferences of interest and websites of relevant organisations.

Search strategies will be developed by an information specialist (AB) in collaboration with other members of the project team, and will be informed by previous reviews in the field and guided by the approach described in the Cochrane handbook (15). Searches will combine keywords and, where appropriate, thesaurus (e.g., MeSH, EMTREE) terms, and will be based around the concepts of learning disabilities and medicines adherence (to include (non-)adherence, compliance, persistence, usage, self-administration, self-management, medicines management, medicines optimisation, prescribing appropriateness, knowledge and understanding). No language restrictions, date limits or study type filters (other than the exclusion of animal studies, where appropriate) will be applied. The search strategy will initially be developed in Ovid MEDLINE; a draft MEDLINE search strategy is provided in the Appendix 1. This will be peer reviewed by another information specialist not otherwise involved in the project, before being adapted for other databases/interfaces.

Reference lists of included studies and a selection of recent, relevant qualitative systematic reviews will be checked. Forwards citation tracking from key publications of included studies (to identify citing papers) will also be undertaken. Supplemental searches will be developed iteratively, as additional search terms, concepts and sources are identified; these may include specific projects, interventions, key authors, theories or organisations.

Types of study to be included

Inclusion Criteria:

- Qualitative studies or mixed methods research that has a clearly identified and reported qualitative element
- Studies published in English (or with available English translation). A record will be kept for potentially relevant studies published in non-English language to ensure that no important topics are neglected due to the language restriction
- Studies which provide insight into the challenges that people (children and adults) with a learning disability and their carers experience regarding the optimal use and

management of medications required for their chronic condition, mental health issues or challenging behaviour

- Studies from Low- and middle-income countries (LMIC) will be included when considered applicable to the UK (this will be assessed by two researchers, and disputes resolved by third person, a senior researcher)

Exclusion:

- Quantitative or mixed methods systematic reviews or literature reviews which are not systematic (e.g. narrative reviews) or commentary and opinion pieces without reporting new qualitative data
- Studies that do not provide insight into the challenges that people (children and adults) with a disability and their carers experience regarding the optimal use and management of medications required for their chronic condition (e.g. medication required for acute illness), mental health issues or challenging behaviour
- Studies exclusively focusing on individual conditions such as autism and epilepsy without referring to learning disability
- Studies from low- and middle-income countries (LMIC) will be excluded when considered not applicable to the UK (this will be assessed by two researchers, and disputes resolved by third person, a senior researcher)

Condition or domain being studied

- People with a learning disability and a physical long-term condition (e.g. diabetes, chronic obstructive pulmonary disease, arthritis, hypertension), for which there is currently no cure and which are managed with drugs or other treatment
- People with a learning disability and mental health issues and/or challenging behaviour for which medication is prescribed

Participants/population

Children, adolescents and adults with a learning disability and carers of people with a learning disability. A learning disability is defined by three core criteria as mentioned earlier (2).

We will not include populations which have what is defined in the United Kingdom as learning difficulty (e.g., dyslexia, agraphia, dyscalculia). We will also not include populations which have autism or attention deficit hyperactivity disorder (ADHD) or epilepsy but no learning disability.

Intervention(s), exposure(s)

Not applicable

Comparator(s)/control

We will include studies that compare the experiences of people with a learning disability to the experiences of carers. We will also include studies without a comparator.

Context

This meta-ethnography will include studies which provide insight into the experiences and perceptions of people with a learning disability and their carers on the challenges they face regarding the optimal use and management of medications required for their long-term condition, mental health issues or challenging behaviour.

Main outcome

Patient Outcomes:

- Experiences and perceptions regarding the optimal use and management of medications (e.g. adhering to medication for long-term conditions, mental health issues and challenging behaviour, and of under-and over-prescribing of medications, knowledge and understanding of prescribed medication)

Carer outcomes:

- Experiences and perceptions of supporting people with a learning disability to optimise their use and management of medications (e.g. adhering to their medication for chronic diseases, mental health issues and challenging behaviour; dealing with over- or under-prescribing of medication and issues related to supply, storage and administration; and improving knowledge and understanding of prescribed medication)

Measures of effect:

n/a – a qualitative evidence synthesis

Additional outcome(s):

NA

Data extraction (Selection and Coding)

After search completion, all references will be imported into 'EndNote' and will be deduplicated. All references will be screened at title/abstract level against the inclusion criteria by at least two reviewers in 'Covidence'. Discrepancies will be resolved through discussion or a further reviewer. All papers which meet the inclusion criteria at abstract stage will then be screened at full text and exclusion will have to be justified. When no consensus can be reached between the reviewers, a further reviewer will be consulted. Data will be extracted using a data extraction form.

Studies in any language other than English will be excluded at study selection stage (i.e. relevant non-English articles will get through title/abstract screening but will be excluded before full-text stage). The intention is to note whether any topics are better covered in non-English literature and hence received insufficient attention in English literature, particularly for issues related to culture/religion/ethnicity etc. Hence, we will not be reviewing non-English literature, but we will briefly describe topics covered.

For the first 10 studies or until good levels of agreement between reviewers are achieved, two reviewers will extract the following types of data: title, author, year of publication, country, setting (home, school, institution), population (number of study participants, level of learning disability, age of participants, type of chronic disease(s) or long-term

condition(s)), outcomes (patient and carers), and themes and concepts identified from primary papers. The remaining studies will be extracted by only one reviewer but checked by another.

Risk of bias (quality assessment)

Once the data is analysed, we will use the CASP (Critical Appraisal Skills Programme) checklist for qualitative studies to assess the quality of included primary studies to provide context to the reader (16). Additionally, the CERQual (Confidence in the Evidence from Reviews of Qualitative research) approach will be used through the iSoQ (Version 1.0) online tool by two reviewers to assess how confident we can be in our findings (17,18). The four domains of the GRADE-CERQual framework: (1) methodological limitation, (2) relevance, (3) adequacy of data ('richness and quantity of data'), and (4) coherence ('consistency across studies') will be used to encourage reflection. Discrepancies between the two reviewers will be resolved by discussion or arbitration.

Strategy for data analysis and synthesis

The planned strategy for data analysis and synthesis is a meta-ethnography. The synthesis will be guided by Noblit and Hare's (1988) seven stage process for conducting meta-ethnography, which comprises of the following stages: [1] getting started, [2] describing what is relevant to the initial interest, [3] reading included studies, [4] determining how the studies are related, [5] translating the studies into one another, [6] synthesising translations, and [7] expressing the synthesis. (19).

In the initial stages of the data synthesis, interpretations are developed based on the primary studies and in the latter stages the data synthesis seeks to produce novel interpretations that move beyond the individual, primary study findings and contribute to an increased understanding of collaborative approaches (20). This meta-ethnography will also draw upon France et al.'s (2019) eMERge guidelines for improving the reporting of meta-ethnographies (20).

The findings of this review will be integrated with the findings of the wider project using the Pillar Integration Process (11) or Metrices and/or a narrative (12–14) in order to

develop recommendations on how interventions need to be designed to support people with a learning disability and their carers to use and manage their medication.

Analysis of subgroups or subsets

The narrative synthesis may be guided by presentation according to the following groupings of interest:

- Population type (patient and carers)

  Issues related to medication use may be perceived and experienced differently from different perspectives by different people. It is therefore important to explore the similarities and differences between people with a learning disability, their carers who may be members of their families or friends or paid carers, and other health and social care staff who support them.

- Patient age group and other personal contexts

  Adults and children may experience different challenges regarding the optimal use and management of medication. Further, we assume that people experience different challenges regarding the optimal use and management of medication depending on the level of learning disability and the type and severity of chronic condition(s) or long-term conditions that they are living with.

- Living arrangement and setting

  The challenges that people with a learning disability face in the optimal use and management of medication are also likely to vary depending on their living arrangements (e.g. living independently; assisted care facilities; long-term care institutions) and the setting where the needs for medication occur (e.g. at home or school).

Dissemination

Findings of this project will be presented in key conferences associated with people with learning disability, and be published in academic journals and in NIHR Journals Library. We

will generate infographics to highlight common issues related to medication usage in people with learning disabilities and a summary of evidence on potential interventions. These will be disseminated through charities (the Foundation for People with Learning Disabilities, People First Dorset and Sunderland People First which are directly involved in this project, but also key organisations and wider networks with whom they have collaborated such as Mencap, Learning Disability England), Royal College of General Practitioners and Royal Pharmaceutical Society and be promoted through relevant social media such as Twitter and discussion forums.

In order to ensure that findings of the project can be communicated directly to people with learning disability, members of our PAG and our Learning Disability PPI Group will help us to co-create dissemination materials in formats that are more accessible for people with learning disability. We plan to produce a video for communicating key findings more relevant to them. The contents will be chosen by people with learning disability who will be directly involved in the production. We will also produce easy-read versions of key findings and recommendations.

We will create a project website to be hosted by the University of Warwick. The website will include information about the project and the project team; ways for interested people to get involved; updates on the progress of the project; and will provide access to findings and outputs of the project when they are produced.

Contact details for further information

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Prof Kate Seers. Professor, Warwick Medical School, University of Warwick

Type and method of review

Synthesis of qualitative studies, Systematic Review

Anticipated or actual start date

September 2022

Anticipated completion date

July 2024

Funding sources/ sponsors

National Institute for Health and Care Research (NIHR) Health Technology Assessment (HTA)

Programme

Conflict of interest

None known

Language

English

Country

England

Stage of review

Completed, under peer review

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Appendix

Appendix 1: Draft Medline Search

Ovid MEDLINE(R) ALL <1946 to July 22, 2022>

Date searched: 25/07/22

1 Developmental Disabilities/ or exp Learning Disabilities/ or Persons with Mental Disabilities/ or exp Intellectual Disability/ 144901

2 Neurodevelopmental Disorders/ or exp Child Development Disorders, Pervasive/ 48270

3 ((learning or intellectual* or developmental* or neurodevelopmental*) adj (disabilit* or disabled or handicap* or impair* or retard* or deficien* or disorder* or subnormal*)).kf,tw. 68799

4 (mental* adj (disabilit* or disabled or handicap* or impair* or retard* or deficien* or subnormal*)).kf,tw. 44722

5 (development* adj1 delay*).kf,tw. 21027

6 (down* syndrome or fragile x or william* syndrome or angelman or cri du chat or smith magenis or de lange syndrome or rubinstein taybi or prader willi or patau* syndrome or trisomy 13 syndrome or wagr syndrome* or wilms tumo?r aniridia).kf,tw. 41074

7 "profound intellectual and multiple disab*".kf,tw. 123

8 (PMLD or PIMD).kf,tw. 262

9 (autis* or asperger* or neurofibromatos* or hypothyroid* or phenylketonuria or digeorge or lesch nyhan or rett* syndrome or overgrowth syndrome* or pervasive development* disorder* or f?etal alcohol or prenatal alcohol exposure or fasd or velocardiofacial or velo cardio facial or velo cardiofacial or velocardio facial or klinefelter* or childhood disintegrative or static encephalopath*).kf,tw. 140549

10 (22q11?2 adj1 deletion).kf,tw. 1826

11 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 336013

12 exp Medication Adherence/ or Self-Management/ or Medication Review/ or Medication Therapy Management/ or Deprescriptions/ or Inappropriate Prescribing/ or Polypharmacy/ or Self Administration/ 53452

13 ((medication? or medicine?) adj support).kf,tw. 193

14 ((medication? or medicine? or drug?) adj4 (adheren* or nonadheren* or persisten* or complian* or noncomplian*)).kf,tw. 34530

15 ((medication? or medicine? or drug?) adj3 (understand* or knowledg*)).kf,tw. 14592

16 ((medicine? or medication?) adj management).kf,tw. 4989

17 ((medicine? or medication?) adj review?).kf,tw. 2839

18 (selfmanagement or self management).kf,tw. 24535

19 ((medication? or medicine?) adj3 (administ* or selfadminist*)).kf,tw. 13214

20 ((medication? or medicine? or drug? or prescri*) adj2 (optim* or appropriate* or inappropriate*)).kf,tw. 22997

21 ((medication? or medicine? or drug?) adj1 (discontinu* or taper* or withdraw* or reduc* or decreas*)).kf,tw. 23003

22 (deprescri* or de prescri*).kf,tw. 1768

23 (overprescri* or over prescri* or underprescri* or under prescri*).kf,tw. 2542

24 polypharmacy.kf,tw. 10065

25 ("medication? use" or "medication? usage" or "medicine? use" or "medicine? usage").kf,tw. 24225

26 ((medication? or medicine?) adj (reminder? or list? or information)).kf,tw. 3395

27 ((medication? or medicine? or drug?) adj3 decision making).kf,tw. 1468

28 Pharmacists/ or "pharmacist*".kf,tw. 44457

29 "Off-Label Use"/ or off label.kf,tw. 11336

30 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 238704

31 11 and 30 1961

32 exp animals/ not humans/ 5039010

33 31 not 32 1908

Search strategies and filters from the following studies were consulted in development of this search strategy:

Sheerin F, Eustace-Cook J, Wuytack F, Doyle C. Medication management in intellectual disability settings: a systematic review. Journal of Intellectual Disabilities 2019;25(2):242-76. http://dx.doi.org/10.1177/1744629519886184

Morel T, Nguyen-Soenen J, Thompson W, Fournier J-P. Development and validation of search filters to identify articles on deprescribing in Medline and Embase. BMC Med Res Methodol 2022;22:79. https://doi.org/10.1186/s12874-022-01515-x

Adams D, Hastings R, Maidment I, Shah C and Langdon P. Deprescribing psychotropic medicines for behaviours that challenge in people with intellectual disabilities: a systematic review. [unpublished; personal communication].

The following tools were used to identify search terms and refine the search strategy: Systematic Review Accelerator SearchRefinery.

https://sr-accelerator.com/#/searchrefinery

Scells H, Zuccon G. Searchrefiner: a query visualisation and understanding tool for systematic reviews. Proceedings of the 27th ACM International Conference on Information and Knowledge Management. 2018 Oct 17:1939–42.

Sinclair S, Rockwell G. Voyant Tools. 2016. http://voyant-tools.org/

The effectiveness and cost-effectiveness of interventions designed to support people with a learning disability and their carers to optimise their medication usage: A quantitative systematic review

Dr Julia Gauly, Iman Ghosh, Anna Brown, Danielle Adams, Daniel Sutherland, Dr Samantha Flynn, Kerry Martin, Stephen Patterson, David Mahon, Dr Peter Auguste, Dr Samuel Tromans, Prof Paramjit Gill, Prof Eddie Chaplin, Prof Peter Langdon, Prof Kate Seers, Dr Yen-Fu Chen

Version & date

Version 2.1, 6 October 2024

Background

People with a learning disability might have some difficulty in understanding complicated information, learning certain skills, and/or looking after themselves or living alone (1). A learning disability is defined by three core criteria: lower intellectual ability (usually defined as an IQ of less than 70), significant impairment of social or adaptive functioning and onset in childhood (2). Terminology used to describe a learning disability varies over time and by geographical location. The term 'learning disability' is the preferred term used in the UK including governmental documents and official guidelines. For this project, we will adopt this preferred term and follow recommendations made by the NHS England for the choice of words to describe people with a learning disability (3). Internationally, the alternative term 'intellectual disability' has been widely used and is adopted in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-V) (4). The International Classification of Diseases 11th Revision (ICD-11) uses a slightly different term 'disorder of intellectual development'. Historically, the term 'mental retardation' was used in DSM-IV and ICD-10 and older literature (4).

People with a learning disability often require medications for their chronic conditions, mental health issues or challenging behaviour (5)(6). A large population-based study indicated that the mean number of conditions is as high as 11 and the prevalence of multiple long-term chronic health conditions (MLTC) is 98.7% (6) . Adhering to medication as prescribed can be challenging for various reasons related to their disability and a lack of support and reasonable adjustments. Likewise, being exposed to under- and overprescribing of medication can be a challenge experienced by people with a disability and their carers. A high proportion of people with learning disabilities further receive psychotropic medications (7). Many of these people receive them for behavioural issues, even though the medications have not been indicated for this use (7). Additionally, diagnostic overshadowing is increasingly recognised to contribute to health inequalities experienced by people with a learning disability (8). Diagnostic overshadowing refers to when symptoms arising from physical or mental health problems are wrongly attributed to learning disability, leading to delayed diagnosis and treatment (9). A recent scoping review further showed that people with a learning disability often lack understanding of their medication, including its name, purpose and when and how to take it (10). Lack of routine monitoring of prescribed medication and follow-up; and issue of administration and storage of prescribed medication are further potential problems that people with a learning disability may encounter.

Different strategies have been developed in order to support people with a learning disability and their carers to optimise their medication use. The aim of this review is to summarise and analyse what is known about the effectiveness and cost-effectiveness of intervention designed to support people with a learning disability and their carers to optimise their medication use. The findings will help those who are currently delivering strategies or planning to implement strategies for people with a learning disability and their carers to decide which strategies are most effective and cost-effective in supporting them to optimise the use of their medication.

This review is part of a larger mixed methods evidence synthesis project on the optimal use and management of medication for people with a learning disability and their carers. The findings of this review will be integrated with the findings of the wider project (a scoping

review of all relevant literature; a meta-ethnography of issues related to medication use experienced by people with a learning disability and their carers; and a mixed methods review of feasibility, acceptability and barriers and facilitators of medication support interventions) using the Pillar Integration Process (8) or Metrices (9–11) in order to develop recommendations on what interventions are effective and cost-effective and how interventions need to be designed to support people with a learning disability and their carers to use and manage their medication.

Patient and public involvement (PPI)

We aim to co-produce this review protocol and the protocols of the other components of the broader evidence synthesis (scoping review; meta-ethnography; mixed methods review) with people with a learning disability, their family and carers and health and social care professionals working with them. We will therefore establish two PPI groups to facilitate the co-production process: a Learning Disability PPI Group which consists of members of people with a learning disability and a Stakeholder PPI Group which includes family members and health and social care professionals who care for or work with people with a learning disability. In addition, we will also establish a Project Advisory Group which includes two members of people with a learning disability and other stakeholders to advise on practical challenges and provide strategic guidance for this review.

Our PPI lead (DM) will work with the two PPI Groups to obtain their feedback on our project scope and terminologies used in the protocols. We will also share the protocols with our Project Advisory Group and ask for their feedback. Further inputs will be sought from the Project Advisory Group and the PPI Groups throughout the process of our project. These include verifying the comprehensiveness of our literature search in terms of type of literature and topic areas covered; helping with making sense of our initial review findings; formulating practice and research recommendations based on review findings; and creating materials to facilitate dissemination.

Review Question

What is known about the effectiveness and cost-effectiveness of interventions designed to support people with a learning disability and their carers to optimise their medication use?

Searches

The electronic databases MEDLINE All (via Ovid), Embase (Ovid), CINAHL (EbscoHost), Science, Social Science and Conference Proceedings Citation Indices (Web of Science), Cochrane Library (all databases, via Wiley) and PsycINFO (Ovid) will be searched, from database inception to the current issue. Grey literature will be identified via internet (Google) searches, ProQuest Dissertations & Theses database, proceedings of selected conferences of interest and websites of relevant organisations.

Search strategies will be developed by an information specialist (AB) in collaboration with other members of the project team, and will be informed by previous reviews in the field and guided by the approach described in the Cochrane handbook (12). Searches will combine keywords and, where appropriate, thesaurus (e.g., MeSH, EMTREE) terms, and will be based around the concepts of learning disabilities and medicines optimisation (to include (non-) adherence, compliance, persistence, usage, self-administration, self-management, medicines management, prescribing appropriateness, knowledge and understanding of medication). No language restrictions, date limits or study type filters (other than the exclusion of animal studies, where appropriate) will be applied. The search strategy will initially be developed in Ovid MEDLINE; a draft MEDLINE search strategy is provided in the Appendix 1. This will be peer reviewed by another information specialist not otherwise involved in the project, before being adapted for other databases/interfaces.

Reference lists of included studies and a selection of recent, relevant quantitative systematic reviews will be checked. Forwards citation tracking from key publications of included studies (to identify citing papers) will also be undertaken. Supplemental searches will be developed iteratively, as additional search terms, concepts and sources are identified; these may include specific projects, interventions, key authors, theories or organisations.

Types of study to be included

Inclusion Criteria:

- Quantitative effectiveness studies (e.g., randomised controlled trials, non-randomised controlled trials); mixed methods research that has a clearly identified and reported quantitative element; economic evaluations (cost-effectiveness, cost-benefit, cost-utility, and cost-consequence studies); systematic reviews that have reported quantitative estimates of intervention effectiveness or cost-effectiveness.
- Before-and-after studies of intervention effectiveness without a control group, and UK-based cost studies of medication support interventions for people with a learning disability will be considered if no evidence of better quality is found for a particular intervention.
- Studies published in English (or with available English translation). A record will be kept for potentially relevant studies published in non-English language to ensure that no important topics are neglected due to the language restriction.
- Studies from Low- and middle-income countries (LMIC) will be included when considered applicable to the UK (this will be assessed by two researchers, and disputes resolved by third person, a senior researcher).

Exclusion:

- Qualitative studies; qualitative or mixed methods reviews that do not cover quantitative estimates of effectiveness and cost-effectiveness
- Studies that do not provide quantitative estimates of the effectiveness and/or cost-effectiveness of strategies developed to support people (children and adults) with a learning disability and their carers to optimise the usage of medications required for their chronic condition, mental health issues or challenging behaviour (e.g. medication required for acute illness)

- Studies exclusively focusing on individual conditions such as autism and epilepsy without referring to learning disability
- Studies from low- and middle-income countries (LMIC) will be excluded when considered not applicable to the UK (this will be assessed by two researchers, and disputes resolved by third person, a senior researcher)

Condition or domain being studied

- People with a learning disability and a physical long-term condition (e.g. diabetes, chronic obstructive pulmonary disease, arthritis, hypertension), for which there is currently no cure and which are managed with drugs or other treatment
- People with a learning disability and mental health issues and/or challenging behaviour for which medication is prescribed

Participants/population

Children, adolescents and adults with a learning disability and carers of people with a learning disability. A learning disability is defined by three core criteria as mentioned earlier (13). We will not include populations which have what is defined in the United Kingdom as learning difficulty (e.g., dyslexia, agraphia, dyscalculia). We will also not include populations which have autism or attention deficit hyperactivity disorder (ADHD) or epilepsy but no learning disability.

Intervention(s), exposure(s)

Strategies/interventions that are developed to support people (children and adults) with a learning disability and their carers to optimise the usage of medications required for their chronic condition, mental health issues or challenging behaviour.

Comparator(s)/control

We will include reviews or studies that compare the effectiveness or cost-effectiveness of strategies developed to support the optimisation of medication usage of people with a learning disability with usual care or with different interventions. We may consider

before-and-after studies without a comparator group where no controlled studies are found for a particular intervention.

Context

This systematic review will include studies which provide insight into the effectiveness and/or cost-effectiveness of strategies that are developed to support people (children and adults) with a learning disability and their carers to optimise the usage of medications required for their chronic condition, mental health issues or challenging behaviour.

Main outcome

- Effectiveness of interventions (e.g. measurement of patient or carer's knowledge about medication; measurement of medication adherence (e.g. whether the medications have been taken according to doctor's or non-medical prescriber's instructions), medication errors, or prescribing appropriateness, including under- and over use of medications; adequacy of monitoring; clinical outcomes of patients; adverse events; quality of life for people with learning disability and/or their carers
- Costs and cost-effectiveness of interventions; use of resources

Measures of effect:

Measures of effect may include percentages, risk ratios and risk difference (for dichotomous or binary outcomes); mean and standardised mean differences (for continuous outcomes).

Additional outcome(s):

NA

Data extraction (Selection and Coding)

After search completion, all references will be imported into 'Endnote' and will be deduplicated. All references will be screened at title/abstract level against the inclusion criteria by at least two reviewers in 'Covidence'. Discrepancies will be resolved through discussion or a further reviewer. All papers which meet the inclusion criteria at abstract

stage will then be screened at full text and exclusion will have to be justified. When no consensus can be reached between the reviewers, a further reviewer will be consulted. Data will be extracted using a data extraction form.

Studies in any language other than English will be excluded at study selection stage (i.e. relevant non-English articles will get through title/abstract screening but will be excluded before full-text stage). The intention is note whether any topics are better covered non-English literature and hence received insufficient attention in English literature, particularly for issues related to culture/religion/ethnicity etc. Hence, we will not be reviewing non-English literature, but we will briefly describe topics covered.

Where a published systematic review of intervention effectiveness or cost-effectiveness that covers the subject area being evaluated in this review is found, we will firstly assess the quality of the systematic review. Findings from this assessment will be used to inform a decision, in consultation with the Project Advisory Group, with regard to how data and findings from the systematic review will be used. For example, if the published systematic review is comprehensive and of high quality, we will not assess the primary studies already included in the systematic review again in our systematic review. Instead, we will summary findings from the systematic review alongside findings from new primary studies that would have met the inclusion criteria for the original review, if identified. If the systematic review is of good quality but there is scope for alternative or further synthesis of evidence covered by the review, we may utilise data from the systematic review and partially update them with new data or analyses. Where a systematic review is found to be of poor quality, we may use the review only as an additional source for identifying primary studies.

For the first 10 studies meeting our inclusion criteria or until good levels of agreement between reviewers are achieved, two reviewers will extract the following types of data: title, author, year of publication, country, population (number of study participants, severity of learning disability, age of participants, type of chronic disease(s) or long-term condition(s)), type of medications, setting (home, assisted living, long-term care institute), details of the interventions, outcome measures, quantitative estimates of the effectiveness

and cost-effectiveness of interventions. The remaining studies will be extracted by only one reviewer but checked by another.

Risk of bias (quality assessment)

Quality assessment for studies on effectiveness of interventions:

Randomised controlled trials will be assessed using the Cochrane Risk of Bias 2 (RoB 2) Tool. Non-randomised studies will be appraised using the ROBINS-I tool (14). If systematic reviews are found, they will be assessed using AMSTAR-2 (15).

Quality assessment for studies on the cost-effectiveness of interventions:

All studies will be appraised against best practice guidance. The CHEERS 2022 checklist will be used to assess reporting of economic evaluation studies (16). The Philips checklist will be used for the appraisal of any decision analytic models (17). The framework developed by Phillips and colleagues sets out best practice guidance for the conduct of model-based economic evaluations under the dimensions of structure, data, and consistency.

Strategy for data analysis and synthesis

Data analysis and synthesis of studies on the effectiveness of interventions:

We envisage a high level of heterogeneity between studies, in which case narrative synthesis of the findings facilitated by grouping, tabulation and graphical presentation of the data will be undertaken.

Given the diverse nature of health conditions and issues related to medication use, different tools and measures are likely to have been used and reported in previous studies. We will firstly group these outcomes for individual health conditions (indications) and meta-analyse them for each intervention against standard practice separately where suitable data are available. For similar issues across different health conditions (e.g. medication adherence), we may undertake exploratory meta-analyses to assess the effectiveness and effect modifiers for a given intervention across different health conditions. Where studies comparing different interventions are found, the head-to-head comparisons will be analysed and presented separately. We expect that the heterogeneous

nature of the health conditions, interventions and contexts would not be conducive for undertaking network meta-analyses between different interventions, but may explore the possibility of such analyses through a protocol amendment after discussion with PAG and the NIHR if potentially suitable data are found.

A random effects model will be used for meta-analyses of binary, continuous or time-to-event outcomes. Use of standardised mean difference for meta-analysis may be considered for studies that utilised different scales to measure similar constructs.

Data analysis and synthesis of studies on the cost-effectiveness of strategies:

We do not anticipate that there would be sufficient effectiveness and cost-effectiveness evidence to warrant a de novo economic evaluation but will identify priority interventions and settings for further research on cost-effectiveness. Given the nature of economic analyses being highly context-specific, the conduct and findings from individual studies will be summarised narratively.

If sufficient evidence is available to determine the cost-effectiveness of specific interventions, we will evaluate and describe the (un)certainty of the evidence and its applicability with respect to current practice in the UK, and highlight any caveats. If evidence for different interventions addressing similar issues is found, we will comment on their relative cost-effectiveness where evidence permits, or provide details for the conduct of future economic analyses that aim to compare these interventions against each other. We will outline the key components that should be considered and highlight any areas of concern, which may require undertaking further research in order to support the evidence linkage (e.g. linking the process measure of medication adherence to clinical outcomes and quality of life) that is likely to be required for a future economic analysis. Output from the systematic review of the health economic literature can be used to explore how the cost-effectiveness of interventions being compared might vary when applied to a specific setting and what the drivers are for cost-effectiveness. These will help inform service planners and practitioners about the trade-offs between alternative interventions in their own settings. if no economic evaluations on medication support interventions specifically for people with learning disability are found, we will provide commentaries to highlight methodological

challenges that may need to be overcome to facilitate future economic evaluations by consulting existing economic literature on medication support interventions for other patient populations (18).

Data integration

The findings of this review will be integrated with the findings of the wider project using the Pillar Integration Process (8) or Metrices and/or a narrative (9–11) in order to develop recommendations on what interventions are effective and cost-effective and how interventions need to be designed to support people with a learning disability and their carers to use and manage their medication.

Analysis of subgroups or subsets

Exploratory subgroup analyses may be conducted to compare the effectiveness of different types of interventions for a given medication use issues, or to explore whether the effectiveness of a given type of interventions may be modified by various attributes related to people with a learning disability, the intervention and other contextual factors, including:

- Targeted group(s) of people with learning disability: by severity of learning disability or mental capacity; by conditions associated with learning disability; by age and sex; by ethnicity and cultural / religious background
- Targeted health conditions for which the medications are described / targeted medications
- Settings in which the interventions are to be implemented: e.g. at home (living arrangement: independent, supported), long-term care institutions, hospitals, schools
- Country: existing health care provision for people with a learning disability may vary substantially between different countries and may impact on intervention effectiveness

- Intervention features (e.g. type of intervention, key personnel for delivery/implementation etc)

Dissemination

Findings of this project will be presented in key conferences associated with people with learning disability, and be published in academic journals and in NIHR Journals Library. We will generate infographics to highlight common issues related to medication usage in people with learning disabilities and a summary of evidence on potential interventions. These will be disseminated through charities (the Foundation for People with Learning Disabilities, People First Dorset and Sunderland People First which are directly involved in this project, but also key organisations and wider networks with whom they have collaborated such as Mencap, Learning Disability England), Royal College of General Practitioners and Royal Pharmaceutical Society and be promoted through relevant social media such as Twitter and discussion forums.

In order to ensure that findings of the project can be communicated directly to people with learning disability, members of our PAG and our Learning Disability PPI Group will help us to co-create dissemination materials in formats that are more accessible for people with learning disability. We plan to produce a video for communicating key findings more relevant to them. The contents will be chosen by people with learning disability who will be directly involved in the production. We will also produce easy-read versions of key findings and recommendations.

We will create a project website to be hosted by the University of Warwick. The website will include information about the project and the project team; ways for interested people to get involved; updates on the progress of the project; and will provide access to findings and outputs of the project when they are produced.

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Type and method of review

Synthesis of quantitative studies, Systematic Review

Anticipated or actual start date

September 2022

Anticipated completion date

December 2024

Funding sources/ sponsors

National Institute for Health and Care Research (NIHR) Health Technology Assessment (HTA)

Programme

Conflict of interest

None known

Language

English

Country

England

Stage of review

Data synthesis

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Appendix

Appendix 1: Draft Medline Search

Ovid MEDLINE(R) ALL <1946 to July 22, 2022>

Date searched: 25/07/22

1 Developmental Disabilities/ or exp Learning Disabilities/ or Persons with Mental Disabilities/ or exp Intellectual Disability/ 144901

2 Neurodevelopmental Disorders/ or exp Child Development Disorders, Pervasive/ 48270

3 ((learning or intellectual* or developmental* or neurodevelopmental*) adj (disabilit* or disabled or handicap* or impair* or retard* or deficien* or disorder* or subnormal*)).kf,tw. 68799

4 (mental* adj (disabilit* or disabled or handicap* or impair* or retard* or deficien* or subnormal*)).kf,tw. 44722

5 (development* adj1 delay*).kf,tw. 21027

6 (down* syndrome or fragile x or william* syndrome or angelman or cri du chat or smith magenis or de lange syndrome or rubinstein taybi or prader willi or patau* syndrome or trisomy 13 syndrome or wagr syndrome* or wilms tumo?r aniridia).kf,tw. 41074

7 "profound intellectual and multiple disab*".kf,tw. 123

8 (PMLD or PIMD).kf,tw. 262

9 (autis* or asperger* or neurofibromatos* or hypothyroid* or phenylketonuria or digeorge or lesch nyhan or rett* syndrome or overgrowth syndrome* or pervasive development* disorder* or f?etal alcohol or prenatal alcohol exposure or fasd or velocardiofacial or velo cardio facial or velo cardiofacial or velocardio facial or klinefelter* or childhood disintegrative or static encephalopath*).kf,tw. 140549

10 (22q11?2 adj1 deletion).kf,tw. 1826

11 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 336013

12 exp Medication Adherence/ or Self-Management/ or Medication Review/ or Medication Therapy Management/ or Deprescriptions/ or Inappropriate Prescribing/ or Polypharmacy/ or Self Administration/ 53452

13 ((medication? or medicine?) adj support).kf,tw. 193

14 ((medication? or medicine? or drug?) adj4 (adheren* or nonadheren* or persisten* or complian* or noncomplian*)).kf,tw. 34530

15 ((medication? or medicine? or drug?) adj3 (understand* or knowledg*)).kf,tw. 14592

16 ((medicine? or medication?) adj management).kf,tw. 4989

17 ((medicine? or medication?) adj review?).kf,tw. 2839

18 (selfmanagement or self management).kf,tw. 24535

19 ((medication? or medicine?) adj3 (administ* or selfadminist*)).kf,tw. 13214

20 ((medication? or medicine? or drug? or prescri*) adj2 (optim* or appropriate* or inappropriate*)).kf,tw. 22997

21 ((medication? or medicine? or drug?) adj1 (discontinu* or taper* or withdraw* or reduc* or decreas*)).kf,tw. 23003

22 (deprescri* or de prescri*).kf,tw. 1768

23 (overprescri* or over prescri* or underprescri* or under prescri*).kf,tw. 2542

24 polypharmacy.kf,tw. 10065

25 ("medication? use" or "medication? usage" or "medicine? use" or "medicine? usage").kf,tw. 24225

26 ((medication? or medicine?) adj (reminder? or list? or information)).kf,tw. 3395

27 ((medication? or medicine? or drug?) adj3 decision making).kf,tw. 1468

28 Pharmacists/ or "pharmacist*".kf,tw. 44457

29 "Off-Label Use"/ or off label.kf,tw. 11336

30 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 238704

31 11 and 30 1961

32 exp animals/ not humans/ 5039010

33 31 not 32 1908

Search strategies and filters from the following studies were consulted in development of this search strategy:

Sheerin F, Eustace-Cook J, Wuytack F, Doyle C. Medication management in intellectual disability settings: a systematic review. Journal of Intellectual Disabilities 2019;25(2):242-76. http://dx.doi.org/10.1177/1744629519886184

Morel T, Nguyen-Soenen J, Thompson W, Fournier J-P. Development and validation of search filters to identify articles on deprescribing in Medline and Embase. BMC Med Res Methodol 2022;22:79. https://doi.org/10.1186/s12874-022-01515-x

Adams D, Hastings R, Maidment I, Shah C and Langdon P. Deprescribing psychotropic medicines for behaviours that challenge in people with intellectual disabilities: a systematic review. [unpublished; personal communication].

The following tools were used to identify search terms and refine the search strategy: Systematic Review Accelerator SearchRefinery.

https://sr-accelerator.com/#/searchrefinery

Scells H, Zuccon G. Searchrefiner: a query visualisation and understanding tool for systematic reviews. Proceedings of the 27th ACM International Conference on Information and Knowledge Management. 2018 Oct 17:1939–42.

Sinclair S, Rockwell G. Voyant Tools. 2016. http://voyant-tools.org/

The feasibility, acceptability, uptake and barriers and facilitators of implementation for interventions designed to optimise medication use for people with a learning disability: A mixed methods systematic review

Dr Julia Gauly, Iman Ghosh, Anna Brown, Danielle Adams, Daniel Sutherland, Dr Samantha Flynn, Kerry Martin, Stephen Patterson, David Mahon, Peter Auguste, Dr Samuel Tromans, Prof Paramjit Gill, Prof Eddie Chaplin, Prof Peter Langdon, Prof Kate Seers, Dr Yen-Fu Chen

Version & date

Version 2.1, 6 October 2024

Background

People with a learning disability might have some difficulty in understanding complicated information, learning certain skills, and/or looking after themselves or living alone (1). A learning disability is defined by three core criteria: lower intellectual ability (usually defined as an IQ of less than 70), significant impairment of social or adaptive functioning and onset in childhood (2). Terminology used to describe a learning disability varies over time and by geographical location. The term 'learning disability' is the preferred term used in the UK including governmental documents and official guidelines. For this project, we will adopt this preferred term and follow recommendations made by the NHS England for the choice of words to describe people with a learning disability (3). Internationally, the alternative term 'intellectual disability' has been widely used and is adopted in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-V) (4). The International Classification of Diseases 11th Revision (ICD-11) uses a slightly different term 'disorder of intellectual development'. Historically, the term 'mental retardation' was used in DSM-IV and ICD-10 and older literature (4).

People with a learning disability often require medications for their chronic conditions, mental health issues or challenging behaviour (5)(6). A large population-based study indicated that the mean number of conditions is as high as 11 and the prevalence of multiple long-term chronic health conditions (MLTC) is 98.7% (6). Adhering to medication as prescribed can be challenging for various reasons related to their disability and a lack of support and reasonable adjustments. Likewise, being exposed to under- and overprescribing of medication can be a challenge experienced by people with a disability and their carers. A high proportion of people with learning disabilities further receive psychotropic medications (7). Many of these people receive them for behavioural issues, even though the medications have not been indicated for this use (7). Additionally, diagnostic overshadowing is increasingly recognised to contribute to health inequalities experienced by people with a learning disability (8). Diagnostic overshadowing refers to when symptoms arising from physical or mental health problems are wrongly attributed to learning disability, leading to delayed diagnosis and treatment (9). A recent scoping review further showed that people with a learning disability often lack understanding of their medication, including its name, purpose and when and how to take it (10). Lack of routine monitoring of prescribed medication and follow-up; and issue of administration and storage of prescribed medication are further potential problems that people with a learning disability may encounter.

This mixed methods review aims to summarise what is known about the feasibility, acceptability, uptake and barriers and facilitators of implementation for interventions designed to optimise medication use for people with a learning disability.

This review is part of a larger mixed methods evidence synthesis project on the optimal use and management of medication for people with a learning disability. The review will be informed by a scoping review and will be integrated with other reviews (a meta-ethnography of issues related to medication usage a; quantitative review of effectiveness and cost-effectiveness of interventions) from the wider project using the Pillar Integration Process (11) or Metrices (12–14) in order to develop recommendations on what interventions are effective and cost-effective and how

interventions need to be designed to support people with a learning disability and their carers to use and manage their medication.

Patient and public involvement (PPI)

We aim to co-produce this study protocol and the protocols of the other study components (scoping review; meta-ethnography; quantitative review) with people with a learning disability, their family and carers and health and social care professionals working with them. We will therefore establish two PPI groups to facilitate the co-production process: a Learning Disability PPI Group which consists of members of people with a learning disability and a Stakeholder PPI Group which includes family members and health and social care professionals who care for or work with people with a learning disability. In addition, we will also establish a Project Advisory Group which includes two members of people with a learning disability and other stakeholders to advise on practical challenges and provide strategic guidance for this review.

Our PPI lead (DMa) will work with the two PPI Groups to obtain their feedback on our project scope and terminologies used in the protocol. We will also share the protocols with our Project Advisory Group and ask for their feedback. Further inputs will be sought from the Project Advisory Group and the PPI Groups throughout the process of our project. These include verifying the comprehensiveness of our literature search in terms of type of literature and topic areas covered; helping with making sense of our initial review findings; formulating practice and research recommendations based on review findings; and creating materials to facilitate dissemination.

Review Question

- What is known about the feasibility, acceptability, uptake and barriers and facilitators of implementation for interventions designed to optimise medication use for people with a learning disability?

Searches

The electronic databases MEDLINE All (via Ovid), Embase (Ovid), CINAHL (EbscoHost), Science, Social Science and Conference Proceedings Citation Indices (Web of Science),

Cochrane Library (all databases, via Wiley) and PsycINFO (Ovid) will be searched, from database inception to the current issue. Grey literature will be identified via internet (Google) searches, ProQuest Dissertations & Theses database, proceedings of selected conferences of interest and websites of relevant organisations.

Search strategies will be developed by an information specialist (AB) in collaboration with other members of the project team, and will be informed by previous reviews in the field and guided by the approach described in the Cochrane handbook (15). Searches will combine keywords and, where appropriate, thesaurus (e.g., MeSH, EMTREE) terms, and will be based around the concepts of learning disabilities and medicines optimisation (to include (non-) adherence), compliance, persistence, usage, self-administration, self-management, medicines management, prescribing appropriateness, knowledge and understanding of medication). No language restrictions, date limits or study type filters (other than the exclusion of animal studies, where appropriate) will be applied. The search strategy will initially be developed in Ovid MEDLINE; a draft MEDLINE search strategy is provided in the Appendix 1. This will be peer reviewed by another information specialist not otherwise involved in the project, before being adapted for other databases/interfaces.

Reference lists of included studies and a selection of recent, relevant systematic reviews will be checked. Forwards citation tracking from key publications of included studies (to identify citing papers) will also be undertaken. Supplemental searches will be developed iteratively, as additional search terms, concepts and sources are identified; these may include specific projects, interventions, key authors, theories or organisations.

Types of study to be included

Inclusion Criteria:

- Qualitative, quantitative and/or mixed methods studies
- Studies published in English (or with available English translation). A record will be kept for potentially relevant studies published in non-English language to ensure that no important topics are neglected due to the language restriction

- Studies which provide insight into the feasibility, acceptability, uptake and barriers and facilitators of implementation for interventions specifically designed to help people with a learning disability to use and manage the medications they require for their long-term condition, mental health issues or challenging behaviour
- Studies from Low- and middle-income countries (LMIC) will be included when considered applicable to the UK (this will be assessed by two researchers, and disputes resolved by third person, a senior researcher)

Exclusion:

- Studies which do not provide insight into the feasibility, acceptability, uptake and barriers and facilitators of implementation for interventions designed to optimise medication use for people with a learning disability
- Studies exclusively focusing on individual conditions such as autism and epilepsy without referring to learning disability
- Studies from low- and middle-income countries (LMIC) will be excluded when considered not applicable to the UK (this will be assessed by two researchers, and disputes resolved by third person, a senior researcher)

Condition or domain being studied

- People with a learning disability and a physical long-term condition (e.g. diabetes, chronic obstructive pulmonary disease, arthritis, hypertension), for which there is currently no cure and which are managed with drugs or other treatment
- People with a learning disability and mental health issues and/or challenging behaviour for which medication is prescribed

Participants/population

Children, adolescents and adults with a learning disability and carers of people with a learning disability. A learning disability is defined by three core criteria as mentioned earlier (2).

We will not include populations which have what is defined in the United Kingdom as learning difficulty (e.g., dyslexia, agraphia, dyscalculia). We will also not include populations which have autism or attention deficit hyperactivity disorder (ADHD) or epilepsy but no learning disability.

Intervention(s), exposure(s)

Strategies/interventions that are developed to support people (children and adults) with a learning disability and their carers to optimise the usage of medications required for their chronic condition, mental health issues or challenging behaviour.

Comparator(s)/control

Studies need to focus on at least one specific strategy or intervention to support people with a learning disability to use and manage their medication to be included. Having a comparator is not a requirement for inclusion in this review.

Context

This study will include studies which provide insight into the feasibility, acceptability, uptake and barriers and facilitators of interventions specifically designed to help people with a learning disability to use and manage the medication that they require for their long-term condition(s) or learning disability.

Main outcome

- Intervention description: this includes type of interventions (e.g. patient and carer education to improve knowledge and understanding of prescribed medication, prompting and reminders, adherence monitoring and feedback, habit analysis, multicomponent approaches, dose simplification, special medication packaging, medication review), key personnel for delivery/implementation of the interventions (where applicable), recipients of the interventions (people with

learning disability; their carers or support workers; health professionals; others); specific tools (where applicable), e.g. dosing devices, other materials such as checklists, leaflets, video clips, and processes (e.g. standard operation procedures) required for the interventions; intensity (including duration and frequency) of the intervention); resources required for the intervention.

- Feasibility of interventions
- Acceptability of interventions
- Uptake of interventions
- Barriers and facilitators for the implementation of interventions

Measures of effect:

Dichotomous outcomes will be presented as percentages (e.g. uptake rate of the intervention); continuous outcomes (e.g. rating of acceptability) will be presented as means and standard deviations.

Additional outcome(s):

NA

Data extraction (Selection and Coding)

After search completion, all references will be imported into 'EndNote' and will be deduplicated. All references will be screened at title/abstract level against the inclusion criteria by at least two reviewers in 'Covidence'. Discrepancies will be resolved through discussion or a further reviewer. All papers which meet the inclusion criteria at abstract stage will then be screened at full text and exclusion will have to be justified. When no consensus can be reached between the reviewers, a further reviewer will be consulted. The study selection process will be described in a PRISMA flow chart. The reviewers will independently extract relevant data from all studies included using a data extraction form specifically designed for this systematic review. The design of the data extraction form will be informed by the TIDieR checklist (16) and the Consolidated Framework for Implementation Research (CFIR) (17). Extracted data will include:

- Author
- Title
- Year of publication
- Country
- Population description (number of study participants, severity of learning disability, age of participants, type of chronic disease(s)/ long-term condition(s), medication used
- Settings
- Intervention description (as stated above)
- Results (e.g., feasibility of interventions, acceptability of interventions, uptake of interventions, facilitators and barriers for the implementation of interventions)

Risk of bias (quality assessment)

The Mixed Methods Appraisal Tool (MMAT) – Version 2018 will be used for quality assessment (18). Two reviewers will independently assess the quality of included studies. If the reviewers disagree over the quality assessment, this will be resolved by consulting a third reviewer. The quality assessment will not be used to exclude studies from this review but to offer a context for the synthesised findings.

Strategy for data analysis and synthesis

A narrative synthesis will be conducted to summarise the evidence. Narrative synthesis has been chosen as strategy for data synthesis since the included studies will be heterogenous in study design and outcomes. The findings will be presented via text and tables (19). The findings of this review will be integrated with the findings of the wider project using the Pillar Integration Process (11) or Metrices and/or a narrative (12–14) in order to develop recommendations on how interventions need to be designed to support people with a learning disability and their carers to use and manage their medication.

Analysis of subgroups or subsets

The narrative synthesis will be guided by presentation according to the following groupings of interest:

- Intervention type
- Population type (patient, carers, health and social care professionals)
- Patient age group, sex, and other personal contexts such as level of disability, living arrangement, ethnicity, cultural or religious background.

Dissemination

Findings of this project will be presented in key conferences associated with people with learning disability, and be published in academic journals and in NIHR Journals Library. We will generate infographics to highlight common issues related to medication usage in people with learning disabilities and a summary of evidence on potential interventions. These will be disseminated through charities (the Foundation for People with Learning Disabilities, People First Dorset and Sunderland People First which are directly involved in this project, but also key organisations and wider networks with whom they have collaborated such as Mencap, Learning Disability England), Royal College of General Practitioners and Royal Pharmaceutical Society and be promoted through relevant social media such as Twitter and discussion forums.

In order to ensure that findings of the project can be communicated directly to people with learning disability, members of our PAG and our Learning Disability PPI Group will help us to co-create dissemination materials in formats that are more accessible for people with learning disability. We plan to produce a video for communicating key findings more relevant to them. The contents will be chosen by people with learning disability who will be directly involved in the production. We will also produce easy-read versions of key findings and recommendations.

We will create a project website to be hosted by the University of Warwick. The website will include information about the project and the project team; ways for interested

people to get involved; updates on the progress of the project; and will provide access to findings and outputs of the project when they are produced.

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Mixed methods study, Systematic Review

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Programme

Conflict of interest

None known

Language

English

Country

England

Stage of review

Writing-up

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Appendix

Appendix 1: Draft Medline Search

Ovid MEDLINE(R) ALL <1946 to July 22, 2022>

Date searched: 25/07/22

1 Developmental Disabilities/ or exp Learning Disabilities/ or Persons with Mental Disabilities/ or exp Intellectual Disability/ 144901

2 Neurodevelopmental Disorders/ or exp Child Development Disorders, Pervasive/ 48270

3 ((learning or intellectual* or developmental* or neurodevelopmental*) adj (disabilit* or disabled or handicap* or impair* or retard* or deficien* or disorder* or subnormal*)).kf,tw. 68799

4 (mental* adj (disabilit* or disabled or handicap* or impair* or retard* or deficien* or subnormal*)).kf,tw. 44722

5 (development* adj1 delay*).kf,tw. 21027

6 (down* syndrome or fragile x or william* syndrome or angelman or cri du chat or smith magenis or de lange syndrome or rubinstein taybi or prader willi or patau* syndrome or trisomy 13 syndrome or wagr syndrome* or wilms tumo?r aniridia).kf,tw. 41074

7 "profound intellectual and multiple disab*".kf,tw. 123

8 (PMLD or PIMD).kf,tw. 262

9 (autis* or asperger* or neurofibromatos* or hypothyroid* or phenylketonuria or digeorge or lesch nyhan or rett* syndrome or overgrowth syndrome* or pervasive development* disorder* or f?etal alcohol or prenatal alcohol exposure or fasd or velocardiofacial or velo cardio facial or velo cardiofacial or velocardio facial or klinefelter* or childhood disintegrative or static encephalopath*).kf,tw. 140549

10 (22q11?2 adj1 deletion).kf,tw. 1826

11 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 336013

12 exp Medication Adherence/ or Self-Management/ or Medication Review/ or Medication Therapy Management/ or Deprescriptions/ or Inappropriate Prescribing/ or Polypharmacy/ or Self Administration/ 53452

13 ((medication? or medicine?) adj support).kf,tw. 193

14 ((medication? or medicine? or drug?) adj4 (adheren* or nonadheren* or persisten* or complian* or noncomplian*)).kf,tw. 34530

15 ((medication? or medicine? or drug?) adj3 (understand* or knowledg*)).kf,tw. 14592

16 ((medicine? or medication?) adj management).kf,tw. 4989

17 ((medicine? or medication?) adj review?).kf,tw. 2839

18 (selfmanagement or self management).kf,tw. 24535

19 ((medication? or medicine?) adj3 (administ* or selfadminist*)).kf,tw. 13214

20 ((medication? or medicine? or drug? or prescri*) adj2 (optim* or appropriate* or inappropriate*)).kf,tw. 22997

21 ((medication? or medicine? or drug?) adj1 (discontinu* or taper* or withdraw* or reduc* or decreas*)).kf,tw. 23003

22 (deprescri* or de prescri*).kf,tw. 1768

23 (overprescri* or over prescri* or underprescri* or under prescri*).kf,tw. 2542

24 polypharmacy.kf,tw. 10065

25 ("medication? use" or "medication? usage" or "medicine? use" or "medicine? usage").kf,tw. 24225

26 ((medication? or medicine?) adj (reminder? or list? or information)).kf,tw. 3395

27 ((medication? or medicine? or drug?) adj3 decision making).kf,tw. 1468

28 Pharmacists/ or "pharmacist*".kf,tw. 44457

29 "Off-Label Use"/ or off label.kf,tw. 11336

30 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 238704

31 11 and 30 1961

32 exp animals/ not humans/ 5039010

33 31 not 32 1908

Search strategies and filters from the following studies were consulted in development of this search strategy:

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The following tools were used to identify search terms and refine the search strategy: Systematic Review Accelerator SearchRefinery.

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