

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Interventions for mental health problems in children and adults with severe intellectual disabilities: A systematic review
AUTHORS	Vereenoghe, Leen; Flynn, Samantha; Hastings, Richard; Adams, Dawn; Chauhan, Umesh; Cooper, Sally-Ann; Gore, Nick; Hatton, Chris; Hood, Kerensa; Jahoda, Andrew; Langdon, PE; McNamara, Rachel; Oliver, Chris; Roy, Ashok; Totsika, Vasiliki; Waite, Jane

VERSION 1 – REVIEW

REVIEWER	Dr Gracia Fellmeth University of Oxford
REVIEW RETURNED	19-Feb-2018

GENERAL COMMENTS	<p>Thank you for the opportunity to review this interesting and well-conducted review on a neglected topic. I only have two very minor comments:</p> <ol style="list-style-type: none">1. Did you include cohort studies? Perhaps none were identified, but I did not see these mentioned in your inclusion criteria.2. In the discussion section, you do discuss the limitations of the review. Personally I would find it helpful to have this sign-posted more clearly - i.e. "Limitations of the review were...". As it stands the potential limitations of the review are not clearly demarcated from the limitations of the existing evidence more broadly. <p>Other than these very minor comments this is a rigorously-conducted piece of work on an important topic and I would recommend its publication.</p>
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REVIEWER	Prof Angela Hassiotis UCL Psychiatry, UK
REVIEW RETURNED	19-Feb-2018

GENERAL COMMENTS	<p>The paper is an important contribution to the literature in the field of intellectual disabilities as it focuses on the intractable difficulties of evidence based care (I think the issue of precision medicine goes a bit too far at this stage; p27 line 42) for people with severe to profound ID across the lifespan. The treatment follows on from the identification of a problem and ascertainment remains a considerable challenge as acknowledged by the authors. Nevertheless, bringing the issue to the fore and making a reasoned argument about the importance of further and much needed research is an important first step for improving mental and physical health care of people with IDD.</p> <p>The methods of the review are rigorous and show clearly the paucity</p>
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	<p>of available research. However, the authors do not include limitations in their discussion although some mention particular points is made in various sections of the manuscript (e.g. p28-29; p14 lines 64-68). It would be better to pull all potential problems together in the discussion.</p> <p>The extensive research strategy should, in my opinion, be an appendix or supplementary material.</p> <p>I noted that the references for some mental health difficulties are rather old, e.g. reference #9. I suggest that a more up to date reference may be included (e.g. https://www.futuremedicine.com/doi/full/10.2217/epi.14.52?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub%3Dpubmed&). By the same token, is the 2004 Hastings et al study a better fit or the 2008 Hulbert-Williams and Hastings one?</p>
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REVIEWER	Bernd Puschner Ulm University, Germany
REVIEW RETURNED	21-Feb-2018

GENERAL COMMENTS	<p>This paper aims at giving a systematic review of studies on interventions to improve mental health problems of people with severe intellectual disabilities. The paper is well-written and follows current standards (PRISMA guidelines). Only a few outdated studies of low quality were identified. I believe that apart from the finding that there is no relevant evidence the paper does not add anything. This is no trivial finding, but it should have stopped there. I do not see a reason for presenting extensive descriptions of poorly conducted studies from 30 years ago. As is, the paper is much too long. It should be reduced to a brief report or similar.</p> <p>Minor comments:</p> <ul style="list-style-type: none"> • “Treatment of mental health problems in people with severe...” is no strength or limitation. • A current review could have been mentioned (https://doi.org/10.1192/bjp.bp.114.162313) • Table 1 (search strategy) has 5 pages should go into an online appendix.
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REVIEWER	Dave Dagnan Cumbria Partnership NHS Foundation Trust & Lancaster University, UK
REVIEW RETURNED	28-Feb-2018

GENERAL COMMENTS	<p>This is clearly an important area and is clearly methodologically rigorous. My overall question is concerned with the balance in the paper of the excellent and detailed methodology and very small amount of data, I wonder whether the authors considered a briefer report of the systematic absence of data?</p> <p>I have a small number of specific comments:</p> <ol style="list-style-type: none"> 1. The requirement for a reversal element in a single case experimental design precludes some more successful behavioural approaches. For example, I note a small number of single case studies in the area of phobia where graded exposure and other counter-conditioning approaches show clear success but are treatment approaches for which it is hard to demonstrate reversal. The single case included of environmental enrichment lends itself to a reversal design; beginning a graded exposure with counter-conditioning does not. This would not introduce a large number of papers to the review but papers such as Conyers, C., Miltenberger,
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	<p>R. G., Peterson, B., Gubin, A., Jurgens, M., Selders, A., et al. (2004). An evaluation of in vivo desensitization and video modelling to increase compliance with dental procedures in persons with mental retardation. <i>Journal of Applied Behavior Analysis</i>, 37, 233–238. describe successful behavioural interventions of this type.</p> <p>2. The criterion used to identify outcomes (and by default the core mental health problem) also needs a little clarification. It is not absolutely clear whether the method describes a requirement for studies to have had symptoms assessed by a qualified clinician as part of the original study or whether this was carried out by the study team.</p> <p>3. Related to the above, is there a risk that search approach which uses diagnostics labels may miss some studies (such as the example above) where the issue is described behaviourally but which probably fits the criteria for phobia (for example studies in Hagopian’s review of phobia treatments in people with intellectual disabilities [which finds at least 50% of the participants in the papers reviewed had severe or profound disabilities] often use terms such as avoidance or aversion rather than phobia)?</p> <p>4. A minor point but the strengths and limitations of the study (page 4) somewhat underplays the major weakness for any generalizable statements about interventions of such a small number of studies reviewed in psychosocial and pharmacological areas.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Dr Gracia Fellmeth

Institution and Country: University of Oxford

Please state any competing interests: None declared

Please leave your comments for the authors below

Thank you for the opportunity to review this interesting and well-conducted review on a neglected topic. I only have two very minor comments:

1. Did you include cohort studies? Perhaps none were identified, but I did not see these mentioned in your inclusion criteria.

- Thank you for your comment. Observational cohort studies were not eligible for inclusion in this review. We have now clarified this in the study eligibility criteria section.
- Addition: ‘Observational and retrospective cohort studies, as well as case studies without a control condition or a return to baseline were excluded.’ (p. 7)

2. In the discussion section, you do discuss the limitations of the review. Personally I would find it helpful to have this sign-posted more clearly - i.e. "Limitations of the review were...". As it stands the potential limitations of the review are not clearly demarcated from the limitations of the existing evidence more broadly.

- Thank you for your comment. We have now signposted the limitations of the review under a new heading and differentiated it from the limitations of the evidence.
- Addition: subheadings ‘Strengths and limitations’, and ‘Explanations and implications’. (p. 24)

Other than these very minor comments this is a rigorously-conducted piece of work on an important topic and I would recommend its publication.

- Thank you for your consideration.

Reviewer: 2

Reviewer Name: Prof Angela Hassiotis

Institution and Country: UCL Psychiatry, UK

Please state any competing interests: None declared (I know and have worked with some of the authors in the past)

Please leave your comments for the authors below

The paper is an important contribution to the literature in the field of intellectual disabilities as it focuses on the intractable difficulties of evidence based care (I think the issue of precision medicine goes a bit too far at this stage; p27 line 42) for people with severe to profound ID across the lifespan. The treatment follows on from the identification of a problem and ascertainment remains a considerable challenge as acknowledged by the authors. Nevertheless, bringing the issue to the fore and making a reasoned argument about the importance of further and much needed research is an important first step for improving mental and physical health care of people with IDD.

- Thank you for your comment. We have removed this information from the discussion.
- Removal: 'Whilst precision medicine is recognised to be of crucial importance, the evidence allows for no precision in management of the mental health problems so frequently experienced by people with severe intellectual disabilities.' (p. 22)

The methods of the review are rigorous and show clearly the paucity of available research. However, the authors do not include limitations in their discussion although some mention of particular points is made in various sections of the manuscript (e.g. p28-29; p14 lines 64-68). It would be better to pull all potential problems together in the discussion.

- Thank you for your comment. We have now signposted the limitations of the review under a new heading and differentiated it from the limitations of the evidence.
- Addition: subheadings 'Strengths and limitations', and 'Explanations and implications'. (p. 24)

The extensive research strategy should, in my opinion, be an appendix or supplementary material.

- We have taken up this suggestion and moved Table 1 to the Appendix. (p. 7 & Appendix)

I noted that the references for some mental health difficulties are rather old, e.g. reference #9. I suggest that a more up to date reference may be included (e.g. https://www.futuremedicine.com/doi/full/10.2217/epi.14.52?url_ver=Z39.88-2003&rft_id=ori%3Arid%3Aacrossref.org&rft_dat=cr_pub%3Dpubmed&). By the same token, is the 2004 Hastings et al study a better fit or the 2008 Hulbert-Williams and Hastings one?

- Thank you for your comment. We have updated our references.
- Addition: Krefft M, Frydecka D, Adamowski T, Misiak B. From Prader–Willi syndrome to psychosis: translating parent-of-origin effects into schizophrenia research. *Futur Med.* 2014;6(6):677–88. (p. 5)

- Addition: Hulbert-Williams L, Hastings RP. Life events as a risk factor for psychological problems in individuals with intellectual disabilities: A critical review. *J Intellect Disabil Res.* 2008 Nov;52(11):883–95. (p. 5)

Reviewer: 3

Reviewer Name: Bernd Puschner

Institution and Country: Ulm University, Germany

Please state any competing interests: None declared.

Please leave your comments for the authors below

This paper aims at giving a systematic review of studies on interventions to improve mental health problems of people with severe intellectual disabilities. The paper is well-written and follows current standards (PRISMA guidelines). Only a few outdated studies of low quality were identified. I believe that apart from the finding that there is no relevant evidence the paper does not add anything. This is no trivial finding, but it should have stopped there. I do not see a reason for presenting extensive descriptions of poorly conducted studies from 30 years ago. As is, the paper is much too long. It should be reduced to a brief report or similar.

- Thank you for your consideration. We are aware that the number of studies identified through this systematic review is disappointing but have tried to make a case about the importance of research directed at this particular population.

Minor comments:

- “Treatment of mental health problems in people with severe...” is no strength or limitation.
 - Thank you for your comment. We have revised this statement in our strengths and limitations section.
 - Revision: ‘The body of evidence we identified was very slim and does not allow for generalisation of findings for either psychological or pharmacological interventions.’ (p. 4)
- A current review could have been mentioned (<https://doi.org/10.1192/bjp.bp.114.162313>)
 - Thank you for your comment. We are aware of this very interesting and recent systematic review. However, the review by Koslowski et al. (2016) also includes systemic interventions, which fall outside the scope of the current review, and excluded interventions relating to children or to people with severe or profound intellectual disabilities.
- Table 1 (search strategy) has 5 pages should go into an online appendix.
 - We have taken up this suggestion and moved Table 1 to the Appendix. (p. 7 & Appendix)

Reviewer: 4

Reviewer Name: Dave Dagnan

Institution and Country: Cumbria Partnership NHS Foundation Trust & Lancaster University, UK

Please state any competing interests: None declared

Please leave your comments for the authors below

This is clearly an important area and is clearly methodologically rigorous. My overall question is concerned with the balance in the paper of the excellent and detailed methodology and very small amount of data, I wonder whether the authors considered a briefer report of the systematic absence of data?

- Thank you for your consideration. We are aware that the number of studies identified through this systematic review is disappointing but have tried to make a case about the importance of research directed at this particular population.

I have a small number of specific comments:

1. The requirement for a reversal element in a single case experimental design precludes some more successful behavioural approaches. For example, I note a small number of single case studies in the area of phobia where graded exposure and other counter-conditioning approaches show clear success but are treatment approaches for which it is hard to demonstrate reversal. The single case included of environmental enrichment lends itself to a reversal design; beginning a graded exposure with counter-conditioning does not. This would not introduce a large number of papers to the review but papers such as Conyers, C., Miltenberger, R. G., Peterson, B., Gubin, A., Jurgens, M., Selders, A., et al. (2004). An evaluation of in vivo desensitization and video modelling to increase compliance with dental procedures in persons with mental retardation. *Journal of Applied Behavior Analysis*, 37, 233–238. describe successful behavioural interventions of this type.

- Thank you for your comment. We are aware of the body of evidence relating to phobias of medical procedures in this population. For the present review, the focus was on mental health problems that significantly impact daily functioning rather than compliance with certain procedures where problems with compliance may be related to mental health symptoms such as anxiety. Thus, this literature did not meet the inclusion criteria. In addition, other single case experimental design approaches (multiple baseline designs in particular) could have been used to evaluate behavioural approaches for mental health problems. However, such studies did not emerge from the searches.

2. The criterion used to identify outcomes (and by default the core mental health problem) also needs a little clarification. It is not absolutely clear whether the method describes a requirement for studies to have had symptoms assessed by a qualified clinician as part of the original study or whether this was carried out by the study team.

- Thank you for your comment. We have revised this criterion to clarify that the original studies required a qualified clinician to deliver the intervention. Outcomes were to be reported using standardised assessments but could be administered by non-clinicians (e.g. researchers).
- Revision: 'Eligible outcomes were standardised assessments of mental disorders or their key symptoms which have a significant impact on daily functioning'. (p. 8)

3. Related to the above, is there a risk that search approach which uses diagnostics labels may miss some studies (such as the example above) where the issue is described behaviourally but which probably fits the criteria for phobia (for example studies in Hagopian's review of phobia treatments in people with intellectual disabilities [which finds at least 50% of the participants in the papers reviewed had severe or profound disabilities] often use terms such as avoidance or aversion rather than phobia)?

- Thank you for your comment. We have added this as a limitation to our study. We are confident however that our additional search methods, including use of the ancestry method and contact with authors, would have identified relevant studies that met all review eligibility criteria. Numerous studies of interventions for phobia in people with severe and profound intellectual disabilities have targeted avoidance of and compliance with medical procedures. Such interventions, however, fall outside the scope of this review (see earlier responses).
- Revision: 'The systematic search did not include terms for every specific possible disorder or potential treatment, neither did it include a wide range of behavioural descriptions. In spite of this, we identified a considerably large number of potential records.' (p. 24)

4. A minor point but the strengths and limitations of the study (page 4) somewhat underplays the major weakness for any generalizable statements about interventions of such a small number of studies reviewed in psychosocial and pharmacological areas.

- Thank you for your comment. We have revised this statement in our strengths and limitations section.
- Revision: 'The body of evidence we identified was very slim and does not allow for generalisation of findings from either psychological or pharmacological interventions.' (p. 4)
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VERSION 2 – REVIEW

REVIEWER	Dave Dagnan Cumbria Partnership NHS Foundation Trust & Lancaster University, UK
REVIEW RETURNED	03-Apr-2018

GENERAL COMMENTS	The authors have addressed my questions. On balance I still feel this is a complex paper with a simple message of no recent or substantial published treatment research! However, the authors have answered my queries and I would recommend publication.
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REVIEWER	Dr Gracia Fellmeth University of Oxford, UK
REVIEW RETURNED	09-Apr-2018

GENERAL COMMENTS	The authors have taken on board the various comments provided by reviewers. The limitations section is now clearer but more could be added to this section, e.g. the comment by one reviewer that only few relevant studies were found and that these were out of date and that overall the review does not add many new findings. This should be commented upon in the limitations section. The authors also state that the search strategy "did not include terms for every specific possible disorder or potential treatment". If this is going to be listed as a short-coming, it would be helpful if there was also a justification for having adopted this approach (rather than applying a more comprehensive search strategy).
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VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Dr Gracia Fellmeth

Institution and Country: University of Oxford

Please state any competing interests: None declared

Please leave your comments for the authors below

The authors have taken on board the various comments provided by reviewers. The limitations section is now clearer but more could be added to this section, e.g. the comment by one reviewer that only few relevant studies were found and that these were out of date and that overall the review does not add many new findings. This should be commented upon in the limitations section. The authors also state that the search strategy "did not include terms for every specific possible disorder or potential treatment". If this is going to be listed as a short-coming, it would be helpful if there was also a justification for having adopted this approach (rather than applying a more comprehensive search strategy).

- Thank you for considering the changes we have made to our original manuscript. We have revised the limitations section to stress the limited findings and to justify our search strategy.
- Revision, p. 24: 'In spite of this, our findings show that this area of research has received very little attention over the years with no recent treatments studies being identified and pharmacological interventions having employed drugs that would no longer comply with today's medical standards.'
- Revision, p. 7: 'Instead of listing all potential diagnosis and treatments the search strategy included the most common diagnoses and treatments in conjunction with more general mental health descriptions. This approach could limit the initial records to be screened, whereas relevant studies would still be identified through the ancestry method which screens citing and cited articles of included studies and through contact with authors.'

Reviewer: 4

Reviewer Name: Dave Dagnan

Institution and Country: Cumbria Partnership NHS Foundation Trust & Lancaster University, UK

Please state any competing interests: None declared

Please leave your comments for the authors below

The authors have addressed my questions. On balance I still feel this is a complex paper with a simple message of no recent or substantial published treatment research! However, the authors have answered my queries and I would recommend publication.

- Thank you for considering the changes to our manuscript. We have revised the limitations section to stress the limited findings.
- Revision, p. 24: 'In spite of this, our findings show that this area of research has received very little attention over the years with no recent treatments studies being identified and pharmacological interventions having employed drugs that would no longer comply with today's medical standards.'
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