PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	A rapid systematic review of measures to protect older people in long term care facilities from COVID-19
AUTHORS	Frazer, Kate; Mitchell, Lachlan; Stokes, Diarmuid; Lacey, Ella; Crowley, Eibhlin; Kelleher, Cecily

VERSION 1 – REVIEW

REVIEWER	Low, Lee Fay University of Sydney
REVIEW RETURNED	11-Jan-2021

GENERAL COMMENTS	Thank you for conducting this important rapid review, it is important to generate evidence with regards to reducing COVID transmission in care homes. 1) It is not clear how the eligibility criteria "report an assessment of measures to reduce transmission of COVID-19 (including SARS or MERS) in residents, employees, or visitors" is was operationalised. My interpretation is that 'measures to reduce transmission' would require active and probably new measures, whereas many of the included papers reported on existing facility characteristics (e.g. size, profit status). To me, many of the included papers would not meet inclusion criteria, and should be excluded or the inclusion criteria are broadened 2) On outcome measures, I'm not sure about the value of table 3 (point prevalence of COVID, point prevalence of symptoms, mortality) in terms of addressing the review aim. While it does contain some useful information, it doesn't provide sufficient context around the other conditions most e.g. community prevalence of COVID-19 in that region which might help interpret these data, and the stage of outbreak in a facility (i.e. were point prevalence data taken after the outbreak had run it's course, or in the middle of the outbreak?). 3) In terms of measures which were instituted to prevent COVID-19 transmissions, such as mass testing, use of PPE, single-site work policies, these were often instituted together, and it would be difficult to disentangle the effects of individual measures. 4) The major limitation of the paper is that while it presents a summary of data between facility characteristics and COVID outcomes, it does not present a summary of measures to prevent COVID-19 transmissions and COVID-19 outcomes. It appears that there are not sufficient data on these relationships in the published literature, and if this is the case it should be stated.

	5) Suggest that SARS related studies are not included, as the transmissibility of SARS and COVID are different. 6) The grey literature (e.g. country specific reports on COVID transmission strategies and outcomes that have been produced by different departments of health) might provide additional trustworthy data. 7) A minor point that in the introduction it states that the reasons that older people are more susceptible to COVID-19 are unclear, I believe this is not accurate and that there are some biological reasons why older people are at higher risk.

REVIEWER	Chamberlain , Stephanie University of Alberta, Nursing
REVIEW RETURNED	11-Jan-2021

GENERAL COMMENTS	Thank you for the opportunity to review this paper. It is important work and highlights to intense vulnerability of the long-term care sector to Covid-19 and measures that must be considered in future outbreaks. The focus on organizational and facility characteristics is particularly important. I have offered a few suggestions and areas for you to consider. Background The background is complete but given the understandable lag between submission and review some information needs to be updated. This includes the number of covid-19 cases and deaths worldwide. The discussion of the vaccine should also be updated to indicate that there are several vaccines that have been approved in various countries (i.e., Pfizer, Moderna) and that are currently being administered in acute care and LTC homes. I would also reference the prevalence of Covid-19 in LTC in Canada and the US. It is particularly relevant to include Canada because over 80% of Covid-19 deaths have occurred in LTC residents. Much higher than in other EU countries. Methods The authors should highlight how this rapid review differs from a traditional systematic review for readers (e.g., which stages are simplified/omitted). Can the authors clarify if their search included or excluded National reports? One of the included studies is by the Office for National Statistics (ref. 39) but the PRISMA diagram and the study Methods indicate that Reports were excluded. Given that pre-published studies were included and the rapid nature of current government reporting it might have been advisable to include Reports. However, I understand the need to limit the search for a rapid review. The Limitations should then reflect the exclusion of unpublished reports. Results In the various Tables there were some issues with spacing in the columns that made it hard to know when reference to one study ended and another began.

	Discussion One measure that was not described in the Discussion was the regional/public health directive that restricted care aides to working in only one facility. This was an early measure taken to limit spread after it was found that many staff worked in multiple homes and this was driving transmission. It was a broader public health directive that influenced all facilities so it is understandable why it wasn't described in the individual studies but should be referenced in the Discussion as a measure to reduce transmission.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1 Lee Fay Low, University of Sydney Comments to the Author:	
Thank you for conducting this important rapid review, it is important to generate evidence with regards to reducing COVID transmission in care homes.	Thank you for your comments.
1) It is not clear how the eligibility criteria "report an assessment of measures to reduce transmission of COVID-19 (including SARS or MERS) in residents, employees, or visitors" is was operationalised. My interpretation is that 'measures to reduce transmission' would require active and probably new measures, whereas many of the included papers reported on existing facility characteristics (e.g. size, profit status). To me, many of the included papers would not meet inclusion criteria, and should be excluded or the inclusion criteria are broadened	Many thanks for your comments; however, we respectfully disagree that the papers did not meet the inclusion criteria for the reasons set out below. Our review was to establish what measures existed in long term care facilities to reduce risk of transmission. Specifically, we stated: 'aim of this rapid review of the literature was to assess the extent to which measures implemented in LTCF reduced transmission of COVID-19 (SARS-CoV-2) among residents, staff, and visitors, and the effect of these measures on morbidity and mortality outcomes. The review was initially undertaken when knowledge of measures or activities effective against a novel virus were not known. This certainly might include existing infection prevention and control measures as well as

	new strategies. We deliberately sought to identify what interventions had been reported and applied a broad interpretation of 'intervention' to enable inclusion of real time reporting of current papers. Our inclusion criteria are broad and encompassing. *Eligibility criteria* All study designs (experimental, observational, and qualitative) are included, and no exclusions placed on language. Included studies report an assessment of measures to reduce transmission of COVID-19 (including SARS or MERS) in residents, employees, or visitors of LTCF. Is it important in congregated settings to understand how the facilities in themselves confer or mitigate risk. To provide as comprehensive a review of the evidence we included any intervention implemented to reduce the transmission of COVID-19 in long-term residential care facilities, including facility measures, social distancing, use of personal protective equipment, and hand hygiene.
On outcome measures, I'm not sure about the value of table 3 (point prevalence of COVID, point prevalence of symptoms, mortality) in terms of addressing the review aim. While it does contain some useful information, it doesn't provide sufficient context around the other conditions most e.g. community prevalence of COVID-19 in that region which might help interpret these data, and the stage of outbreak in a facility (i.e. were point prevalence data taken after the outbreak had run it's course, or in the middle of the outbreak?).	Thank you for your comments. We consider Table 3 to be justified as it contains novel information of policy relevance. We can only report the information as published, many of the papers do not give information on wider community incidence or prevalence, we submit that is outside the scope of this review.
In terms of measures which were instituted to prevent COVID-19 transmissions, such as mass testing, use of PPE, single-site work policies, these were often instituted together, and it would be difficult to	We agree and acknowledge that public health measures are not instituted singly. In real-time public health practice these measures are not put in place and evaluated separately.

disentangle the effects of individual measures.	
The major limitation of the paper is that while it presents a summary of data between facility characteristics and COVID outcomes, it does not present a summary of measures to prevent COVID-19 transmissions and COVID-19 outcomes. It appears that there are not sufficient data on these relationships in the published literature, and if this is the case it should be stated	Thank you. We have included the following sentence in our limitations section page 37. We acknowledge that while a summary of facility characteristics and COVID-19 outcomes are presented, data do not allow for presentation of specific measures.
Suggest that SARS related studies are not included, as the transmissibility of SARS and COVID are different.	This is a valid point we did consider. However, we did learn information from SARS and MERS that was useful in the evolving understanding of COVID-19. At the outset of the pandemic experience of SARS was an influence in public health measures put in place. Heung et al. and Ho et al. studies provided data on droplet and contact transmissions and on use of cohorting and PPE. These studies met the inclusion criteria that we applied rigorously and systematically.
The grey literature (e.g. country specific reports on COVID transmission strategies and outcomes that have been produced by different departments of health) might provide additional trustworthy data.	We agree on the importance of such data. Our earlier published systematic review for the Republic of Ireland's Department of Health Nursing Homes Expert Panel included grey literature based on the International experience. However, we confined this review to published research papers, not reports. We reference our report for Expert Panel in the discussion P.38 and is reference 55. In our quality rating review table (supplementary table 2) we note the one paper that remains from Medrxiv. We acknowledge in our review of quality P.37.

A minor point that in the introduction it states that the reasons that older people are more susceptible to COVID-19 are unclear, I believe this is not accurate and that there are some biological reasons why older people are at higher risk.	Thank you, we provide additional explanation, and an additional reference is included in the introduction p.5: The specific rationale for their increased susceptibility is less clear. Comorbidities including cardiovascular disease and diabetes *may increase the chances of fatal disease, but they alone do not explain why age is an independent risk factor* (Mueller et al. 2020 p. 9959). Molecular, biological and immunological changes inform emergent viable hypotheses (Mueller et al. 2020 p. 9968). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7288963/pdf/aging-12-103344.pdf
Reviewer: 2 Dr. Stephanie Chamberlain , University of Alberta	
Thank you for the opportunity to review this paper. It is important work and highlights to intense vulnerability of the long-term care sector to Covid-19 and measures that must be considered in future outbreaks. The focus on organizational and facility characteristics is particularly important. I have offered a few suggestions and areas for you to consider.	Thank you for your encouraging feedback.
Background The background is complete but given the understandable lag between submission and review some information needs to be updated. This includes the number of covid-19 cases and deaths worldwide.	Thank you we have updated the infection and mortality numbers to the introduction and have included information regarding vaccinations in the discussion. As vaccines are an important development, particularly for the LTCF population, we feel the inclusion of vaccine information is an important one to highlight. P4 and updated reference 7. Globally, up to March 25 2021 there are 123 636 852 cases of COVID-19 (following the applied case definitions and testing strategies in the affected countries) including 2 721 891 deaths. Within Europe,

The discussion of the vaccine should also be updated to indicate that there are several vaccines that have been approved in various countries (i.e., Pfizer, Moderna) and that are currently being administered in acute care and LTC homes.	over 25 220 376 cases are reported, with 592 929 deaths. P36 Rapid development of COVID-19 vaccines was recognised in early March 2020 (Lurie et al. 2020). Lurie et al. (2020) noted previous success in development of a H1N1 vaccination, and similarly the challenges for SARS, Ebola and Zika vaccines. The speed of developments is acknowledged, and Public Health England (2021) reported that at the end of February 2021 up to 5900 deaths were averted in people aged 80 years and older, with over 200 deaths prevented in those aged 70 to 79 years. Montano (2021) advises that an accelerated pace of vaccine developments may not lead to full eradication of the virus citing smallpox as the only virus that is worldwide. Given this, the transmission reduction measures highlighted in the present review are of key importance for continued management of COVID-19 in LTCF.
I would also reference the prevalence of Covid-19 in LTC in Canada and the US. It is particularly relevant to include Canada because over 80% of Covid-19 deaths have occurred in LTC residents. Much higher than in other EU countries.	Thank you. This is also noted in the Irish Expert Panel Report. We added the following text on p 35/36. Sepulveda (2020) reports the disproportionately higher risk of contracting COVID-19 for residents of LTCFs, calculating a 12- country average mortality rate of 2772 per 100,000 LTFC residents compared to 122 per 100,000 for community dwelling older persons. This represented an average 24.2 fold higher rate of death (range 14.2 (Germany) to 73.7 (Canada). Higher mortality rates in Canada (78.4% V the OECD 12 country average 47.3%) are explained by poorer services in care facilities including limited staffing and funding (Sepulveda 2020).
The authors should highlight how this rapid review differs from a traditional systematic review for readers (e.g., which stages are simplified/omitted).	The review was rapid in nature as it was important to contribute to ongoing public health policy initiatives in a formative way. An initial review for the Irish Expert Panel had a time frame of 6 weeks. We then updated our searches up to 27th July for this publication. We believe we employed rigorous methodological standards.

	Four databases were included in this review only. All other criteria associated with PRISMA guidelines on reviews is complete. We included a PRISMA guidelines form as a supplementary file.
Can the authors clarify if their search included or excluded National reports? One of the included studies is by the Office for National Statistics (ref. 39) but the PRISMA diagram and the study Methods indicate that Reports were excluded. Given that pre-published studies were included and the rapid nature of current government reporting it might have been advisable to include Reports. However, I understand the need to limit the search for a rapid review. The Limitations should then reflect the exclusion of unpublished reports.	This review does not include national reports as detailed in our methods and protocol, see earlier comments. Reference 39 (now reference 40) has been amended and thank you for bringing this to our attention. The data from this study was published by Office for National Statistics. However, this is based on a funded study from University College London, led by Professor Smallcross. Publishing of their data on an official site is in their published protocol. https://www.ucl.ac.uk/health-informatics/research/vivaldi-study We will amend our reference to include the title of the study. National reports are included in the review published for Expert Panel in Ireland. Ref. 55 (was reference 58 in first submission). This review includes empirical studies and we have included those listed in Medrxiv to enable rapid reporting of this evidence.
Results In the various Tables there were some issues with spacing in the columns that made it hard to know when reference to one study ended and another began.	Thank you. We have revised Tables to ensure that grid lines are included for all.
Discussion One measure that was not described in the Discussion was the regional/public health directive that restricted care aides to working in only one facility. This was an early measure taken to limit spread after it was found that many staff worked in multiple homes and this was driving transmission. It was a broader public health directive that	Thank you. We have revised a sentence on p 35 to include this information and include ref 55 (Irish Expert Panel Report). These included guidance on hand hygiene, and contact and droplet precautions, and restricting staff, including agency workers, to working in only one facility.

influenced all facilities so it is understandable why it wasn't described in the individual studies but should be referenced in the Discussion as a measure to reduce transmission.	

VERSION 2 – REVIEW

REVIEWER	Chamberlain , Stephanie University of Alberta, Nursing
REVIEW RETURNED	04-May-2021

GENERAL COMMENTS	Briefly describe what the authors define as LTC facility in the background as the definition of the setting varies considerably across and within countries. Remove facility characteristics from the primary outcome and in Table 1 outcome column. The outcome is covid-19 related information such as cases, mortality, symptoms, etc. Facility characteristics may be an independent factor associated with the outcome of interest but they are not an outcome (see Abrams as well as Stall wording in Table 1). In fact, they are appropriately described as more an independent factor in both the Results and Discussion section. The wording in the Results (Page 25-Characteristics of LTCFs on Covid-19 transmission) and in the Discussion echo this sentiment with facility characteristic being linked with risk of cases, not facility characteristics being an outcome. The outcome column in Table 1 should be more streamlined to highlight the specific covid-19 related outcomes and facility characteristics in other columns.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2

- Briefly describe what the authors define as LTC facility in the background as the definition of the setting varies considerably across and within countries.

Authors' response: *Thank you for your suggestion. We have added a description on* ***page 6 (line 130****) adopting ECDC May 2020 guidance used for our review.*

"A broad definition of LTCFs was adopted for this review noting ECDC guidance [8] including institutions such as nursing homes, skilled nursing facilities, retirement homes, assisted-living facilities, residential care homes or other facilities providing care in congregated setting for older aged adults.".

Reviewer: 2

Remove facility characteristics from the primary outcome and in Table 1 outcome column. The outcome is covid-19 related information such as cases, mortality, symptoms, etc. Facility characteristics may be an independent factor associated with the outcome of interest, but they are not an outcome (see Abrams as well as Stall wording in Table 1). In fact, they are appropriately described as more an independent factor in both the Results and Discussion section. The wording in the Results (Page 25-Characteristics of LTCFs on Covid-19 transmission) and in the Discussion echo this sentiment with facility characteristic being linked with risk of cases, not facility characteristics being an outcome.

The outcome column in Table 1 should be more streamlined to highlight the specific covid-19 related outcomes and facility characteristics in other columns.

Authors' response: *We confirm that facility characteristics were an outcome for reporting noted in our published protocol. CRD42020191569. Following your suggestion, we have revised the reporting of outcomes in our paper –* ***see page 6 (lines 134-138)*** *and include a 'Secondary outcome' heading and have moved our wording on facility characteristics to here instead:*

"Primary outcome measures

Primary outcome measures are morbidity data, case fatality rates, and reductions in reported transmission rates.

Secondary outcomes

Secondary outcomes reported are facility characteristics associated with COVID-19 incidence." (line 138)

We have added a column to Table 1 and include text on facility outcome reporting.

Table 1 outcomes are separated and are reported in two separate columns as suggested. ***(Pages 9 to 22)***