



**Health
Information
and Quality
Authority**

An tÚdarás Um Fhaisnéis
agus Cáilíocht Sláinte

**What is the evidence underpinning the
categorisation of 'extremely medically
vulnerable' groups, who may be at risk
of severe illness from COVID-19?**

**Advice to the National Public Health
Emergency Team**

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About the Health Information and Quality Authority

The Health Information and Quality Authority (HIQA) is an independent statutory authority established to promote safety and quality in the provision of health and social care services for the benefit of the health and welfare of the public.

HIQA's mandate to date extends across a wide range of public, private and voluntary sector services. Reporting to the Minister for Health and engaging with the Minister for Children and Youth Affairs, HIQA has responsibility for the following:

- **Setting standards for health and social care services** — Developing person-centred standards and guidance, based on evidence and international best practice, for health and social care services in Ireland.
- **Regulating social care services** — The Chief Inspector within HIQA is responsible for registering and inspecting residential services for older people and people with a disability, and children's special care units.
- **Regulating health services** — Regulating medical exposure to ionising radiation.
- **Monitoring services** — Monitoring the safety and quality of health services and children's social services, and investigating as necessary serious concerns about the health and welfare of people who use these services.
- **Health technology assessment** — Evaluating the clinical and cost-effectiveness of health programmes, policies, medicines, medical equipment, diagnostic and surgical techniques, health promotion and protection activities, and providing advice to enable the best use of resources and the best outcomes for people who use our health service.
- **Health information** — Advising on the efficient and secure collection and sharing of health information, setting standards, evaluating information resources and publishing information on the delivery and performance of Ireland's health and social care services.
- **National Care Experience Programme** — Carrying out national service-user experience surveys across a range of health services, in conjunction with the Department of Health and the HSE.

Foreword

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a highly infectious virus which has caused tens of millions of cases of COVID-19 since its emergence in 2019, with a considerable level of associated mortality. In the context of the ongoing COVID-19 pandemic, SARS-CoV-2 constitutes a significant public health concern due to its high basic reproduction rate, the absence of immunity in the human population, and the current lack of an effective vaccination or treatment approaches.

The National Public Health Emergency Team (NPHE) oversees and provides national direction, guidance, support and expert advice on the development and implementation of strategies to contain COVID-19 in Ireland. Since March 2020, HIQA's COVID-19 Evidence Synthesis Team has provided research evidence to support the work of NPHE and associated groups and inform the development of national public health guidance. The COVID-19 Evidence Synthesis Team which is drawn from the Health Technology Assessment Directorate in HIQA, conducts evidence synthesis incorporating the scientific literature, international public health recommendations, and existing data sources as appropriate.

From September 2020, as part of the move towards a sustainable response to the public health emergency, HIQA provides evidence based advice in response to requests from NPHE. The advice provided to NPHE is informed by research evidence developed by HIQA's COVID-19 Evidence Synthesis Team and with expert input from HIQA's COVID-19 Expert Advisory Group (EAG). Topics for consideration are outlined and prioritised by NPHE. This process helps to ensure rapid access to the best available evidence relevant to the SARS-CoV-2 outbreak to inform decision-making at each stage of the pandemic.

The purpose of this report is to outline the advice provided to NPHE by HIQA regarding the categorisation of groups as 'extremely medically vulnerable', that is, groups at risk of severe illness from COVID-19.

HIQA would like to thank its COVID-19 Evidence Synthesis Team, the members of the COVID-19 EAG and all who contributed to the preparation of this report.



Dr Máirín Ryan

Deputy CEO & Director of Health Technology Assessment

Health Information and Quality Authority

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Particular thanks are due to the Expert Advisory Group (EAG) and the individuals within the organisations listed below who provided advice and information.

The membership of the EAG was as follows:

Dr Máirín Ryan (Chairperson)	Director of Health Technology Assessment & Deputy Chief Executive Officer, HIQA
Dr Niamh Bambury	Specialist Registrar in Public Health Medicine, HSE-Health Protection Surveillance Centre (HPSC)
Prof Karina Butler	Consultant Paediatrician and Infectious Diseases Specialist, Children's Health Ireland & Chair of the National Immunisation Advisory Committee
Dr Jeff Connell	Assistant Director, UCD National Virus Reference Laboratory, University College Dublin
Dr Eibhlín Connolly	Deputy Chief Medical Officer, Department of Health
Prof Máire Connolly	Specialist Public Health Adviser, Department of Health & Adjunct Professor of Global Health and Development, National University of Ireland, Galway
Prof Martin Cormican	Consultant Microbiologist & National Clinical Lead, HSE Antimicrobial Resistance and Infection Control Team
Ms Sinead Creagh	Laboratory Manager, Cork University Hospital & Academy of Clinical Science and Laboratory Medicine
Dr Ellen Crushell*	Consultant Paediatrician, Dean, Faculty of Paediatrics, Royal College of Physicians of Ireland & Co-Clinical Lead, Paediatric/Neonatology National Clinical Programme

Dr John Cuddihy	Specialist in Public Health Medicine & Interim Director, HSE- Health Protection Surveillance Centre (HPSC)
Dr Cillian de Gascun	Consultant Virologist & Director of the National Virus Reference Laboratory, University College Dublin
Dr Lorraine Doherty	National Clinical Director Health Protection, HSE- Health Protection Surveillance Centre (HPSC)
Ms Josephine Galway	National Director of Nursing, Infection Prevention Control and Antimicrobial Resistance, AMRIC Division, HSE- Health Protection Surveillance Centre (HPSC)
Dr Vida Hamilton	Consultant Anaesthetist & National Clinical Advisor and Group Lead, Acute Hospital Operations Division, HSE
Dr David Hanlon	General Practitioner & National Clinical Advisor and Group Lead, Primary Care/Clinical Strategy and Programmes, HSE
Dr Patricia Harrington	Head of Assessment, Health Technology Assessment, HIQA
Dr Muiris Houston*	Specialist in Occupational Medicine, Clinical Strategist – Pandemic, Workplace Health & Wellbeing, HSE
Dr Derval Igoe	Specialist in Public Health Medicine, HSE- Health Protection Surveillance Centre (HPSC)
Prof Mary Keogan	Consultant Immunologist, Beaumont Hospital & Clinical Lead , National Clinical Programme for Pathology, HSE
Dr Siobhán Kennelly	Consultant Geriatrician & National Clinical & Advisory Group Lead, Older Persons, HSE
Ms Sarah Lennon	Executive Director, SAGE Advocacy
Mr Andrew Lynch	Business Manager, Office of the National Clinical Advisor and Group Lead - Mental Health, HSE

Dr Gerry McCarthy *	Consultant in Emergency Medicine, Cork University Hospital & Clinical Lead, National Clinical Programme for Emergency Medicine, HSE
Prof Paddy Mallon*	Consultant in Infectious Diseases, St Vincent's University Hospital & National Clinical Programme for Infectious Diseases, HSE
Dr Eavan Muldoon*	Consultant in Infectious Diseases, Mater Misericordiae University Hospital, National Clinical Lead for CIT and OPAT programmes & National Clinical Programme for Infectious Diseases, HSE
Dr Desmond Murphy	Consultant Respiratory Physician & Clinical Lead, National Clinical Programme for Respiratory Medicine, HSE
Dr John Murphy*	Consultant Paediatrician & Co-Clinical Lead, Paediatric/Neonatology National Clinical Programme, HSE
Dr Sarah M. O'Brien	Specialist in Public Health Medicine, Office of National Clinical Advisor & Group Lead (NCAGL) for Chronic Disease
Dr Gerard O'Connor*	Consultant in Emergency Medicine, Mater Misericordiae University Hospital & National Clinical Programme for Emergency Medicine, HSE
Ms Michelle O'Neill	HRB-CICER Programme Manager, Health Technology Assessment, HIQA
Dr Margaret B. O'Sullivan	Specialist in Public Health Medicine, Department of Public Health, HSE South & Chair, National Zoonoses Committee
Dr Michael Power	Consultant Intensivist, Beaumont Hospital & Clinical Lead, National Clinical Programme for Critical Care, HSE
Dr Lynda Sisson*	Consultant in Occupational Medicine, Dean of Faculty of Occupational Medicine, RCPI & National Clinical Lead for Workplace Health and Well Being, HSE
Prof Susan Smith	General Practitioner & Professor of Primary Care Medicine, Royal College of Surgeons in Ireland

Dr Patrick Stapleton	Consultant Microbiologist, UL Hospitals Group, Limerick & Irish Society of Clinical Microbiologists
Dr Conor Teljeur	Chief Scientist, Health Technology Assessment, HIQA
Ms Anne Tobin	Assessment and Surveillance Manager, Medical Devices, Health Products Regulatory Authority

* Alternate nominee for programme /association

Members of HIQA's Evidence Synthesis Team:

Susan Ahern, Natasha Broderick, Paula Byrne, Karen Cardwell, Paul Carty, Barbara Clyne, Laura Comber, Christopher Fawsitt, Patricia Harrington, Karen Jordan, Michael McCarthy, Kirsty O'Brien, Eamon O'Murchu, Michelle O'Neill, Sinead O'Neill, Máirín Ryan, Debra Spillane, Susan Spillane, Conor Teljeur, Barrie Tyner, Kieran Walsh.

The advice is developed by the HIQA Evidence Synthesis Team with support from the Expert Advisory Group. Not all members of the Expert Advisory Group and Evidence Synthesis Team are involved in the response to each research question. The findings set out in the advice represent the interpretation by HIQA of the available evidence and do not necessarily reflect the opinion of all members of the Expert Advisory Group.

Conflicts of Interest

None declared.

Advice to the National Public Health Emergency Team

The purpose of this evidence synthesis is to provide advice to the National Public Health Emergency Team (NPHET) on the following policy question:

“Based on the available international evidence, is the current definition of what constitutes ‘extremely medically vulnerable’ (that is, those who were previously asked to cocoon) in relation to COVID-19 appropriate?”

The response to the policy question is informed by an evidence synthesis considering two elements:

1. evidence underpinning the categorisation of ‘extremely medically vulnerable’ groups who may be at risk of severe illness from COVID-19 identified from the following document categories:
 - a. public health guidance and policy documents
 - b. reviews
 - c. original research studies
 - d. international disease registries.
2. input from the COVID-19 Expert Advisory Group.

The key points of this evidence synthesis, which informed HIQA's advice, are as follows:

Evidence underpinning the categorisation of ‘extremely medically vulnerable’ groups who may be at risk of severe illness from COVID-19

- SARS-CoV-2 is a highly infectious virus, which has caused tens of millions of cases of COVID-19, and over one million deaths, globally.
- The Health Protection Surveillance Centre (HPSC) and Health Service Executive (HSE) have categorised groups of individuals as ‘extremely medically vulnerable’, who may be at highest risk of severe illness from COVID-19.
- The groups included were based upon Public Health England’s definitions, which were originally based on those groups at highest risk of complications from influenza. As the pandemic has progressed, the course of COVID-19 has been investigated and more evidence is becoming available on those at risk of severe illness.
- The scoping methodology applied in the review identified:

- Eight international organisations that reported the underpinning evidence that informed the categorisation of groups at highest risk of severe illness due to COVID-19.
- Four systematic reviews and meta-analyses and one rapid review provided evidence relevant to two groups defined as extremely medically vulnerable: people aged 70 years or older (n=4) and people with specific cancers (n=1).
- Twenty four primary research studies that provided evidence on six extremely medically vulnerable groups: people aged 70 years and older (n=9); solid organ transplant recipients (n=4); people with specific cancers (n=18); people with severe respiratory conditions (n=2); people on immunosuppression therapies sufficient to significantly increase risk of infection (n=1); and patients with end stage renal failure or dialysis patients (n=3).
- Findings arising from the evidence included in the review (conducted using scoping methodology) are that:
 - All included reviews and eight out of nine primary studies that explored the relationship between age and risk of severe illness from COVID-19 were consistent in reporting a significantly increased risk of severe illness in those aged 70 years and older.
 - Three of the four studies on organ transplantation reported a significantly increased risk of mortality in transplant patients with COVID-19, compared with those who had not had a transplant.
 - Pooled evidence on patients with cancer (from one systematic review and meta-analysis) together with evidence from 18 primary studies (six of which were also included in the systematic review) relevant to this group, were inconclusive. The most consistent finding was that among cancer patients, those receiving chemotherapy (compared to those who are not) are at a significantly increased risk of severe illness due to COVID-19.
 - A small number of primary studies of people with severe respiratory conditions, people on immunosuppression therapies sufficient to significantly increase risk of infection, and patients with end stage renal failure or undergoing dialysis, consistently identified that these conditions were associated with a significantly increased risk of severe illness from COVID-19. Although consistent in their findings, the evidence is of low

certainty due to the small number and nature of the study designs; therefore the results should be interpreted with caution.

- Of the extremely medically vulnerable groups included in this evidence summary, no evidence (from systematic or rapid reviews or primary studies) was identified for people with rare diseases and inborn errors of metabolism or pregnant women with significant heart disease.
- It should be noted that the classification of risk varies across organisations and thus is not directly comparable. Most included organisations have only one overall 'high risk' group, whereas Ireland has two, those at high risk and those at very high risk. A number of international guidance documents identify additional groups in their highest risk category (cardiovascular disease, type 1 diabetes, type 2 diabetes, chronic liver disease, chronic obstructive pulmonary disease (COPD), chronic kidney disease, HIV infection with low CD4 counts, obesity, severe obesity, stage B Child Pugh score cirrhosis, motor neuron disease, myasthenia gravis, multiple sclerosis, Parkinson's disease, cerebral palsy, quadriplegia or hemiplegia, primary cerebral malignancy, progressive cerebellar disease), which are included in the Irish guidance as 'high risk' rather than 'very high risk'. Four further groups, women who are pregnant and their unborn children, those with dementia, those who smoke and adults with Down syndrome are included in the highest risk group of some international guidance documents; these are not included in either of the at-risk groups in Ireland.
- Overall, considering existing guidance and reviews of primary research identified using the applied scoping methodology:
 - Evidence was available for six of the eight groups listed by the HPSC and HSE as being 'extremely medically vulnerable' with the strongest evidence supporting the inclusion of those aged 70 years and older in the highest risk category.
 - Evidence was not identified for people with rare diseases and inborn errors of metabolism or for pregnant women who have significant heart disease. Given the rarity of some conditions and the likely ongoing cocooning of certain patient groups which has reduced their exposure to SARS-CoV-2, an absence of evidence of severe COVID-19 in these conditions should not be interpreted as an absence of a true association.

COVID-19 Expert Advisory Group

- A meeting of the COVID-19 Expert Advisory Group (EAG) was convened for clinical and technical interpretation of the evidence provided.
- Based on the evidence presented, the COVID-19 EAG reasoned that:
 - No sufficiently consistent evidence was identified to support the removal of any group categorised as 'extremely medically vulnerable'.
 - The group acknowledged the significant implications that cocooning may have on those categorised as 'extremely medically vulnerable' and the implications for the wider society. For example, those defined to be 'extremely medically vulnerable' may need to be facilitated to work at home, which present challenges for work force planning. They may also be advised to reduce or limit social interactions, leading to significant social isolation if implemented over a prolonged period of time.
 - There is a need for clear communication regarding the risks (with respect to COVID-19) associated with varying levels of immunosuppression. This communication should include clarification, where possible, on risk attributed to different immunosuppressant treatment regimens. Furthermore, patients receiving immunosuppressant medication should be provided with information regarding the risks and benefits of their current treatment(s) and the potential risks, including with respect to COVID-19, of electing to discontinue or change their current treatment regime.
 - The group highlighted that guidance from the US CDC was updated on 2 November 2020. It was felt that this illustrates the ongoing emergence of evidence and the need to establish processes that enable timely updates to Irish guidance, where appropriate and for communicating change to the wider system.
 - It was noted that there is a lack of consensus on the definition of severe respiratory disease within the literature at large and within clinical practice. This indicates the requirement to clearly stratify and communicate risk in relation to this group.
 - There is a lack of data relating to paediatric populations. While the risk of severe disease is increased in children with specific underlying medical conditions relative to children without these conditions, this risk must be interpreted in the context of the overall burden associated with COVID-19. Compared with adults, national and international data indicate that the absolute risk of severe disease is substantially lower in children. As such, it

was highlighted that there needs to be careful messaging relating to this population. It was noted that current HSE advice is that children who are ordinarily considered well enough to attend school can continue to attend in-person classes in the context of COVID-19.

- The term 'risk of infection' was noted to be extremely broad and may not be appropriate (for example, following splenectomy, there is a specific risk of severe infection from encapsulated bacteria, but this does not necessarily mean there is an increased risk of severe infection from other organisms). Consideration should be given to refining the language to specify that it is conditions or treatments that significantly increase the risk of *viral* infections.
- The COVID-19 EAG identified additional factors which should be considered to inform both this policy question and potential further research and policy questions. These included:
 - There may be important contextual issues that limit the applicability of international data. Where available, Irish data should be evaluated to ensure that conditions associated with severe illness in Irish populations are reflected in the risk categorisations.
 - It was highlighted that there is a danger of medicalisation of older people who are in good health, and that the current age cut- point of 70 years for higher risk may require more nuanced communication. There is a concern that the current broad approach results in a poor risk-benefit balance in those older adults who are otherwise healthy and in individuals for whom actions such as cocooning may have a significant negative impact on their wellbeing.
 - It was noted that less healthy adults (for example, those aged 50 years and older with multiple chronic conditions, living under circumstances of increased deprivation) are at an increased risk of severe disease, yet this risk may not be sufficiently acknowledged. Danish guidance on people at higher risk was highlighted as an example of guidance that is more person-centred. This guidance, directed towards individuals, considers the effect of health status within different age groups.
 - Guidance from the HPSC has evolved since the start of the pandemic. The changes in the guidance, which includes a more person-centred approach that supports people to live with COVID-19, need to be clearly communicated to those identified as extremely medically vulnerable, along with the risk mitigation strategies to allow them to optimise their

wellbeing. Moreover, the composition of the groups and messaging around behaviours needs to be standardised in national guidance across agencies in Ireland.

- The absolute risk of serious illness from COVID-19 may differ between and within the identified medically vulnerable groups, particularly for risk groups that comprise large and heterogeneous cohorts (for example, those over the age of 70 years, people with immunosuppression).
- It was noted that the categorisation of groups as 'extremely medically vulnerable' will have important implications for future COVID-19 vaccine policy.
- A framework should be established that outlines the process by which risk categorisations are changed (how a very high risk group (extremely medically vulnerable group) moves to become a high risk group and vice versa). The framework should be considered a live document that takes consideration of the certainty and applicability of emerging evidence including the estimated relative and absolute risks, where available. Any resulting changes to the risk categorisation of groups should be incorporated into Irish guidance and communicated to all stakeholders.

Advice

Arising from the findings above, HIQA's advice to the National Public Health Emergency Team is as follows:

- The evidence identified and included in this scoping review does not currently support the removal of any of the groups categorised as 'extremely medically vulnerable'.
- Category descriptors representing those at increased risk of SARS-CoV-2 infection should be refined to specify that they relate to conditions with an increased risk of viral infection (as opposed to other pathogens).
- Further clarity is required in the public health advice on terms that cover heterogeneous groups (including those taking immunosuppressant medication, those who are otherwise immunocompromised, and those with respiratory conditions). This should take consideration of national and international evidence and be developed in conjunction with the relevant clinical programmes.

- A framework is required outlining the process by which emerging evidence is considered to ensure updates or refinements to the composition of the risk groups. Consideration should be given to the implications for individuals of being included in the extremely medically vulnerable groups. The process should be informed by the expert interpretation by the clinical programmes of:
 - changes in international practices identified through the horizon scanning provided by the ongoing HIQA review of international guidance on vulnerable groups
 - Irish data on morbidity and mortality from COVID-19
 - the certainty and applicability of emerging evidence including the relative and absolute risk of serious illness from COVID-19.
- Interpretation of clinical vulnerability for individuals identified as being at increased risk of serious illness from COVID-19 needs to also take account of the impact of any multimorbidity, frailty, disability, or poverty and social deprivation.
- There is a need to ensure consistency across all current documents (for example, from the HPSC and HSE) with respect to the composition of groups defined as extremely medically vulnerable and the recommendations to support people living with COVID-19. Any updates to the risk categories should be clearly communicated to all stakeholders.

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For further information please contact:

Health Information and Quality Authority

George's Court

George's Lane

Smithfield

Dublin 7

D07 E98Y

+353 (0)1 8147400

info@hiqa.ie

www.hiqa.ie

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