Joint Committee on Vaccination and Immunisation: advice on priority groups for COVID-19 vaccination

2 December 2020

Introduction

This advice is provided to facilitate the development of policy on COVID-19 vaccination in the UK.

JCVI advises that the first priorities for any COVID-19 vaccination programme should be the prevention of COVID-19 mortality and the protection of health and social care staff and systems. Secondary priorities could include vaccination of those at increased risk of hospitalisation and at increased risk of exposure, and to maintain resilience in essential public services. This document sets out a framework for refining future advice on a national COVID-19 vaccination strategy.

This advice has been developed based on a review of UK epidemiological data on the impact of the COVID-19 pandemic so far (1), data on demographic and clinical risk factors for mortality and hospitalisation from COVID-19 (2-3), data on occupational exposure(4-7), a review on inequalities associated with COVID-19 (8), Phase I, II and III data on the Pfizer-BioNTech mRNA vaccine and headline phase III results on the AstraZeneca vaccine, Phase I and II data on other developmental COVID-19 vaccines (9-18), and mathematical modelling on the potential impact of different vaccination programmes (19).

Considerations

Pfizer-BioNTech vaccine

The Committee has reviewed unpublished Phase I/II/III safety and efficacy data for the Pfizer BioNTech mRNA vaccine. The vaccine appears to be safe and well-tolerated, and there were no clinically concerning safety observations. The data indicate high efficacy in all age groups (16

years and over), including encouraging results in older adults. The Committee advises that this vaccine be used in the first phase of the programme, according to the priority order set out below. While there is some evidence to indicate high levels of short-term protection from a single dose of vaccine, a two-dose vaccine schedule is currently advised in accordance with regulatory approval.

This statement will be updated following consideration of Phase III safety and efficacy data on other COVID-19 vaccines.

Direct protection vs transmission reduction

JCVI has considered a number of different vaccination strategies, including those targeting transmission and those targeted at providing direct protection to persons most at risk.

In order to interrupt transmission, mathematical modelling indicates that we would need to vaccinate a large proportion of the population with a vaccine which is highly effective at preventing infection (transmission). At the start of the vaccination programme, good evidence on the effects of vaccination on transmission will not be available, and vaccine availability will be more limited. The best use of available vaccine will also, in part, be dependent on the point in the pandemic the UK is at.

Given the current epidemiological situation in the UK, all evidence indicates that the best option for preventing morbidity and mortality in the initial phase of the programme is to directly protect persons most at risk of morbidity and mortality.

Age

Current evidence strongly indicates that the single greatest risk of mortality from COVID-19 is increasing age and that the risk increases exponentially with age (1-3). Mathematical modelling indicates that the optimal strategy for minimising future deaths or quality adjusted life year (QALY) losses is to offer vaccination to older age groups first. These models assume an available vaccine is both safe and effective in older adults. (19). Data also indicate that the absolute risk of mortality is higher in those over 65 years than that seen in the majority of younger

adults with an underlying health condition (see below). Accordingly, the Committee's advice largely prioritises based on age.

Age-based programmes are usually easier to implement and therefore achieve higher vaccine uptake. An age-based programme is also likely to increase uptake in those with clinical risk factors as the prevalence of these increases with age.

Older adults resident in care homes

There is clear evidence that those living in residential care homes for older adults have been disproportionately affected by COVID-19 (20-23) as they have had a high risk of exposure to infection and are at higher clinical risk of severe disease and mortality. Given the increased risk of outbreaks, morbidity and mortality in these closed settings, these adults are considered to be at very high risk. The Committee's advice is that this group should be the highest priority for vaccination. Vaccination of residents and staff at the same time is considered to be a highly efficient strategy within a mass vaccination programme with the greatest potential impact (see below).

Health and social care workers

Frontline health and social care workers are at increased personal risk of exposure to infection with COVID-19 and of transmitting that infection to susceptible and vulnerable patients in health and social care settings. The Committee considers frontline health and social care workers who provide care to vulnerable people a high priority for vaccination. Protecting them protects the health and social care service and recognises the risks that they face in this service. Even a small reduction in transmission arising from vaccination would add to the benefits of vaccinating this population, by reducing transmission from health and social care workers to multiple vulnerable patients and other staff members. This group includes those working in hospice care and those working temporarily in the COVID-19 vaccination programme who provide face-to-face clinical care.

There is evidence that infection rates are higher in residential care home staff (20-23), than in those providing domiciliary care or in healthcare workers. Care home workers are therefore considered a very high priority for vaccination.

Prioritisation amongst health and social care workers

Frontline health and social care workers at high risk of acquiring infection, at high individual risk of developing serious disease, or at risk of transmitting infection to multiple vulnerable persons or other staff in a healthcare environment, are considered of higher priority for vaccination than those at lower risk. This prioritisation should be taken into account during vaccine deployment.

Clinically Extremely Vulnerable (Shielding patients)

Individuals considered extremely clinically vulnerable have been shielding for much of the pandemic (24). This means that available data are likely to underestimate the risk in this group. Many of those who are clinically extremely vulnerable are in the oldest age groups and will be among the first to receive vaccine. Considering data from the first wave in the UK, the overall risk of mortality for clinically extremely vulnerable younger adults is estimated to be roughly the same as the risk to persons aged 70 – 74 years. Given the level of risk seen in this group as a whole, JCVI advises that persons aged less than 70 years who are clinically extremely vulnerable should be offered vaccine alongside those aged 70-74 years of age. There are two key exceptions to this, pregnant women with heart disease and children (see below).

Many individuals who are clinically extremely vulnerable will have some degree of immunosuppression or be immunocompromised and may not respond as well to the vaccine. Therefore, those who are clinically extremely vulnerable should continue to follow Government advice on reducing their risk of infection. Consideration has been given to vaccination of household contacts of immunosuppressed individuals. However, at this time there are no data on the size of the effect of COVID-19 vaccines on transmission. Evidence is expected to accrue during the course of the vaccine programme, and until that time the committee is not in a position to advise vaccination solely on the basis of indirect protection. Once sufficient evidence becomes available the committee will consider options for a cocooning strategy for immunosuppressed individuals, including whether any specific vaccine is preferred in this population.

Pregnancy

There are no data as yet on the safety of COVID-19 vaccines in pregnancy, either from human or animal studies. Given the lack of evidence, JCVI favours a precautionary approach, and does not currently advise COVID-19 vaccination in pregnancy.

Women should be advised not to come forward for vaccination if they may be pregnant or are planning a pregnancy within three months of the first dose.

Data are anticipated which will inform discussions on vaccination in pregnancy. JCVI will review these as soon as they become available.

Children

Following infection, almost all children will have asymptomatic infection or mild disease. There are very limited data on vaccination in adolescents, with no data on vaccination in younger children, at this time. The Committee advises that only those children at very high risk of exposure and serious outcomes, such as older children with severe neuro-disabilities that require residential care, should be offered vaccination. Clinicians should discuss the risks and benefits of vaccination with a person with parental responsibility, who should be told about the paucity of safety data for the vaccine in children aged < 16 years. More detail on vaccination in children is set out in the Green Book – Immunisation Against Infectious Disease.

Underlying health conditions

There is good evidence that certain underlying health conditions increase the risk of morbidity and mortality from COVID-19. When compared to persons without underlying health conditions, the absolute increased risk in those with underlying health conditions is considered generally to be lower than the increased risk in persons over the age of 65 years (with the exception of the clinically extremely vulnerable – see above). The Committee's advice is to offer vaccination to those aged 65 years and over followed by those in clinical risk groups aged 16 years and over. The risk groups identified by the Committee are set out below.

- Chronic respiratory disease, including chronic obstructive pulmonary disease (COPD), cystic fibrosis and severe asthma
- Chronic heart disease (and vascular disease)

- Chronic kidney disease
- Chronic liver disease
- Chronic neurological disease including epilepsy
- Down's syndrome
- Severe and profound learning disability
- Diabetes
- Solid organ, bone marrow and stem cell transplant recipients
- People with specific cancers
- Immunosuppression due to disease or treatment
- Asplenia and splenic dysfunction
- Morbid obesity
- Severe mental illness

Individuals within these risk groups who are clinically extremely vulnerable are discussed separately (see above). Further advice on risk groups, including clear definitions, are set out in the Green Book - Immunisation Against Infectious Disease.

Mitigating inequalities

Multiple social and societal drivers are recognised to contribute towards increased risk from COVID-19. JCVI considered it important to understand the factors underlying health inequalities in COVID-19 giving due consideration to relevant scientific evidence, ethical principles and vaccine programme deliverability. The issues considered are set out in Annex A.

There is clear evidence that certain Black, Asian and minority ethnic (BAME) groups have higher rates of infection, and higher rates of serious disease, morbidity and mortality. There is no strong evidence that ethnicity by itself (or genetics) is the sole explanation for observed differences in rates of severe illness and deaths. What is clear is that certain health conditions are associated with increased risk of serious disease, and these health conditions are often overrepresented in certain Black, Asian and minority ethnic groups. It is also clear that societal factors, such as occupation, household size, deprivation, and access to healthcare can increase susceptibility to COVID-19 and worsen outcomes following infection. These factors are playing a large role in the inequalities being seen with COVID-19.

Good vaccine coverage in Black, Asian and minority ethnic groups will be the most important factor within a vaccine programme in reducing inequalities for this group. Prioritisation of persons with underlying health conditions (see above) will also provide for greater vaccination of BAME communities who are disproportionately affected by such health conditions.

The Committee's advice is for NHS England and Improvement, the Department of Health and Social Care, Public Health England and the devolved administrations to work together to ensure that inequalities are identified and addressed in implementation. This could be through culturally competent and tailored communications and flexible models of delivery, aimed at ensuring everything possible is done to promote good uptake in Black, Asian and minority ethnic groups and in groups who may experience inequalities in access to, or engagement with, healthcare services. These tailored implementation measures should be applied across all priority groups during the vaccination programme.

Occupational vaccination (other than frontline health and social care workers)

The Committee considered evidence on the risk of exposure and risk of mortality by occupation. Under the priority groups advised below, those over 50 years of age, and all those 16 years of age and over in a risk group, would be eligible for vaccination within the first phase of the programme. This prioritisation captures almost all preventable deaths from COVID-19, including those associated with occupational exposure to infection. As such, JCVI does not advise further prioritisation by occupation during the first phase of the programme.

Occupational prioritisation could form part of a second phase of the programme, which would include healthy individuals from 16 years of age up to 50 years of age, subject to consideration of the latest data on vaccine safety and effectiveness.

The impact of vaccine delivery on non-pharmaceutical interventions.

In a situation of constrained vaccine supply, population level protection will not be achievable immediately.

Once we have evidence of the impact of the programme on morbidity and mortality amongst vulnerable persons, the initial phase of the vaccination programme could allow the subsequent relaxation of non-pharmaceutical interventions in some sectors of the population. Government advice on non-pharmaceutical interventions should continue to be followed.

Vaccine priority groups: advice on 2 December 2020

Phase 1 – direct prevention of mortality and supporting the NHS and social care system

JCVI advises that the first priorities for the COVID-19 vaccination programme should be the prevention of mortality and the maintenance of the health and social care systems. As the risk of mortality from COVID-19 increases with age, prioritisation is primarily based on age. The order of priority for each group in the population corresponds with data on the number of individuals who would need to be vaccinated to prevent one death, estimated from UK data obtained from March to June 2020 (3)

1	Residents in a care home for older adults and their carers
2	All those 80 years of age and over Frontline health and social care workers
3	All those 75 years of age and over
4	All those 70 years of age and over Clinically extremely vulnerable individuals*
5	All those 65 years of age and over
6	All individuals aged 16 years to 64 years with underlying health conditions which put them at higher risk of serious disease and mortality
7	All those 60 years of age and over
8	All those 55 years of age and over
9	All those 50 years of age and over
*	Clinically extremely vulnerable individuals are described here. This advice on vaccination does not include pregnant women and those under the age of 16 years (see above)

It is estimated that taken together, these groups represent around 99% of preventable mortality from COVID-19.

JCVI advises that implementation of the COVID-19 vaccine programme should aim to achieve high vaccine uptake. An age-based programme will likely result in faster delivery and better uptake in those at the highest risk. Implementation should also involve flexibility in vaccine deployment at a local level with due attention to:

- mitigating health inequalities, such as might occur in relation to access to healthcare and ethnicity;
- vaccine product storage, transport and administration constraints;
- exceptional individualised circumstances; and
- availability of suitable approved vaccines e.g. for specific age cohorts.

JCVI appreciates that operational considerations, such as minimising wastage, may require a flexible approach, where decisions are taken in consultation with national or local public health experts. To be assured that outcome is maximised however, JCVI would like to see early and regular comprehensive vaccine coverage data so that the Committee can respond if high priority risk groups are unable to access vaccination in a reasonable time frame.

The next phase – further reduction in hospitalisation and targeted vaccination of those at high risk of exposure and/or those delivering key public services

As the first phase of the programme is rolled out in the UK, additional data will become available on the safety and effectiveness of COVID-19 vaccines. These data will provide the basis for consideration of vaccination in groups that are at lower risk of mortality from COVID-19. The Committee is currently of the view that the key focus for the second phase of vaccination could be on further preventing hospitalisation.

Vaccination of those at increased risk of exposure to SARS-CoV-2 due to their occupation could also be a priority in the next phase. This could include first responders, the military, those involved in the justice system, teachers, transport workers, and public servants essential to the

pandemic response. Priority occupations for vaccination are considered an issue of policy, rather than for JCVI to advise on. JCVI asks that the Department of Health and Social Care consider occupational vaccination in collaboration with other Government departments.

Wider use of COVID-19 vaccines will provide a better understanding of whether they can prevent infection and onward transmission in the population. Data on vaccine impact on transmission, along with data on vaccine safety and effectiveness, will potentially allow for consideration of vaccination across the rest of the population.

As trials in children and pregnant women are completed, we will also gain a better understanding of the safety and effectiveness of the vaccines in these persons.

Further work

JCVI will continually monitor data on vaccines in development. As more Phase III data become available on candidate COVID-19 vaccines the Committee will be able to prepare further advice for policy makers in the UK.

JCVI will review data on vaccine coverage, in particular focussing on inequalities, and the impact of actions being undertaken to mitigate inequalities. Vaccine safety will be continually monitored by the MHRA and PHE, and JCVI will regularly review data on vaccine safety as the programme rolls out. Vaccine efficacy and any potential impacts on transmission will be monitored by PHE. Data will be considered at the earliest opportunity to facilitate discussions on prioritisation after the first phase of the programme.

Background

JCVI met to consider COVID-19 vaccination on 7 May, 3 June, 6 July, 1 September, 29 November, 30 November and 1 December 2020. Between 24 September 2020 and 19 November 2020, a JCVI COVID-19 sub-committee met weekly to consider key issues in greater depth. The advice provided is to support the government in development of a

vaccine strategy for the procurement and delivery of a vaccination programme to the population.

SARS-CoV-2 (COVID-19)

COVID-19 disease first emerged as a cause of severe respiratory infection in Wuhan, China in late 2019. The first two cases in the UK were seen in late January 2020. In March 2020, the WHO declared a SARS-Cov-2 pandemic.

In adults, the clinical picture varies widely. A significant proportion of individuals are likely to have mild symptoms and may be asymptomatic at the time of diagnosis. Symptoms are commonly reported as a new onset of cough and fever, but may include headache, loss of smell, nasal obstruction, lethargy, myalgia, rhinorrhoea, taste dysfunction, sore throat, diarrhoea, vomiting and confusion. Fever may not be reported in all symptomatic individuals. Progression of disease, multiple organ failure and death will occur in some individuals.

As with other Coronaviruses, SARS-CoV-2 is an RNA virus which encodes four major structural proteins. Most vaccine candidates focus on immunisation with the spike glycoprotein, which is the main target for neutralising antibodies following infection. Neutralising antibodies that block viral entry into host cells by preventing interaction between the spike protein and the host cell are expected to be protective.

Pfizer-BioNTech vaccine

The Pfizer-BioNTech vaccine is a lipid nanoparticle–formulated mRNA vaccine. The mRNA encodes the SARS-CoV-2 receptor-binding domain of the spike protein. The mRNA in the vaccine is translated and transcribed by the body to produce this key part of the spike protein. The protein then acts as an intracellular antigen to stimulate the immune response. The mRNA in the vaccine is normally degraded within a few days and cannot incorporate into the host genome. Data from the Pfizer-BioNTech vaccine trials undertaken in over 40,000 individuals indicate high vaccine efficacy, with no serious safety concerns observed.

AstraZeneca COVID-19 vaccine

AstraZeneca COVID-19 vaccine uses a replication deficient chimpanzee adenovirus as a vector that encodes the full-length SARS-CoV2 spike

protein. Chimpanzee adenoviruses are non-enveloped viruses, meaning that the glycoprotein antigen is not present on the surface of the vector, but is only expressed at high levels once the vector enters the target cells. Genes are inserted to render the virus replication incompetent, and to enhance immunogenicity. Once the vector is in the nucleus, mRNA encoding the spike protein is produced that then enters the cytoplasm. This leads to translation of the target protein which acts as an intracellular antigen. Headline data from vaccine trials undertaken indicate high vaccine efficacy, with no serious safety events related to the vaccine.

After JCVI has been given the opportunity to review Phase III data on this vaccine, this statement will be updated.

Other vaccines in development

Other COVID-19 vaccines are in development, with some in late stage trials. When sufficient data on vaccine safety and efficacy are available, these will be considered by JCVI and this statement will be updated.

References

1. National COVID-19 surveillance reports
2. Williamson EJ, Walker AJ, Bhaskaran K, *et al.* Factors associated with COVID-19-related death using OpenSAFELY. Nature. 2020 Aug;584(7821):430-436.
3. Clift AK, Coupland CAC, Keogh RH *et al*. Living risk prediction algorithm (QCOVID) for risk of hospital admission and mortality from coronavirus 19 in adults: national derivation and validation cohort study. BMJ. 2020 Oct 20;371:m3731.
4. Coronavirus (COVID-19) related deaths by occupation, before and during lockdown, England and Wales: deaths registered between 9 March and 30 June 2020, Office for National Statistics
5. Meyerowitz EA, Richterman A, Gandhi RT *et al*. Transmission of SARS-CoV-2: A Review of Viral, Host, and Environmental Factors. Ann Intern Med. 2020 Sep 17:M20-5008.

6. Lally C. COVID-19 and occupational risk
7. Mutambudzi M, Niedzwiedz C, Macdonald *et al*. Occupation and risk of severe COVID-19: prospective cohort study of 120,075 UK Biobank participants medRxiv 2020.05.22.20109892; doi: https://doi.org/10.1101/2020.05.22.20109892
8. Public Heath England report - Beyond the data: Understanding the impact of COVID-19 on BAME groups
9. Jackson LA, Anderson EJ, Rouphael NG *et al*. An mRNA Vaccine against SARS-CoV-2 - Preliminary Report. N Engl J Med. 2020 Nov 12;383(20):1920-1931.
10. Corbett KS, Flynn B, Foulds KE *et al*. Evaluation of the mRNA-1273 Vaccine against SARS-CoV-2 in Nonhuman Primates. N Engl J Med. 2020 Oct 15;383(16):1544-1555.
11. Anderson EJ, Rouphael NG, Widge AT *et al*. mRNA-1273 Study Group. Safety and Immunogenicity of SARS-CoV-2 mRNA-1273 Vaccine in Older Adults. N Engl J Med. 2020 Sep 29.
12. van Doremalen N, Lambe T, Spencer A et al. ChAdOx1 nCoV-19 vaccine prevents SARS-CoV-2 pneumonia in rhesus macaques. Nature. 2020 Jul 30.
13. Folegatti PM, Ewer KJ, Aley PK *et al*. Oxford COVID Vaccine Trial Group. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial. Lancet. 2020 Aug 15;396(10249):467-478.
14. Ramasamy M, Minassian A, Ewer K *et al*. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. Lancet Nov 18 2020.
15. Mulligan MJ, Lyke KE, Kitchin N *et al*. Phase 1/2 study of COVID-19 RNA vaccine BNT162b1 in adults. Nature. 2020 Aug 12.
16. Sahin U, Muik A, Derhovanessian E *et al*. Concurrent human antibody and T H 1 type T-cell responses elicited by a COVID-19 RNA vaccine. medRxiv [Preprint]. 2020 July 20.
17. Walsh EE, Frenck R, Falsey AR *et al*. RNA-Based COVID-19 Vaccine BNT162b2 Selected for a Pivotal Efficacy Study. medRxiv [Preprint]. 2020 Aug 20.

18. Keech C, Albert G, Cho I et al. Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine. N Engl J Med. 2020 Sep 2.
19. Moore S, Hill E, Dyson L et al. Modelling optimal vaccination strategy for SARS-CoV-2 in the UK. MedRxiv 2020.09.22.20194183; doi: https://doi.org/10.1101/2020.09.22.20194183
20. Ladhani SN, Chow JY, Janarthanan R et al. Investigation of SARS-CoV-2 outbreaks in six care homes in London, April 2020. EClinicalMedicine. 2020 Sep 9:100533.
21. Ladhani SN, Chow JY, Janarthanan R et al. London Care Home Investigation Team. Increased risk of SARS-CoV-2 infection in staff working across different care homes: enhanced CoVID-19 outbreak investigations in London care Homes. J Infect. 2020 Jul 29;81(4):621–4.
22. Graham NSN, Junghans C, Downes R, et al. SARS-CoV-2 infection, clinical features and outcome of COVID-19 in United Kingdom nursing homes. J Infect. 2020 Sep;81(3):411-419.
23. Vivaldi 1: coronavirus (COVID-19) care homes study report
24. https://www.gov.uk/government/publications/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19

ANNEX A

COVID-19 Vaccine and Health Inequalities: considerations for prioritisation and implementation

5 November 2020; revised 18 November 2020

Authors: Ines Campos-Matos (PHE) and Sema Mandal (PHE)

Contributors: James Wilson (UCL), Julie Yates (PHE), Gayatri Amirthalingam (PHE), Mary Ramsay (PHE), Andrew Earnshaw (PHE)

Purpose of this paper

The purpose of this paper is to consider the impact on and implications for health inequalities in the prioritisation of COVID-19 vaccines when they are introduced in the context of initial supply constraints. This paper expands on the considerations informing the Joint Committee on Vaccination and Immunisation (JCVI) interim advice on priority groups for COVID-19 vaccine (1), which is intended to support the government in planning the vaccine programme, and it offers further considerations for its implementation.

Background

JCVI has considered epidemiological, microbiological and clinical information on the impact of COVID-19 in the United Kingdom (UK) so far, including data on disease incidence, hospitalisation and mortality associated with COVID-19, early data from COVID-19 vaccine clinical trials, and mathematical modelling on the impact of different vaccination strategies. The proposed COVID-19 vaccine programme intends to protect those individuals at highest risk of severe illness and mortality from COVID-19 in the UK either directly or indirectly.

The reality of the situation where novel vaccines are being developed during a global pandemic is that supplies will be limited initially, with increasing stock over time to meet demand. Prioritisation of specific population groups, therefore, becomes a necessary step in the planning process to ensure those most at risk of severe consequences of COVID-19 have early access to vaccine. The UK is not alone in considering vaccine prioritisation; the USA through its Advisory Committee on Immunization Practice (JCVI equivalent) has also adopted a framework for phased allocation of COVID-19 vaccine (2).

Prioritising means unequal access and thus has implications for health inequalities, which presents both opportunities and risks. In addition to considering health inequalities regarding prioritisation of the vaccine, actions to address health inequalities should also be employed during the implementation phase, as with any immunisation programme or other population-based health intervention. Monitoring and evaluation of the programme should therefore include indicators for tracking uptake and acceptability in key underserved groups and across protected characteristics.

When considering population groups to prioritise on the basis of risk, it is also important to recognise that there may be unintended consequences of targeting specific groups, particularly in the context of a pandemic with a novel, potentially stigmatising virus, and

new vaccines, some using novel technologies not deployed in mass programmes, which may be perceived as “experimental”.

Principles of vaccine prioritisation – a conceptual framework

Principles guiding the prioritisation of the vaccine include scientific evidence, ethics and deliverability. Science should provide the evidence and data on risk of COVID-19 severe morbidity and mortality for different population groups, which underpins prioritisation decisions. From an ethical perspective, prioritisation should maximise benefit and reduce harm, be fair and transparent, and address health inequalities. Finally, deliverability should be considered in formulating the prioritisation such that the approach is simple to communicate to the public and professionals and realistic to implement.

This conceptual framework and its application to key population groups that have been disproportionately affected by COVID-19 is discussed below and summarised in Table 1.

Proposed prioritisation

The decision to prioritise one population group over another to have early access to the vaccine is not an easy or straightforward one and should take into account scientific evidence, ethics and deliverability (implementation). Based on preliminary information on the vaccines in development, JCVI agreed that a programme that combines clinical risk stratification, an age-based approach and prioritisation of health and social care workers should optimise both outcomes and deliverability (1). Simple age-based programmes are usually easier to deliver and therefore achieve higher uptake including in the highest risk groups. Table 1 summarises the scientific rationale, ethical considerations for maximising benefits and reducing health inequalities, and deliverability for each of these population groups.

Scientific Evidence

Prioritisation of people in older age groups and with clinical risk factors is based on the current evidence that strongly indicates that the absolute risk of serious disease and death increases exponentially with age (3). Mortality is also higher in those with underlying health conditions, although this is also very strongly related to age with low absolute risks in those under 40 years of age (4). Frontline health and social care workers are at increased risk of exposure, increased risk of transmitting the infection to vulnerable patients, and their health is key to maintain resilience in the NHS and for health and social care providers.

However, other population groups might also be considered for prioritisation of the vaccine. While the evidence indicates that age has the highest absolute risk, studies have also shown that there are several factors which include inequality domains and protected characteristics that are associated with elevated incidence or adjusted risk ratios, such as male sex, Black, Asian and Minority Ethnic (BAME) groups, people with multiple comorbidities and deprivation (5, 6). Indeed, in the OpenSafely risk prediction model, an Asian or a Black person reaches the equivalent age-risk of COVID-19 of a White 65 year old at 60 years without co-morbidities and at 45 years or 43 years, respectively, if they have two co-morbidities (7). If split by sex this equivalent age is lower in men compared to women.

So, the question could be posed: should men or people belonging to BAME groups also be prioritised?

The male-female differences in COVID-19 mortality are not straightforward, with likely interaction of age and sex along with other factors that have a sex differential: co-morbidities, occupation, behavioural factors (including smoking and alcohol use), compliance with social distancing measures and shielding. The explanation for sex differences may reflect social and cultural factors related to gender rather than the biology of sex (8). Additionally, focusing on men's higher death rates compared to women may be misleading since the absolute differences will be higher, despite similar relative risk, given men's higher baseline mortality (9). It is also important to note that, while risk increases with age for both men and women, the age cut off at 50 years is below the age at which absolute risk starts increasing for women (7), therefore capturing everyone at increased risk.

We know that people of BAME groups also tend to have a higher relative risk of having the infection and complications from the disease when compared to their counterparts of White ethnic groups (6). The Scientific Advisory Group for Emergencies (SAGE) ethnicity sub-group recently prepared a paper on the drivers of the higher COVID-19 incidence, morbidity and mortality among minority ethnic groups which concluded that, based on the available evidence at the time, "the relative importance of different pathways that cause ethnic inequalities in COVID-19 is not well understood" (10). Importantly, the authors also point out that they are highly confident that social factors (such as poverty and occupation) make a large contribution to the greater burden of COVID-19 in ethnic minorities; that they have medium confidence that some clinical conditions, which are associated with severe COVID-19 are more common in some ethnic minority groups, may contribute to the ethnic inequalities seen; and that they are highly confident that genetics alone cannot explain the higher burden of COVID-19 of people in some ethnic groups over others.

It is important to note that the data have significant limitations. While OpenSafely has a sample of 17 million people on GP systems, these systems do not include unregistered people (who may belong to underserved groups), ethnicity is not optimally recorded, and they cannot measure some fundamental confounders, such ability to adhere to social distancing measures, shielding, social interactions, occupation, and unknown residual confounders. Furthermore, much of the data that is being used now was obtained in the early part of the pandemic, which presents particular limitations.

Ethics

From an ethical perspective, prioritisation should:

(1) Maximise benefit and reduce harm

Scientific evidence, like the one outlined above, allows us to focus on populations that are at highest risk of infection, hospitalisation, and death from COVID-19. It is important that these population groups are the first to receive the vaccine, as they are the most likely to benefit from them.

But this principle is not just about individual benefit. Maximising benefit and reducing harm is also about protecting some population groups in order to reduce transmission to those at highest individual risk and about maintaining health system resilience. Health and social care workers may not take much personal benefit from the vaccine as a group, but they have close and frequent contacts with those at highest risk and are essential in the COVID-19 response. Ensuring that they remain healthy and able to work is therefore in the interest to the whole of society, allowing us all to benefit.

(2) Promote transparency and fairness

Throughout the process of decision-making, JCVI has aspired to remain transparent. It has done this by publishing its interim advice on prioritisation (1), and by publishing the minutes of the committee's meetings (11). This paper is a further step in ensuring transparency as to how these decisions have been made. Promoting fairness means working towards equitable access of the vaccine for everyone.

(3) Mitigate health inequalities

Health inequalities can be structured across three dimensions: wider determinants of health, protected characteristics and social exclusion (12). The wider determinants of health (the social, economic, and environmental factors that shape mental and physical health) are ubiquitous and create a health gradient across the whole of society. Protected characteristics, such as ethnicity and sex, as outlined in The Equality Act (2010), provide an actionable framework to target those who frequently suffer worse health outcomes. Finally, social exclusion is associated with the poorest health outcomes, putting those affected beyond the extreme end of the gradient of health inequalities. Social exclusion is the basis for the concept of "inclusion heath", which typically encompasses populations such as homeless people, Gypsy, Roma, and Traveller communities, people in contact with the justice system, vulnerable migrants and sex workers, but other groups can be included.

This framework for health inequalities reminds us of our legal duty to prevent discrimination based on protected characteristics, but also of our public health commitment to improving the health of everyone across the population, with a focus on those whose health can benefit more. This means that, to reduce health inequalities, targeted action focussed on some population groups is required. The currently proposed prioritisation supports the reduction of health inequalities between age groups, by actively targeting those of older age groups and with clinical conditions above younger, healthier people.

However, it is important to keep in mind that prioritising some groups over others may have unintended consequences. PHE's Beyond the Data report, which sought to understand the impact of COVID-19 among BAME groups early in the pandemic, reported how stakeholders expressed deep dismay, anger, loss and fear in their communities about the realities of BAME groups being harder hit by the COVID-19 pandemic than others. Some communities also reported increased experiences of stigma and discrimination as they were viewed as being more likely to be infected with the disease (13). It is paramount therefore that prioritisation and roll-out of the vaccine does not reinforce these negative stereotypes and further increase experiences of stigma and discrimination.

A similar discussion has happened with regards to occupational risk, and whether workers of some ethnic groups should be assessed differently to others, as there is a fundamental requirement to ensure people are able to work in the safest way possible. A consensus led by PHE, the Faculty of Occupational Medicine (FOM) and the Health and Safety Executive (HSE) concluded that "risk assessments should be applied equally and consistently across the workforce" and points out that "singling out all ethnic minority members of staff for additional risk assessments could be stigmatising and could deny them opportunities" (14).

Another key consideration for health inequalities is trust. Different communities will have a different degree of trust in the government and in the process of vaccine development and immunisation programmes, related to culture, history and other social factors. In this context of low trust among some groups, being given early access to the vaccine on the grounds of belonging to a certain community may feel like exploitation rather than inclusivity.

Unintended consequences may work to reduce health inequalities. We know that, for example, while 3.4% of the working population in England are of Black ethnic groups, this proportion is 6.1% in the NHS workforce (15). Prioritising health and social care workers will therefore indirectly provide some benefit to people of BAME groups.

Deliverability and Implementation

While scientific and ethical considerations may dominate prioritisation, the ability to operationalise these into a national immunisation programme delivered at an accelerated pace, using existing or enhanced information systems, logistics and infrastructure, is fundamental to its success. A critical component of deliverability is designing a prioritisation approach that builds public trust over time, so while it needs to have some flexibility, there should be minimal changes. The programme should be simple enough, and intuitive enough for both health care professionals and the public (including from underserved groups) to understand and buy in to.

It is important to work to proactively reduce health inequalities at implementation by identifying and addressing barriers to access and uptake of vaccination in the operational design and implementation of the programme. In England, this approach is already enshrined in the role of Screening and Immunisation Teams embedded within in Public Health Commissioning in NHS England, echoed in the PHE Immunisation Strategy vision, aims, tools and resources for implementation, and endorsed by NICE guidance (16).

Ease of identifying and contacting eligible individuals is essential for deliverability. The most comprehensive population-based health information systems are GP systems, which hold lists of patients with identifiers and contact details for the vast majority of the population. Many call and recall systems for immunisation are based on these systems. However, data on inclusion health groups or protected characteristics are variably collected. Age, sex, co-morbidities, socio-economic status (at practice level, not individual level), some behavioural factors (smoking, alcohol) and pregnancy, are comparatively well recorded and directly extractable when compared to ethnicity. Data on inclusion health groups, such as belonging to a Gypsy, Roma or Traveller community, being homeless, or being a refugee, is almost non-existent in GP systems, although in some cases may be held in local authority systems.

Incomplete or inaccurate data and the need for complex data linkages or validation steps to identify and contact eligible people increase the likelihood of increasing existing inequalities, reducing public confidence, and slowing the pace of vaccine roll out.

While prioritising certain ethnic groups has implications in terms of identifying eligible individuals, this is not the case for men as sex is almost universally recorded. However, prioritising men must be weighed against the negative impact of adding complexities to the deliverability, particularly acceptability, of the programme by essentially introducing gender bias. This may impede roll out, erode trust and undermine the higher vaccine uptake observed in the elderly that is associated with having a partner compared to being single (17). A gender-neutral programme is more likely to yield better coverage and is therefore preferable.

Monitoring of vaccine coverage of most routine immunisation programmes relies on data extracted from primary care systems. If there are specific inclusion health or vulnerable groups that are not flagged in information systems (such as rough sleepers or vulnerable migrants), this will limit our ability to identify and address inequalities in vaccine uptake. PHE's national immunisation equity audit (2019) illustrated this point: while the audit identified inequalities in uptake by age, geography, socioeconomic status, ethnicity, religion, disability and health status, travellers, migrants, prisoners, and parental factors (lone parents, large families, parental age), no assessment could be made on adults with learning disability, children or adults with physical disability, mental illness or chronic physical illness, homeless, sexual orientation and gender reassignment due to lack of systematically collected data.

To be able to monitor the impact and effectiveness, as well as safety, and detect inequalities, locally relevant data sources and intelligence therefore need to be exploited. Collaboration with public health colleagues across organisations (particularly with local authority Director of Public Health teams), and the use of population health management approaches, can also ensure that additional datasets held by other system partners can be accessed to support the identification of specific population groups and to target specific activity to ensure improved access and more effective delivery. This would enable the development of locally sensitive approaches to access and delivery, communication, and engagement that reduce inequalities by better meeting the needs of potentially marginalised high-risk individuals and population groups.

PHE's immunisation equity audit also highlighted the complexity of the situation: existing programmes had inequalities not just for overall coverage, but also for timing of vaccines and completion of vaccine schedules and the inequalities varied by vaccine programme, geographic locality and geographic unit of analysis, and the extent of a particular inequality in vaccination such as by ethnicity, may vary when that domain intersects with one or more other domains. These complexities are observed in the shingles vaccination programme, which has a comparable eligible older population to the COVID-19 programme: coverage was lowest in London, decreased with increasing deprivation, and after adjusting for geography and deprivation vaccine coverage was highest for White-British, Indian and Bangladeshi groups and lowest for Mixed White and Black African, and Black-other ethnicities (18). Uptake by sex differed by cohort: shingles vaccine uptake was higher in males for the catch-up cohort but slightly lower in males for the routine cohort (19).

Furthermore, lower vaccine coverage in high risk groups does not always equate to low impact of the vaccine programme. This was borne out in a study in Merseyside looking at rotavirus vaccine uptake and acute gastroenteritis hospitalisations; vaccine impact (i.e. reduction in hospitalisation rates) was greatest among the most deprived populations, despite lower vaccine uptake, because the baseline absolute risk was so high (20). In the context of a COVID-19 vaccine programme, even if vaccine uptake falls short in some high-risk groups, health benefits may still be realised in terms of disease burden reduction.

A socioecological model of factors influencing inequalities in vaccination uptake has been developed (figure 1) based on the audit's findings. This model provides a framework for actions to mitigate inequalities which can be applied to the COVID-19 immunisation programme. For example, intrapersonal and interpersonal factors such as vaccine beliefs around safety should be addressed through a communications strategy that is culturally competent and specific, with resources in multiple languages, and using several media (to avoid digital exclusion). To ensure equitable access for groups where mobility may be a challenge (e.g. elderly and those with physical disabilities), who have poor access to traditional health services, or are essential health and care staff, a policy of multiple models of vaccine delivery (such as domiciliary, community hubs, GP, secondary care and outreach) should be considered. Programmes targeting working-age adults e.g. for influenza, are usually easier to deliver through occupational settings (such as NHS Trusts) and achieve higher vaccine uptake, including in BAME staff through occupational health risk assessments; this delivery model also allows for large volume of stock to be held at vaccination sites with high footfall which can reduce wastage if multi-dose vials are used.

A collaborative approach to delivery of immunisation programmes, with system partners, is a fundamental part of the role of Screening and Immunisation Teams embedded within in Public Health Commissioning in NHS England. These teams in England (and their equivalent in devolved administrations) have knowledge of their local populations and are experienced in implementing both targeted and universal population immunisation programmes at pace, and in applying a variety of tools and actions to address issues related to equity and access. For example, the South West flu team have worked with lower performing GP practices in deprived areas on targeted behavioural change messages and used postcard drops, engaged with networks for migrants and people with learning disabilities, developed toolkits to increase vaccine uptake with learning disability nurses, and worked with GPs, local authorities and CCGs to provide vaccination for the traveller community at traveller sites and commission flexible models of vaccine delivery for homeless people. The skills, knowledge and experience of Screening and Immunisation Teams should be utilised to ensure that mobilisation of the COVID-19 vaccination programme is achieved, not only at pace but in a way that minimises the impact of any potential inequalities arising from a prioritisation approach.

Summary

This paper sets out some considerations regarding the currently proposed prioritisation of COVID-19 vaccine which is necessary due to initial limited supply of vaccine.

The conceptual framework adopted is one based on consideration of scientific evidence, ethics and deliverability, with a focus on the ethical principles of maximising benefit and minimising harm, promoting transparency and fairness, and mitigating inequalities in health.

While age has the absolute highest risk of poor COVID-19 outcomes, many factors are associated with an increased relative risk (such as belonging to a BAME group and being male). These are mediated by a complex web of factors which are not straightforward to disentangle and can be potentially misleading, and if misinterpreted when translated to policy, can be damaging to populations and widen health inequalities.

The current prioritisation achieves an acceptable balance between scientific evidence, ethics and deliverability, based on clinical risk as determined by age, clinical conditions, and health and social care worker status (thus providing NHS resilience). While prioritisation alone cannot address all inequalities in health that are rooted in social determinants, planning and implementation should as a minimum not worsen health inequalities, and present a unique opportunity to mitigate them.

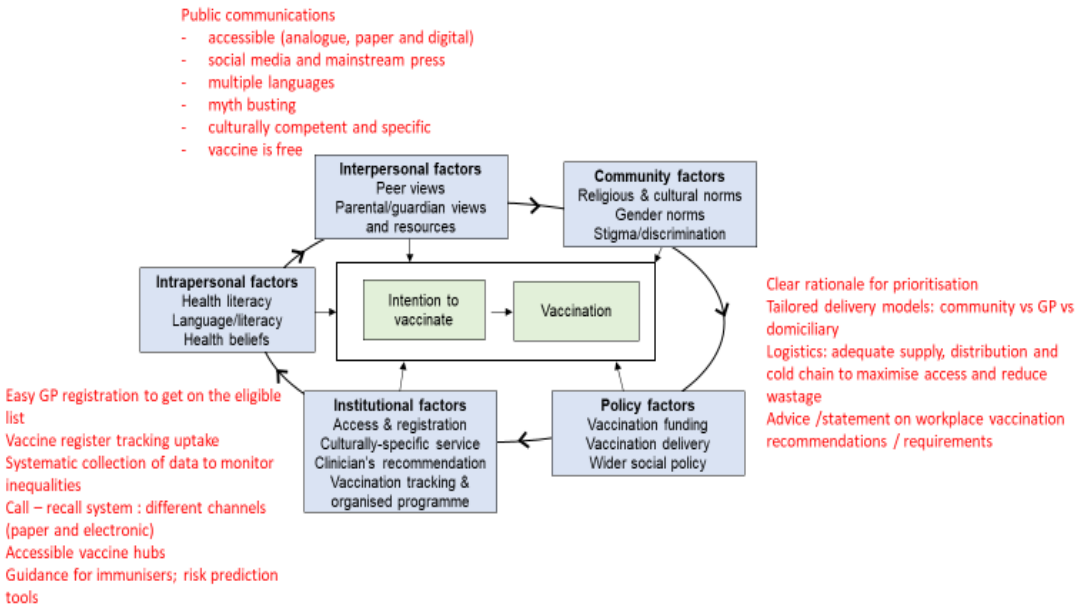
While prioritisation is set nationally, the knowledge, experience, system leadership and collaborative approach with local partners of Screening and Immunisation Teams embedded within in Public Health Commissioning in NHS England (and their equivalent teams in Scotland, Wales and Northern Ireland) should be utilised to improve vaccine uptake and reduce inequalities in the implementation of the COVID-19 immunisation programme.

Table 1. Summary of population groups and considerations for prioritisation

Population group	**Scientific evidence**	**Ethics**	**Deliverability and implementation**
Older age groups	Highest absolute risk of morbidity and mortality	Maximises benefit and reduces health inequalities	Age is almost universally recorded on NHS records, so easy to identify individuals; flexible delivery model to reduce inequalities in vaccine uptake
People with high-risk clinical conditions	Elevated relative risk; comorbidities increase with age; mediated/driven by other factors	Maximises benefit and reduces health inequalities	High risk clinical conditions are well recorded on NHS records, so individuals are easy to identify; flexible delivery model to reduce inequalities in uptake
Health and social care workers	Elevated relative risk – mediated/driven by other factors not just occupation; vaccination of staff protects vulnerable patients	Contributes to individual benefit and population benefits: protect patients and ensure NHS and adult social care resilience	Health and social care workers can be identified through occupational health structures; established delivery model in occupational settings

Population group	Scientific evidence	Ethics	Deliverability and implementation
Men	Elevated relative risk – mediated/driven by other factors, not just biological or genetic	Some benefit achieved by vaccinating older age groups and those with high risk clinical conditions	Sex is almost universally recorded on NHS records, so men would be easy to identify
Black, Asian and Minority Ethnic groups	Elevated relative risk – mediated/driven by other factors, not just biological or genetic	Risks further increasing stigma Some benefit achieved by vaccinating health and social care workers	Ethnicity recording on NHS electronic systems is poor quality, so individuals would be difficult to identify; communications strategy and flexible delivery model to reduce inequalities in vaccine uptake

Figure 1. Socioecological model of factors influencing inequality in vaccination (from immunisation audit) and potential actions to mitigate inequalities in planning and implementation (red)



References

(1) Priority groups for coronavirus (COVID-19) vaccination: advice from the JCVI, 25 September 2020 https://www.gov.uk/government/publications/priority-groups-for-coronavirus-covid-19-vaccination-advice-from-the-jcvi-25-september-2020

(2) Chamberland ME. Ethical Principles for Phased Allocation of COVID-19 Vaccines, ACIP meeting, 20 October 2020 https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2020-10/COVID-Chamberland.pdf

(3) Ward H, Atchison CJ, et al. Antibody prevalence for SARS-CoV-2 in England following first peak of the pandemic: REACT2 study in 100,000 adults medRxiv 2020.08.12.20173690; doi: https://doi.org/10.1101/2020.08.12.20173690

(4) Williamson EJ, Walker AJ, Bhaskaran K et al. Factors associated with COVID-19-related death using OpenSAFELY. Nature. 2020 Aug;584(7821):430-436.

(5) Clift, Ash K., et al. "Living risk prediction algorithm (QCOVID) for risk of hospital admission and mortality from coronavirus 19 in adults: national derivation and validation cohort study." *bmj* 371 (2020).

(6) PHE. 2020. COVID-19: review of disparities in risks and outcomes https://www.gov.uk/government/publications/covid-19-review-of-disparities-in-risks-and-outcomes

(7) OPENSafely. Absolute risks by age, comorbidity and ethnicity. (Unpublished OpenSafely Collaboration paper for JCVI)

(8) Bhopal SS & Bhopal R. Sex differential in COVID-19 mortality varies markedly by age. The Lancet, Volume 396, Issue 10250, 532 - 533 https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31748-7/fulltext

(9) Krieger, Nancy et al. Excess mortality in men and women in Massachusetts during the COVID-19 pandemic. The Lancet, Volume 395, Issue 10240, 1829 https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31234-4/fulltext#back-bib1

(10) SAGE Ethnicity sub group. Drivers of the higher COVID-19 incidence, morbidity and mortality among minority ethnic groups, 23 September 2020 https://www.gov.uk/government/publications/drivers-of-the-higher-covid-19-incidence-morbidity-and-mortality-among-minority-ethnic-groups-23-september-2020

(11) Joint Committee on Vaccination and Immunisation https://www.gov.uk/government/groups/joint-committee-on-vaccination-and-immunisation

(12) Campos-Matos, Ines et al. From health for all to leaving no-one behind: public health agencies, inclusion health, and health inequalities. The Lancet Public Health, Volume 4, Issue 12, e601 - e603https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(19)30227-0/fulltext

(13) PHE 2020. Beyond the data: Understanding the impact of COVID-19 on BAME groups. https://www.gov.uk/government/publications/covid-19-understanding-the-impact-on-bame-communities

(14) Race Disparities Unit, Cabinet Office. Quarterly report on progress to address COVID-19 health inequalities, October 2020

https://www.gov.uk/government/publications/quarterly-report-on-progress-to-address-covid-19-health-inequalities

(15) GOV.UK NHS workforce https://www.ethnicity-facts-figures.service.gov.uk/workforce-and-business/workforce-diversity/nhs-workforce/latest

(16) NICE. Public Health Guidance 21 Immunisations: reducing differences in uptake in under 19s. 2017 https://www.nice.org.uk/guidance/PH21

(17) Schmitz H and Wubker A. What determines influenza vaccine take up in Elderly Europeans? Health Econ 20:1281-1297 2011 https://onlinelibrary.wiley.com/doi/epdf/10.1002/hec.1672

(18) Ward C, Byrne L, White JM, Amirthalingam G, Tiley K, Edelstein M. Sociodemographic predictors of variation in coverage of the national shingles vaccination programme in England, 2014/15. Vaccine. 2017;35(18):2372–8. pmid:28363324

(19) https://www.gov.uk/government/publications/herpes-zoster-shingles-immunisation-programme-2017-to-2018-evaluation-report

(20) Hungerford, D., Vivancos, R., Read, J.M. et al. Rotavirus vaccine impact and socioeconomic deprivation: an interrupted time-series analysis of gastrointestinal disease outcomes across primary and secondary care in the UK. BMC Med 16, 10 (2018). https://doi.org/10.1186/s12916-017-0989-z