

**How to decide on who to vaccinate during a pandemic?**

Theoretically there are roughly two strategies on how to deploy a vaccine during a pandemic, this is or focus on protecting those with the highest risk of severe outcome, or preventing transmission by a focus on those with the highest contribution to transmission, this last strategy should also prevent clinical risk groups due to herd effects. Depending on what is feasible with the vaccine in terms of protecting those with the highest clinical risk (vaccine efficacy among the elderly and clinical risk groups) or preventing transmission (efficacy against transmission endpoints among those healthy) as well as the impact you want to optimize (for example deaths or wider economic impact), you would decide between the two strategies.

However the decision between these two strategies also depends on the available doses of the vaccine over time. To achieve herd immunity it is likely that a larger percentage of the population will need to be vaccinated compared to the specific risk groups. Therefore, in case when vaccine is in short supply it helps to have a tiered strategy where doses are provided to well defined groups which are set in advance, as soon vaccine becomes available. And in which in the process of defining these groups there is a political/compromise component, as not all risks can be exactly calculated.

For example when sufficient number of doses come available at one time you could invite all people aged between 20 to 65 – which will target an important group for transmission. However, if doses will be available in smaller batches targeting a large group might mean that you have to wait until you have sufficient doses before you can start. In this case it might be preferable to have a tiered system. For example based on both risk of clinical outcome and risk to acquire infection. For example: First available vaccine will be provided to people in care homes/hospitals (as the people are both clustered and at high risk for severe outcomes), staff in care homes, 'healthy' people in clustered settings (prisons/asylum centers etc.), clinical risk groups living at home, the rest of the population (depending on the known vaccine efficacy these groups can be defined differently and groups could be switched around).

However, a tiered system is complex, as it will require to define people who are in, and who are out, as well as a requirement to identify and invite these people for vaccination. But these decisions can be made in advance and it could provide clarity. Some of the known risk groups for COVID-19, such as obese people, are likely harder to identify and invite compared to other clinical risk groups.

Furthermore it is important to decide on what you want to optimize. Traditionally cost-effectiveness analysis are conducted to explore the relation between the price of the vaccine and the societal impact. However, in case of a pandemic cost-effectiveness analysis are more complex. The vaccine might already be bought, thus the price is less relevant, and the outstanding question will be reduced if it is worth to provide the vaccine what already has been bought. On the other hand, to estimate the possible costs of the pandemic on society is an open ended analysis, as there are no set methodology to estimate this. It is therefore important to pre-define the endpoints which require to be optimized in this decision making process. On top, the risk of side-effects of this vaccine is a very important consideration when vaccinating many people with a very new vaccine. People perceive the risk of side-effect different compared to normal disease. In standard cost-effectiveness analysis side-effects are poorly included, and if included weighted similar compared to prevented disease (thus 1 prevented QALY by vaccination is off-set by 1 QALY due to induced side-effects) which is not how people think.

Therefore, before the decision process on how to provide the vaccine can start there needs to be a high level, informed discussion about the decision process itself.