The vulnerable to severe COVID-19 & avoiding unlock, relock

The cautious staged lifting of lock-down restrictions accompanies a welcome drop in new cases of infection, hospital admissions for severe disease and deaths. However, fundamental questions at the outset of the lock-down still remain:

- What proportion of the population has already been infected with SARS-COV2?
- Are those who have suffered the virus, no longer able to spread the virus?
- Who and how large is the proportion of the population vulnerable to severe COVID-19?

This epidemic revolves around those vulnerable to severe disease with the restrictions designed to protect those at greatest risk of requiring hospital treatment being the population likely to have to draw on finite health resources if infected.

The R number refers to average number infected as a multiple of each person confirmed to have contracted the virus. As our freedoms slowly return, the spectre in the shadows is the risk of the R number rising above 1 again combined with a large part of the population still being naïve to the virus and capable of spreading it. Should the staged relaxing of social restrictions fail to contain the R number below 1, this will presumably trigger a fresh round of tighter lock-down.

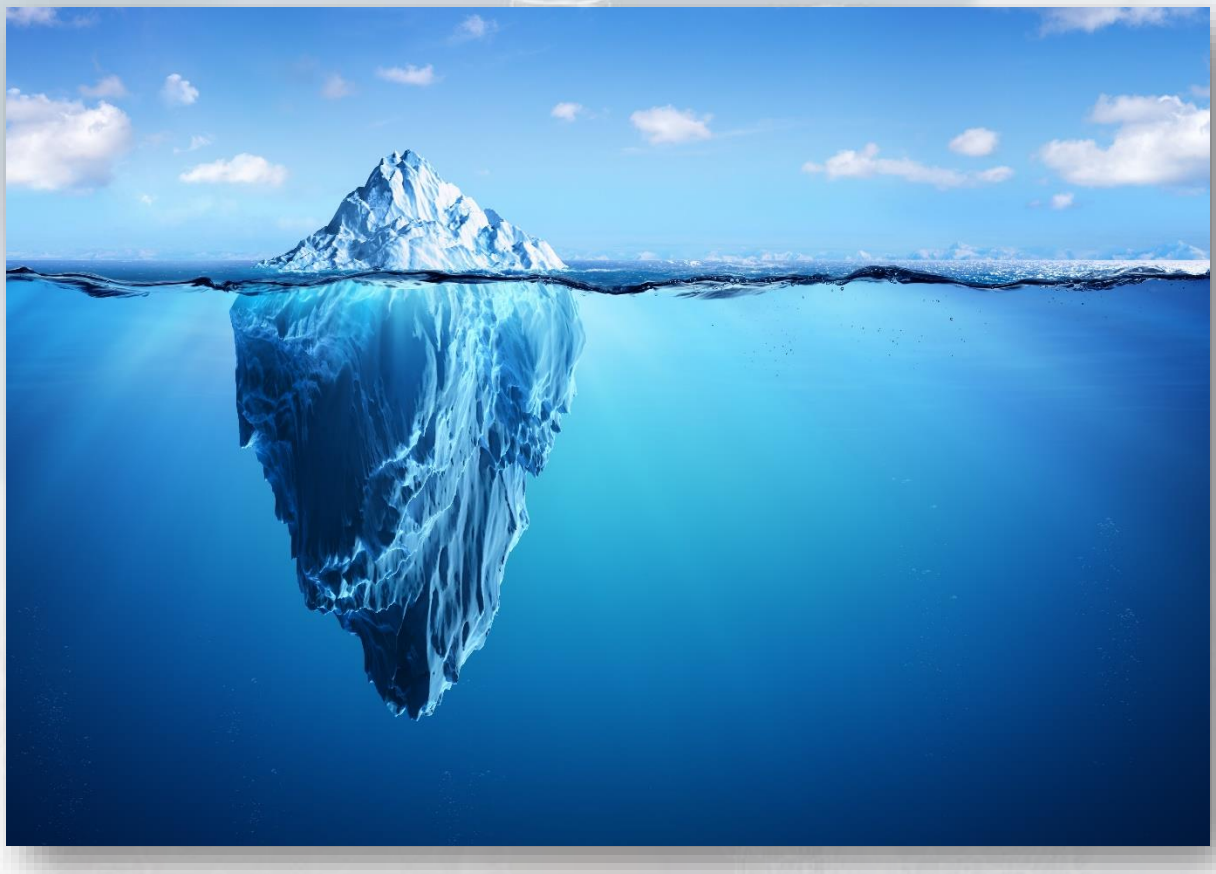
Who are the vulnerable?

A major part of the necessity for such restrictions is associated with the identity and scale of the population who are vulnerable to severe COVID-19. If they are accurately characterised and can be protected (assuming they are willing to live with this over the requisite timeframe) then potentially the balance of the population could be released to induce herd immunity or more ideally for the virus to fizzle out. In the absence of accurate characterisation an escalation of the R number above 1 combined with a sizeable vulnerable population could quickly lead to a spike in severe cases and health services being over-run. Presumably trigger fresh restrictions. Initially the vulnerable were defined as the elderly plus a slightly vague catch-all definition of those with ‘underlying health conditions’.

In a recent article in the Telegraph newspaper in the UK, Dr Aseem Malhotra, a former cardiology registrar provided some more context on what ‘underlying health condition’ may refer to. He reported that the data showed a ten-fold increase in the risk of death for those with obesity and conditions associated with metabolic syndrome e.g. type2 diabetes, high blood pressure, heart disease. He explained this correlation is likely due to such conditions causing a higher incidence of dysregulated immune system. The dysregulated immune system meaning SARS-COV2 infection provokes the excess inflammatory reaction that drives severe COVID-19.

The article goes on to supply statistics that 60% of the UK’s population is now overweight or obese and, alarmingly, in the US only one in three of those with normal or lower Body Mass Index are metabolically healthy. If the US lower Body Mass Index numbers are extrapolated to the UK this would suggest an alarming 80%+ of the population may be vulnerable. This is not spread alarm that this high proportion are vulnerable but it does give an indication of the scale of the possible iceberg

of vulnerability Obviously, before drawing such a conclusion, much more evidence and work is needed but it does provide an indication of the potential scale of vulnerability.



Vaccines, Anti-virals and the vulnerable

The logical conclusion, if even a significant fraction of this proportion of the population proves to be vulnerable, has been sufficiently restricted to just is that social restriction may here for some time. Test and trace offers a means of controlling outbreaks but does not stimulate unrestricted trips to the pub, the football or your favourite band anytime soon. A pattern of ebb and flow may emerge as the authorities react to any upward fluctuations in the R number. The higher the proportion of the population vulnerable to severe COVID-19 the more pronounced this is likely to be.

This implies to obtain a lasting removal of restrictions is either through herd immunity where the majority of the population have had SARS-COV2 infection AND are now immune to spreading it or a scientific innovation is developed capable of dealing with the issue.

Some evidence is emerging that the hyperimmune response may largely occur when the viral load is in decline. This presents a profound question as to the nature of therapeutic innovation needed to address the situation. Is the excess immune reaction a response to the virus itself or a result of damage caused by the virus such as to the epithelial layer of the lung?

The various vaccines being tested are orientated toward compromising the virus and reducing its impact, they do not eradicate infection by the virus. The same is true of the anti-viral drugs being

tested. Whether they can prevent some or all of the vulnerable population with dysfunctional immune systems from escalating into an excessive inflammatory response if infected is unknown. Clearly should the proportion of the population vulnerable to severe COVID-19 be large and these new therapies prove incapable of preventing the excess immune response in a significant proportion of the vulnerable we may still be stuck with social restrictions being relaxed and tightened for some time.

How can unlock, relock be prevented?

Potentially the lock-down restrictions have already restricted the spread sufficiently to an extent that it will not escalate again. However, if this is not the case, what viable solutions can science deliver that can prevent an extended period of fluctuating lock and un-lock? Logically this would appear to be:

- an effective means of tempering the excessive immune response in the vulnerable,
- a vaccine or anti-viral treatment that:
    - renders those inoculated no longer capable of spreading the virus; and/or
    - prevents the vulnerable population from escalating into an excessive immune response.
- significantly reducing the population who are vulnerable, for example by improving their metabolic health.

None are simple, but in the circumstances, given the related human and economic cost, perhaps a parallel focus on all may be prudent.