14) Drugs can also be used as *prophylaxis*. This could be long-term prophylaxis of vulnerable patients providing a form of chemical shielding, occupational prophylaxis for those at high risk of infection for example in healthcare workers, or prophylaxis of contacts of cases as part of a contact tracing system.

15) Currently the priority in clinical trials is to test existing drugs for which we have licensed products, known side effects, drug supply and manufacturing capacity. There is a reasonable chance that this repurposing of older drugs may discover combinations which take the mortality from COVID-19 lower (below 1%) and could suppress transmissibility. We may have initial answers within weeks.

16) It is likely however that drugs that very substantially reduce mortality or are protective enough to change the course of the epidemic will have to be designed and developed specifically for coronavirus. If so this will take at least a year and probably a lot longer, and success cannot be guaranteed.

17) Research to develop new vaccines and drugs must therefore be seen as an essential medium to long-term investment, but is unlikely to change the path of the global pandemic over the next 12 months, and may take much longer. It is an area that the UK is very strong at and we should do everything we can to develop new options and create new infrastructure and industry.

Modifying the epidemic curve through public health interventions.

18) Once the initial peak is under control and new cases are falling, if all social distancing interventions were to stop R would rise rapidly back to close to its initial R_0 value of around 3 and the epidemic would resume exponential growth with a doubling time of a few days. We would rapidly return to a second wave with a risk of ICU capacity being exceeded. The newly increased capacity in the NHS would delay but not prevent reaching the point where it was overwhelmed. Any relaxation of social distancing measures which leads to R>1 as a long-term trend will also lead to exponential growth of the epidemic, albeit at a slower rate at lower values of R.

19) Once the morbidity and mortality rate has dropped from its initial peak and the NHS urgent and critical care capacity has not been exceeded, there are broadly three possible aims.

a) *Suppress the virus to the lowest achievable level*, accepting eradication is not possible. This would imply a more aggressive social distancing policy to get R well below one and more intrusive public health measures. These measures would probably need to be maintained until a sufficiently effective vaccine or drug is available as population immunity would take a very long time to accrue. It would minimise direct coronavirus deaths but is likely to lead to higher rates of other indirect causes of mortality and morbidity.

As a subset of this approach it is possible to consider an approach in which infection is supressed to a very low level through social distancing, and then maintained through rapid case identification and automated efficient contact tracing. Individuals would need to be isolated very actively but the population as a whole would have reduced social distancing measures (see track and trace below), although it is unlikely they could be abandoned. This approach may be very difficult to achieve if the rates of minimally symptomatic or pre-symptomatic transmission are high.

b) *Maintain sufficient social distancing measures, combined with enhanced shielding, and keep R at or just below 1*. With this approach population immunity should gradually accrue (assuming that immunity does occur in everyone infected and that it lasts) whilst the most vulnerable are shielded. There would need to be work to identify more accurately the vulnerable in all age groups. The NHS

epidemiology, but as immunity develops across the population it may be possible to relax social distancing measures for some and still keep R<1.

23) For the next six months period variations on social distancing, possibly enhanced by track and trace, alongside shielding the most vulnerable provide the most realistic routes to controlling the effects of this epidemic. In the longer run (assume >12 months) vaccines or drugs may provide a technological exit strategy, but they will take time and should not be relied on as the easy way out. It is a policy choice whether to run R as low as it can be achieved, implying very long-term suppression of the epidemic or running R as near to 1 as it can be managed within the boundaries the NHS can cope with. The latter would imply an ongoing significant direct COVID-19 mortality but potentially with less social damage and indirect mortality, and quicker although still lengthy exit from the epidemic as population immunity accumulates (assuming it does).

24) If the proportion of asymptomatic infections is much higher than anticipated, the degree of immunity in the community is higher than expected, or the drugs in current clinical trials show reasonable effects then other options could be considered.

25) Five key technologies are likely to provide help with exit – quick accurate testing at scale, data systems to monitor epidemic with regional granularity, automated contact tracing, drugs and vaccines. Of these the two technologies which are sufficiently mature it is currently mainly about operational deployment are tests and data. Drugs, vaccines and automated contact tracing all have discovery and development risks. The UK needs to have a clear approach to all 5.