To- PS/PM

From- CMO

A short note on Long Covid.

1) The PM has asked for a note on Long Covid. In the absence of a settled scientific position this is a personal view of the current state of knowledge. We have a lot of data but very little clarity and still less agreement on Long Covid. There is a however consensus that a significant minority of people infected with Covid go on to have prolonged symptoms, although many of these do improve over the first few months. ONS are about to update their estimates on this (4th June) and this note is written without having seen their new estimates which may change significantly.

What is Long Covid?

- 2) There is a fair degree of agreement that Long Covid is a catchall for more than one syndrome. In general it is taken to mean people who have significant symptoms for more than 12 weeks after their acute Covid episode. There is however a lot of definitional confusion both among professionals and patient support groups.
- 3) Although there is often a common assumption that you either die of infections or get better, for many infections this is not true. The principle that even initially trival infections can cause long-term, and sometimes severe, effects is well established. These vary by infection and often by age. Extreme examples are HPV 16 virus which is asymptomatic but causes cervical cancer some years later, *H. pylori* bacteria which are often asymptomatic but can cause stomach cancer, and chikungunya and Ross River fever, short lived viral infections which can cause severe joint inflammation for months to years after the initial infection has passed.
- 4) A post-infectious fatigue syndrome after other infections has been well recognised for many decades although is poorly understood. Certain infections are particularly liable to cause it such as dengue; in the UK Epstein Barr Virus (EBV) can be associated with it when acquired in early adulthood but not usually in childhood. Most people improve over time and get back to baseline, although this can be slow (months to years), fluctuating and is not invariable. Severity of initial illness is not well correlated with how prolonged symptoms are.
- 5) In my *opinion* the chronic problems that occur after Covid currently termed long Covid fall into at least four categories, described in an NIHR review.
 - A) A post intensive care syndrome. This is well recognised for multiple conditions and essentially is a marker of severity of initial disease, including damage from the disease and sometimes damage from the treatment.
 - B) Permanent organ damage to the lungs, heart and possibly brain which can be identified by imaging or other tests, including in those who did not have obviously severe initial infection.
 - C) A postinfectious fatigue syndrome with a lot of overlap with other postinfectious fatigue.
 - D) Long-term but fluctuating symptoms that seem relatively specific to Covid including intermittent breathlessness and cardiovascular instability.

There may be a subgroup, or groups, among some children, although current data suggest prolonged symptoms are rarer in children.

A lot of work is going on internationally to refine the definition of the syndromes because without this it is very difficult to assess incidence, change over time and the impact of different treatments and vaccines.

How common is Long Covid?

- 6) Estimates of how many people have long Covid vary quite widely probably reflecting the different definitions people use, and are likely to change over time. ONS estimated in April that for the four week period ending 6 March 2020 1.1 million people reported experiencing symptoms persisting more than four weeks. Of these 674,000 were estimated to report ability to undertake day-to-day activities had been affected to some degree, and 196,000 activities had been limited a lot. It is important to note that this is anytime from four weeks after onset and quite a lot of these will resolve relatively early, and that these data represent a period when there was very high circulation of Covid in the community.
- 7) Within the ONS data restricted only to those who had symptoms more than 12 weeks, which is closer to a normal definition of Long Covid, 127,000 people are estimated to have activity limited a lot, 296,000 had activity limited a little and 275,000 with symptoms but no limitation of activity. The peak age was 35-69, more in women than men and with an association with deprivation. Revised ONS data will come out later this week.
- 8) The coronavirus infection survey estimated 13.7% of adults who tested positive Covid had some symptoms at 12 weeks.
- 9) Reviews of the existing literature more widely currently would suggest around 10% of people who are not admitted to hospital have at least one enduring symptom three months later, but for those admitted to hospital between 50 and 90% might have at least one symptom two months after discharge.
- 10) In contrast the ZOE App study suggests only 2.3% of adults who logged symptoms had them at 12 weeks.
- 11) ONS data suggested that in children aged 2 to 11 with Covid 7.4% had symptoms at 12 weeks and for 12 to 16 years 8.2% at 12 weeks (compared to 13.7% in adults).
- 12) We are only now getting to the period we can see how many people with proven COVID have symptoms out to a year- the newest ONS data will be useful on this.
- 13) Many of those who have symptoms at 12 weeks or 6 months will continue to improve. Other than those who have fixed disabilities as a result of Covid such as strokes it is very difficult to tell one year in how long the tail of Long Covid will be. Only a minority of people get prolonged symptoms in the group not admitted to hospital, but because Covid has been so common it is a big enough minority to constitute a significant additional public health problem from Covid on top of acute severe disease and mortality.

What should we do?

14) The short answer: stop people getting COVID; no COVID, no Long COVID.

15) For Long COVID specifically

- i) research into cause and treatment is the medium and long-term priority (NIHR and MRC are funding among others)
- setting up specialist NHS clinics which can provide care for those who need it now, and also accumulate experience of how to manage it. Medicine improves by repeated clinical observation as well as formal scientific studies.
- 16) For those who been vaccinated and then acquire Covid it is highly likely that the vaccine will reduce the probability of the long term problems associated with severe disease (5 A and B above). We cannot yet be confident what the effect of vaccination will be on the prolonged symptoms in those who do not have severe disease (5 C and D). The interaction of the immune system with post-infective syndromes is complex (some are probably caused by prolonged immune activation), and it is therefore not a given that a more active immune response to infection will lead to fewer long-term symptoms. It is more likely to reduce incidence than increase it in my opinion, but this needs data to be confident.
- 17) The scientific and clinical understanding of what is currently called Long Covid is likely to evolve substantially over the next year and beyond. This note should therefore be seen as a very initial summary a complex, evolving and contested field. It is however clear there is a large enough problem to be concerned about over and above mortality and hospitalisation.

Chris. Whitty 31/05/2021