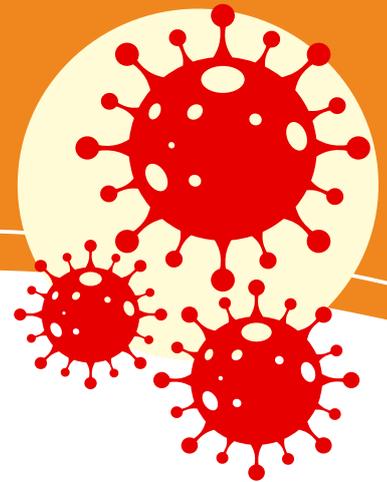


Waldenstrom's macroglobulinaemia (WM) and COVID-19: Are people with WM more at risk of complications?

A WMUK factsheet

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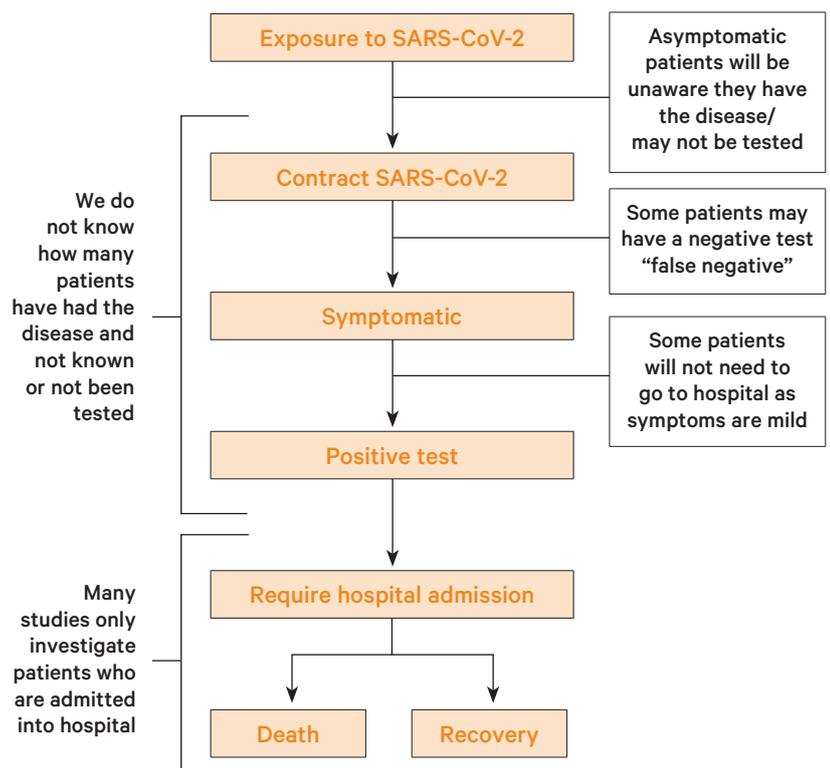
Can I see my grandchildren? Can I go back to work? Is it ok for my partner to go back to work? Is it ok to go out for a meal? Should I delay my treatment? Can you quantify my risk?

Only a few months ago, you would have all been told that you are in the “clinically extremely vulnerable group” and that you should avoid all people outside your household contacts and “shield”. Now that shielding has been paused by the UK government as the rate of people with SARS-CoV-2 in the UK is going down, a large part of my clinic consultations with patients is taken up by questions regarding how much they should still be avoiding others, with the questions above being some of the hundreds of doctors and nurses are asked every week.

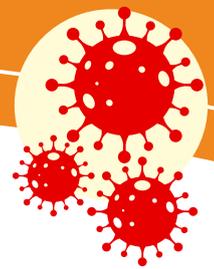
Healthcare professionals practise evidence-based medicine which means that when we are trying to answer these questions and advise patients, we look to the papers that have been published on the subject to give us the actual data that supports what we are saying. The problem is that a lot of the papers on this subject are based on very small numbers of patients and so may not be representative of what is actually happening.

In addition, you only know if you have COVID-19 if you have a test, so even the papers that include hundreds of patients will not capture those patients who maybe only had mild or no symptoms at all, and so this introduces bias into the results (not truly representative) and also skews all the results towards those who have particularly severe symptoms (see diagram opposite).

Finally, all patients with blood cancers are lumped into one “risk group” in many of these papers, and we know that there is a lot of variability in different lymphomas and leukaemias, and also in the patients who get them; you are all of different ages and some of you may have other risk factors such as diabetes. These are some of the reasons why the data published so far should be interpreted with caution and our advice may change with time as we understand more about the disease.



WM and COVID-19: Are people with WM more at risk of complications?



What is my risk of contracting SARS-CoV-2 (the virus that causes COVID-19)?

This is related to lots of factors and to some extent the one thing that we can control.

- **Personal protection:** Hand hygiene, wearing masks, maintaining social distance.
- **Contact with other people/shared surfaces:** dependent on how many different people you see each day; whether you work in shared office space / use public transport etc.

The things beyond our control that can have an impact on this is the infection rate in the general population currently, i.e. if very few people have the virus then the chances of you “catching” it become lower. Obviously if a vaccine becomes available this will also lower the risk of contracting SARS-CoV-2.

Whilst some of the early studies did seem to indicate that patients who were requiring multiple hospital visits or were inpatients, contracted COVID-19 whilst at hospital, certainly in the UK now there are many practices in place to minimise exposure to COVID-19 in the hospital, and the rate is sufficiently low that we can be fairly confident that there is a very low risk of exposure to the virus in the hospital.

What is my risk of severe symptoms if I get COVID-19?

Number of people with severe symptoms with positive COVID-19

Number of people with COVID-19

This is a very important question, but unfortunately we have very little evidence to be able to answer this question, mainly because not everyone with COVID-19 was tested; either because they didn't have symptoms at all, or the symptoms were so mild that they were not tested.

When studies are published, each country has their own national health policy as to who to test dependent on the number of tests and the resources available, and even within a country, this policy can change over time. In the equation above, whilst we have a better idea of the top number, we don't have a good estimate for the bottom number (denominator) and so cannot accurately answer the question regarding risk.

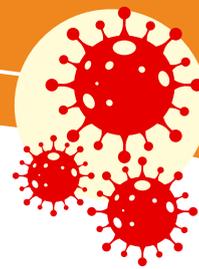
It should also be noted that no test is perfect and so there are going to be a number of false negative tests (people who test negative who actually have COVID-19) and false positive cases.

In patients hospitalised with COVID-19, do patients with blood cancer have a higher risk of death?

This is the question that has been addressed the most in larger studies, as it can be clearly measured.

There does seem to be some evidence that those with blood cancers who are hospitalised with COVID-19 do have increased risk of death when compared to patients with other cancers or the general population.

WM and COVID-19: Are people with WM more at risk of complications?



Do patients with WM have a higher risk of death with COVID-19?

As discussed, most papers have grouped all blood cancers together.

In those that have attempted to look at more detail, there does seem to be some evidence that the risk is higher for those with leukaemia rather than lymphoma or patients that have been more recently diagnosed. In these studies however, it is difficult to know if that is for other reasons (“confounding factors”), e.g the risk of death in patients with some forms of leukaemia is higher and not all the papers published differentiate between patients dying due to COVID-19 or with COVID-19 e.g. due to their blood cancer.

Do patients on treatment have a higher risk of death with COVID-19?

Some of the studies do suggest that those with “active disease”, more recent diagnosis or those patients on treatment have an increased risk of severe complications and death compared to those not on treatment or diagnosed many years ago, but not all studies have found this. Again, this could be due to confounding factors and does not necessarily mean that having treatment increases your risk.

Should I start treatment for WM?

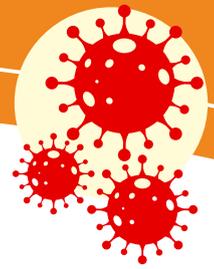
We do not have strong evidence that any treatment is more or less likely to lead to you having severe complications with COVID-19. Obviously, the more times you need to come to hospital for treatments, the increased chance of potential exposure, but as discussed, at present, the risk is quite small in UK hospitals.

When we see patients with WM, we always ask, do they have any reason to need treatment now, and what is the best treatment that we can give. The two questions remain the same, however, for many patients who are approaching needing treatment, for example if you are progressively becoming more anaemic, there is some degree of flexibility in timing of when to start treatment that can be made dependent on what the situation is at that time e.g. infection rate.

If I need treatment, should COVID-19 affect treatment choice?

You may have read a report detailing 6 patients with WM being treated with ibrutinib all of whom were admitted into hospital with COVID-19, and all recovered, but we don't know whether this was at all related to the ibrutinib or not even though there are some plausible theories as to why it may be effective (Treon Blood 2020 135(21) 1912-1915). Trials are underway to know whether BTK inhibitors are useful treatments for COVID-19, until then, it is not advised that you base your treatment decisions on this.

WM and COVID-19: Are people with WM more at risk of complications?



Summary of larger studies

Williamson *et al.* *Nature* 2020 430-436

This study investigated risk factors for death due to COVID-19 by examining the anonymised GP records of approximately 40% of the population of England and comparing the rates of different factors in the general population to the rate of these factors in people who died due to COVID-19. Because the comparison was with the GP records of millions of patients, they could adjust outcomes for age/ sex etc i.e. if a patient has WM and is 90years old, is age more of a risk factor or the fact that he has WM? Multivariable analysis (i.e. when taking other risk factors into account) showed that patients with blood cancers had a 3.5x increased risk in patients who had been diagnosed less than a year ago and 1.88x in those diagnosed over 5 years ago compared to the general population matched for other factors. It also showed that age, diabetes and ethnicity were also risk factors.

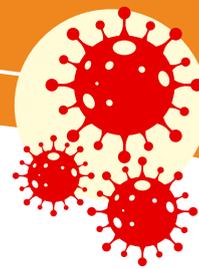
Kuderer *et al* *The Lancet* 2020 395(10241): 1907-1918

This study is from a large cancer consortium (CCC19) between USA, Canada and Spain and looks at the outcome of all patients diagnosed with COVID-19 who also have a cancer diagnosis to try and decide risk factors within this population. In this paper they examined the outcome of 928 patients of whom 167 had a blood cancer. They did not find that patients with blood cancer had a higher risk of death compared to patients with other types of cancer.

Lee *et al* *The Lancet* 2020 395:1919-26

This study is similar to the one above but UK based consortium (UKCCMP) that examined the outcomes of 1044 patients with COVID-19 and a diagnosis of cancer. In this cohort, 79 patients had leukaemia, 79 lymphoma, and 37 myeloma, and 29 other blood cancers. The authors concluded that there were more patients with blood cancers including WM in this cohort than would be expected compared to the general rates of these types of cancer in the national population suggesting that these patients were at increased risk of COVID-19, but this may be due to other reasons, for example were more haematologists involved in entering the data. In this cohort, patients with leukaemia and COVID-19 but not lymphoma or myeloma had an increased rate of death compared to other patients in the consortium. Those who had recent chemotherapy were also at increased risk of death.

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Conclusion

The data suggests that patients with blood cancers do have an increased risk of severe complications with COVID-19, but it is worth remembering that this is still a low risk overall and shouldn't be taken in isolation. When thinking about your own personal risk, you should also consider whether you have other known risk factors eg. age, male sex, high blood pressure, chronic lung disease, and diabetes.

You should try and minimise exposure to lots of different people, e.g. ensure your work-place is COVID-secure, maintain social distancing and wash your hands frequently. It is important you talk through your risk with your clinical team and so you can work out the right solution for you in terms of going back to work / meeting family / socialising.

It is also very important to let your medical team know if you are particularly anxious or the isolation is affecting your mental health, we know that COVID-19 is having lots of indirect consequences. Also remember, if you need to go to hospital, you shouldn't be fearful of this, many new systems have been put in place to protect both patients and staff.

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If you still have questions or have any concerns about the contents of this factsheet and would like to talk to someone, we would always recommend contacting your healthcare professional or WM health care team, or contact us at WMUK.



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