

# Highest risk clinical subgroups upon community infection with SARS-CoV-21

## Down's syndrome and other genetic disorders

- All individuals with Down's Syndrome or other chromosomal disorders known to affect immune competence.

## Solid cancer

- metastatic or locally advanced inoperable cancer.
- lung cancer (at any stage).
- people receiving any chemotherapy (including antibody-drug conjugates), PI3K inhibitors or radiotherapy within 12 months.
- people who have had cancer resected within 3 months and who received no adjuvant chemotherapy or radiotherapy.
- people who have had cancer resected within 3 to 12 months and receiving no adjuvant chemotherapy or radiotherapy are expected to be at less risk (and thus less priority) but still at increased risk compared with the non-cancer populations

## Haematological diseases and recipients of haematological stem cell transplant (HSCT)

- allogeneic HSCT recipients in the last 12 months or active graft versus host disease (GVHD) regardless of time from transplant (including HSCT for non-malignant diseases)
- autologous HSCT recipients in the last 12 months (including HSCT for non-malignant diseases)
- individuals with haematological malignancies who have received CAR-T cell therapy in the last 24 months, or until the lymphocyte count is within the normal range
- individuals with haematological malignancies receiving systemic anti-cancer treatment (SACT) within the last 12 months, or radiotherapy in the last 12 months
- all people who do not fit the criteria above, and are diagnosed with:
  - myeloma (excluding monoclonal gammopathy of undetermined significance (MGUS))
  - AL amyloidosis
  - chronic B-cell lymphoproliferative disorders (chronic lymphocytic leukaemia, follicular lymphoma)
  - myelodysplastic syndrome (MDS)
  - chronic myelomonocytic leukaemia (CMML)

- myelofibrosis
- any mature T-cell malignancy
- all people with sickle cell disease
- people with thalassaemia or rare inherited anaemia with any of the following:
- severe cardiac iron overload (T2 \* less than 10ms)
- severe to moderate iron overload (T2 \* greater than or equal to 10ms) plus an additional co-morbidity of concern (for example, diabetes, chronic liver disease or severe hepatic iron load on MRI)
- individuals with non-malignant haematological disorders (for example, aplastic anaemia or paroxysmal nocturnal haemoglobinuria) receiving B-cell depleting systemic treatment (for example, anti-CD20, anti-thymocyte globulin (ATG) and alemtuzumab) within the last 12 months

### Renal disease

- renal transplant recipients (including those with failed transplants within the past 12 months), particularly those who have:
  - received B cell depleting therapy within the past 12 months (including alemtuzumab, rituximab [anti-CD20], anti-thymocyte globulin)
  - an additional substantial risk factor which would in isolation make them eligible for monoclonals or oral antivirals
- non-transplant renal patients who have received a comparable level of immunosuppression[footnote 3]
- patients with chronic kidney stage (CKD) 4 or 5 (an estimated glomerular filtration rate (eGFR) less than 30ml per min per 1.73m<sup>2</sup>) without immunosuppression

### Liver diseases

- people with cirrhosis Child-Pugh (CP) class A,B and C, whether receiving immune suppressive therapy or not. Those with decompensated liver disease (CP B and C) are at greatest risk
- people with a liver transplant
- people with liver disease on immune suppressive therapy (including people with and without cirrhosis)

### Solid organ transplant recipients

- Solid organ transplant recipients not in any of the above categories.
- Immune mediated inflammatory disorders[footnote 4]
- people who have received a B-cell depleting therapy (anti-CD20 drug for example, rituximab, ocrelizumab, ofatumab, obinutuzumab) in the last 12 months.
- people who have been treated with cyclophosphamide (IV or oral) in the 6 months prior to positive PCR or relevant COVID test.
- people who are on corticosteroids (equivalent to greater than 10mg per day of prednisolone) for at least the 28 days prior to positive PCR.
- people who are on current treatment with mycophenolate mofetil, oral tacrolimus, azathioprine, mercaptopurine (for major organ involvement such as kidney, gastro-intestinal tract, liver and/or interstitial lung disease), methotrexate (for interstitial lung disease or

asthma[footnote 5] only) and/or ciclosporin. No minimum dose threshold is suggested[footnote 6]

- people who exhibit at least one of: (a) uncontrolled or clinically active disease (that is, required recent increase in dose or initiation of new immunosuppressive drug or IM steroid injection or course of oral steroids within the 3 months prior to positive PCR); and/or (b) other high risk comorbidities (for example, body mass index (BMI) greater than 30, diabetes mellitus, hypertension, major organ involvement such as significant kidney, liver or lung inflammation or significantly impaired renal, liver and/or lung function)

## Respiratory

- asthma in people on oral corticosteroids (defined above).
- Any asthma patient taking immunosuppressants for their asthma including but not exclusively methotrexate, ciclosporin.
- COPD on long term home n interstitial lung disease. Patients on long term oxygen therapy. People with moderate or severe disease (FEV1 greater than or equal to 50% predicted) who have required 4 or more courses of prednisolone 30mg for 5 days or greater in last 12 months.
- interstitial lung disease (ILD) - all patients with idiopathic pulmonary fibrosis
- sub-types of ILD - for example, connective tissue disease related, sarcoidosis, hypersensitivity pneumonitis, NSIP (non specific interstitial pneumonia) who have received a B-cell depleting therapy in last 12 months, or IV or oral cyclophosphamide in the 6 months prior to testing positive for COVID-19. Any ILD patient on current treatment with corticosteroids, mycophenolate mofetil, azathioprine, tacrolimus, ciclosporin or methotrexate. No minimum dose criteria
- any people with any type of ILD who may not be on treatment due to intolerance but has severe disease with an FVC predicted less than 60%
- NIV - all patients requiring this type of support regardless of the underlying disorder (which might include COPD, obesity hypoventilation syndrome, scoliosis, bronchiectasis, genetic muscular diseases refer to neurology section)
- lung cancer patients, refer to 'Solid cancer' section above
- lung transplant patients (refer to solid organ transplant section)
- pulmonary hypertension (PH): groups 1 and 4 from PH classification[footnote 10]

## Immune deficiencies

- common variable immunodeficiency (CVID)
- undefined primary antibody deficiency on immunoglobulin (or eligible for Ig)
- hyper-IgM syndromes
- Good's syndrome (thymoma plus B-cell deficiency)
- severe combined immunodeficiency (SCID)
- autoimmune polyglandular syndromes or autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome)
- primary immunodeficiency associated with impaired type I interferon signalling
- x-linked agammaglobulinaemia (and other primary agammaglobulinaemias)
- any person with secondary immunodeficiency receiving, or eligible for, immunoglobulin replacement therapy

## HIV/AIDS

- people with high levels of immune suppression, have uncontrolled or untreated HIV (high viral load) or present acutely with an AIDS defining diagnosis
- people on treatment for HIV with CD4 less than 350 cells per mm<sup>3</sup> and stable on HIV treatment or CD4 greater than 350 cells per mm<sup>3</sup> and additional risk factors (for example, age, diabetes, obesity, cardiovascular, liver or renal disease, homeless, alcoholic dependency)

## Neurological disorders

- Conditions associated with neuromuscular respiratory failure requiring chronic ventilatory support:
  - motor neurone disease
  - Duchenne muscular dystrophy
  - Conditions that require use of specific immunotherapies:[footnote 12]
  - multiple sclerosis (MS)
  - myasthenia gravis (MG)
  - other immune mediated disorders

## Dementia and neurodegenerative disorders when associated with severe frailty

- Alzheimer's disease, vascular disease, Lewy body disease, or frontotemporal atrophy
- Parkinson's disease
- Huntington's disease
- Progressive supranuclear palsy and multiple system atrophy