Article:
Miller, P.D.E., Patel, S.R., Skinner, R. orcid.org/0000-0002-1162-675X et al. (9 more authors) (2023) Joint consensus statement on the vaccination of adult and paediatric haematopoietic stem cell transplant recipients: prepared on behalf of the British society of blood and marrow transplantation and cellular therapy (BSBMTCT), the Children's cancer and Leukaemia Group (CCLG), and British Infection Association (BIA). Journal of Infection, 86 (1). pp. 1-8. ISSN 0163-4453

https://doi.org/10.1016/j.jinf.2022.11.005

Journal of Infection 86 (2023) 1–8

Contents lists available at ScienceDirect

Journal of Infection

journal homepage: www.elsevier.com/locate/jinf

Review

Joint consensus statement on the vaccination of adult and paediatric haematopoietic stem cell transplant recipients: Prepared on behalf of the British society of blood and marrow transplantation and cellular therapy (BSBMTCT), the Children's cancer and Leukaemia Group (CCLG), and British Infection Association (BIA)

PDE Miller[a], SR Patel[b], R Skinner[c], F Dignan[d], A Richter[e], K Jeffery[f], A Khan[g], PT Heath[h], A Clark[i], K Orchard[j], JA Snowden[k,l], TI de Silva[m,*]

[a] British Society of Blood and Marrow Transplantation and Cellular Therapy, UK
[b] Paediatric Department, Croydon Health Services NHS Trust, Croydon, UK
[c] University of Newcastle upon Tyne, Newcastle upon Tyne, UK
[d] Department of Clinical Haematology, University of Manchester, Manchester, UK
[e] Institute of Immunology and Immunotherapy, University of Birmingham, Birmingham, UK
[f] Oxford University Hospitals NHS Foundation Trust, Oxford, UK
[g] St. James' Hospital, Leeds, UK
[h] Vaccine Institute, Institute of Infection and Immunity, St. George's, University of London, London, UK
[i] NHS Greater Glasgow and Clyde, Glasgow, UK
[j] Wessex Blood and Marrow Transplant and Cellular Therapy Program, Department of Haematology, University Hospital Southampton NHS Foundation Trust, Southampton, UK
[k] Department of Haematology, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK
[l] Department of Oncology and Metabolism, Medical School, The University of Sheffield, Sheffield, UK
[m] Department of Infection, Immunity and Cardiovascular Disease, Medical School, The University of Sheffield, Sheffield, UK

ARTICLE INFO

Article history:
Accepted 10 November 2022
Available online 15 November 2022

Keywords:
Haematopoietic stem cell transplant
Vaccination
Immunisation

SUMMARY

Haematopoietic stem cell transplant (HSCT) recipients have deficiencies in their adaptive immunity against vaccine preventable diseases. National and International guidance recommends that HSCT recipients are considered 'never vaccinated' and offered a comprehensive course of revaccination. This position statement aims to draw upon the current evidence base and existing guidelines, and align this with national vaccine availability and licensing considerations in order to recommend a pragmatic and standardised re-vaccination schedule for adult and paediatric HSCT recipients in the UK.

Introduction

Within weeks of haematopoietic stem cell transplant (HSCT) there is a decline in antibody titres against vaccine preventable diseases (VPD).[1–9] This immune defect may persist for years post-HSCT in both autologous and allogeneic settings[10] and infections contribute substantially to mortality.[11] HSCT recipients are susceptible to pathogens against which they were vaccinated pre-transplant; and an increased risk of morbidity and mortality from influenza, measles, *Streptococcus pneumoniae, Haemophilus influenzae* type b, and *Bordetella pertussis* is reported.[12–15] National and international groups therefore recommend that HSCT recipients are considered 'never vaccinated' and offered a comprehensive course of re-vaccination aligned with the national vaccination schedule in their country of residence. Recommendations for re-vaccination of HSCT recipients have been published by several societies including the Infectious Diseases Society of America (IDSA), the American Society for Transplantation and Cellular Therapy (ASTCT) and the European Society for Blood and Marrow Transplantation (EBMT).[16–18] Re-vaccination is also addressed by conference publications from the European Conference on Infections in Leukaemia (ECIL) and the Consensus Conference on Clinical Practice in GvHD (CCCPG).[19,20] Paediatric specific recommendations are made by the Children's Cancer and Leukaemia Group (CCLG) and Royal College of Paedi-

* Corresponding author.
E-mail address: t.desilva@sheffield.ac.uk (T. de Silva).

https://doi.org/10.1016/j.jinf.2022.11.005

atrics and Child Health.[21,22] Despite these resources, surveys of HSCT centres in the UK and Ireland over the last two decades have demonstrated both poor vaccine uptake and heterogeneity in all aspects of re-vaccination practice including vaccine selection, initiation and deferral of vaccination, and vaccination of patients with graft-versus-host-disease (GvHD) and/or receiving immunosuppressive therapy (IST).[23–27] A number of factors may contribute to this, including an evidence base insufficient to inform detailed practical guidance, varying recommendations between existing guidelines, and the practical challenges of implementing international recommendations at a national level.

While in the UK a single National Health Service (NHS) schedule details routine vaccination of children and adults, there is no current schedule in place for re-vaccination of adult HSCT recipients, and paediatric schedules require updating.[21,22] The COVID-19 pandemic has highlighted the importance of vaccination strategies specific to immunocompromised patients including HSCT recipients, and as such a review of evidence and harmonized UK recommendations that cover both routine and SARS-CoV-2 vaccinations are timely.[24]

The aim of this statement is to draw upon the current evidence base and existing guidelines, and align this with national vaccine availability and licensing considerations in order to recommend a pragmatic and standardised re-vaccination schedule for adult and paediatric HSCT recipients in the UK. The recommendation of post-HSCT re-vaccination from the HSCT team has been identified as an important cue for patients[28] and these statements and accompanying schedules should offer a valuable tool to facilitate discussion and promote vaccination uptake.

In as far as evidence allows the recommended schedule has been aligned with the National Health Service (NHS) routine vaccination schedule to ensure it is deliverable within the UK. Vaccine trade names and composition are given. If the named vaccine is not available an alternative with the same composition may be administered.

Commencing and deferring re-vaccination

Commencing re-vaccination

VPD including invasive pneumococcal disease (IPD) and influenza may cause morbidity and mortality in patients in the early post-HSCT period.[13,29–31] Conferring immunity through vaccination at the earliest opportunity is therefore imperative. However, the immune impairment that renders patients susceptible to infection in the early to medium post-HSCT period may also limit the immune response to vaccines. An association between a longer time from HSCT and a greater response to vaccination is reported.[32–34] The optimum timepoint for vaccination post HSCT has not been established. The earliest reported responses are to T cell dependant protein-polysaccharide conjugate vaccines which are immunogenic from as early as 3 months post-HSCT. Biomarkers predictive of vaccine response have not been established. A clear association between CD4+, CD8+ and CD19+ lymphocyte counts and the immune response to a range of vaccines has not emerged.[35–39] Current recommendations are for re-vaccination schedules to commence from 3 to 6 months without routine assessment of markers of immune reconstitution. In practice many UK allogeneic HSCT centres vaccinate from one year post-HSCT.[24,38,40,41] In the UK re-vaccination schedules are almost universally administered in primary care rather than in HSCT centres.[24] Given the frequency of HSCT clinic follow-up and in some cases hospital admission in the first 3–6 months, there may be practical limitations on early delivery of re-vaccination in primary care.

(1) *In the absence of contraindications or reasons for deferral, adult and paediatric HSCT recipients should commence re-vaccination at 6 months post-HSCT with consideration given to vaccination from 3 months where practical.*
(2) *In the absence of evidence, the routine use of markers of immune reconstitution to guide timing of re-vaccination is not recommended.*
(3) *Minimum recommended intervals between vaccine doses should be maintained. If practical considerations around vaccine delivery lead to minor extensions in dosing intervals, this is not expected to negatively impact vaccine responses and the course should be continued to completion.*

Deferring re-vaccination

Recommendations and decisions to defer re-vaccination are largely based on expert opinion rather than on evidence. For example, the impact of GvHD on vaccine immunogenicity has been inconsistently reported.[2,32,38,42–45] Given patients with GvHD or receiving immunosuppressive therapy are at increased risk from infection, current guidelines favour commencing re-vaccination rather than deferring. In practice only a minority of UK HSCT centres proceed with re-vaccination if patients have chronic GvHD.[24] In the absence of evidence prescriptive recommendations are not possible, but the following considerations may be applied:

(1) *If a patient has relapsed disease post-HSCT, take into account the prognosis and future therapeutic options when deciding whether to commence re-vaccination or defer vaccination.*
(2) *Where the re-vaccination schedule is interrupted by disease relapse and the patient receives a subsequent second autologous or allogeneic HSCT, the patient should again be considered 'never vaccinated' and the schedule re-started at the appropriate time after the second HSCT rather than resumed.*
(3) *HSCT recipients with mild cGvHD should commence re-vaccination. Consider re-vaccination of patients with moderate or severe cGvHD but take into account intensity and expected duration of cGvHD targeted therapy.*
(4) *HSCT recipients who are receiving low-dose steroid therapy (<0.5 mg/kg prednisolone or equivalent) should commence re-vaccination. When patients are approaching the end of an immunosuppressive treatment weaning schedule, a short deferral period until weaning is complete may be reasonable.*
(5) *For HSCT recipients who remain on high-dose steroid therapy (prednisolone >0.5 mg/kg) or combination therapy beyond 6 months post-HSCT, take into account indication, intensity and expected duration of IST when deciding whether to vaccinate or defer.*
(6) *If donor lymphocyte infusions are being considered or are scheduled, it is reasonable to defer routine re-vaccination until completed. Prioritisation of specific vaccines (e.g. seasonal inactivated influenza vaccine or SARS-CoV-2 vaccine) should be considered in high-risk epidemiological settings.*

Vaccination selection and vaccine schedule

Non-live vaccines

Safety of non-live vaccines

There is no evidence from prospective trials of seasonal influenza and pneumococcal vaccines that adverse events after are more frequent in HSCT recipients than the general population, nor different in nature or severity.[41,46–49] Neither is there evidence for triggering or worsening of GvHD.[35,41] However, regarding SARS-COV-2 vaccines, a prospective study of the Pfizer mRNA BNT162b2 vaccine reported worsening of GvHD in 4.4% of allogeneic HSCT recipients,[50] while a further study reported exacerbation of GvHD in 4.5% of patients after the first vaccine dose. In a study of the Pfizer

mRNA BNT162b and Moderna mRNA-1273 vaccine new cGvHD was reported in 9.7% of patients and worsening of cGvHD in 3.5% of patients. In the specific setting of autoHSCT for autoimmune disease, non-live vaccines are recommended as there are not data suggesting vaccines may trigger disease reactivation.[51] In conclusion non-live vaccines are safe in the HSCT population. HSCT patients are at increased risk of mortality from SARS-CoV-2 infection and benefits of vaccination are considered to outweigh risk.[52,53]

Diphtheria, tetanus, pertussis, polio, Haemophilus influenzae b, Hepatitis B vaccination in the NHS routine schedule

In the NHS routine schedule primary vaccination against diphtheria, tetanus, pertussis, polio, Haemophilus influenzae type b and Hepatitis B (DTaP/IPV/Hib/HepB) is with either of the combination hexavalent vaccines *Infanrix hexa* or *Vaxelis* given as 3 doses at monthly intervals from eight weeks of age. As summarised below either of these vaccines is the pragmatic choice for re-vaccination of HSCT recipients.

Diphtheria, tetanus, pertussis

Current international guidelines recommend 3 doses of a diphtheria-tetanus-pertussis vaccine from 6 months post-HSCT. In HSCT recipients the immunogenicity of a 3-dose schedule of a tetanus toxoid vaccine is superior to a single dose,[1] and is similarly immunogenic whether administered from 6 or 18 months post HSCT.[54] Low-dose pertussis vaccines (2.5–8mcg pertussis toxoid – designated 'p') are poorly immunogenic when used for primary vaccination.[55,56] Similarly, responses to low-dose diphtheria vaccines (2 IU diphtheria toxoid – designated 'd') appear inferior to high-dose vaccines (not less than 30IU diphtheria toxoid – designated 'D') in HSCT recipients. Both *Infanrix hexa* and *Vaxelis* contain high-dose tetanus, diphtheria and pertussis toxoid (DTaP).

Polio

Current guidelines recommend 3 doses of an inactivated polio vaccine (IPV) from 6 months post HSCT. In HSCT recipients a 3 dose schedule of a polio vaccine is more immunogenic than a single vaccine dose[2–4] with equivalent immunogenicity at 6 or 18 months post HSCT.[4]

Haemophilus influenzae type b (Hib)

Current guidelines recommend 3 doses of a Hib-conjugate vaccine from 6 months post-HSCT. A 3-dose schedule of a Hib conjugate vaccine is immunogenic whether administered at 3 or 6 months post-HSCT.[57] Primary Hib vaccination in the NHS routine schedule is with 3 monthly doses of *Infanrix hexa or Vaxelis* and a booster dose (in combination with Meningococcus C conjugate vaccine) at 12 months of age.

Hepatitis B (HepB)

Current recommendations for HepB vaccination vary with some groups advocating vaccination for all HSCT recipients,[16,58] while others recommend vaccination only for recipients seronegative for HepB pre-HSCT or patients who have lost protective immunity post-HSCT.[17,20] A 3-dose schedule of a HepB vaccine has been found to be immunogenic in allogeneic HSCT recipients.[59] HepB is now part of the hexa-valent vaccine administered as part of the routine UK childhood immunisation programme.

Booster doses

There is little evidence to guide administration of booster doses in HSCT recipients. In the NHS routine vaccination schedule a diphtheria-tetanus-pertussis and polio booster is administered after 3 years 4 months of age using either *Repevax* or *Boostrix-IPV* which are both full dose diphtheria and pertussis vaccines (DTaP/IPV). A further diphtheria-tetanus and polio booster is administered at 14 years of age using *Revaxis* which contains low dose diphtheria toxoid (Td/IPV). In the absence of data specific to this population we recommend following the NHS routine vaccination schedule.

(1) *Adult and paediatric recipients of autologous and allogeneic HSCT should receive 3 doses of a DTaP/IPV/Hib/HepB vaccine (Infranrix Hexa or Vaxelis) one month apart, from 6 months post-transplant.*
(2) *In the absence of evidence in the HSCT population it is reasonable to offer adult and paediatric recipients of autologous and allogeneic HSCT a DTaP/IPV booster vaccine (Repevax or Boostrix-IPV) at 3 years post-HSCT, and to offer a Td/IPV booster vaccine (Revaxis) at 14 years post-HSCT following the NHS routine vaccination schedule.*

Neisseria meningitidis (Meningococcus)

The most recent international guidance advocates the administration of meningococcal vaccines from 6 months post-HSCT following country specific recommendations.[20] This reflects variation in national meningococcal vaccine programmes which are adapted to protect against prevalent serogroups. In the NHS routine vaccination schedule infants receive a primary course of Meningococcal B (MenB) conjugate vaccine with Bexsero at 8 and 16 weeks of age as part of the routine vaccination schedule, and then a further booster dose at 1 year. At 1 year of age one dose of Meningococcal C (MenC) conjugate vaccine (Menitorix) is administered and then one dose of Meningococcal ACWY (MenACWY) conjugate vaccine (Nimenrix or Menveo) at 14 years of age. There are currently no data on immunogenicity of MenB vaccines in HSCT recipients. The immunogenicity of a single dose of MenACWY conjugate vaccine is poor in HSCT recipients, but is improved with a second dose administered after approximately 9 months.[44,60,40,48] We recommend following the NHS routine vaccination schedule for the MenB vaccine, but in view of the poor response to a single dose of MenACWY conjugate in HSCT recipients we recommend a modified schedule using two doses. The 8 and 18 months timepoint for the MenACWY has been chose pragmatically to coincide with adminstration of other vaccines.

(1) *Adult and paediatric recipients of autologous and allogeneic HSCT should receive 2 primary doses of a MenB vaccine (Bexsero) at a 2-month interval from 6 months post-HSCT. A booster dose should be administered at 18 months post-HSCT (or 1 year after primary dose 1).*
(2) *Adult and paediatric recipients of autologous and allogeneic HSCT should receive 2 doses of a MenACWY vaccine (Nimenrix or Menveo), the first from 8 months post-HSCT and the second at 18 months post-HSCT (or 10 months after the first dose).*

Streptococcus pneumoniae (Pneumococcus)

All current guidelines recommend a primary 3 dose course given monthly of a pneumococcal conjugate vaccine (PCV) commencing from 3 to 6 months post-HSCT, followed by a booster dose after a further 6 months. The recommended booster is either a further dose of a PCV or a pneumococcal polysaccharide vaccine (PSV) and selection is determined by whether or not the recipient has active GvHD. In the NHS routine vaccination schedule infants receive the 13-valent PCV (PCV13) Prevenar-13 at 12 weeks of age, and a booster dose at 1 year. Patients aged 65 years are offered the 23-valent PSV *Pneumovax*.

Pneumococcal vaccines are the most extensively studied in HSCT recipients. GvHD is a risk factor for loss of immunity to pneumococcus, and patients with GvHD respond poorly to PSV.[61] However, immunogenicity of PCV is superior to PSV in HSCT recipients,[62] and a 3-dose schedule of 7-valent PCV (PCV7) is more immunogenic than 2 doses when administered from 6 to 9 months

post allogeneic HSCT.[49] Immunogenicity assessed 1 month after a 3-dose PCV7 regimen was equivalent whether administered from 3 or 9 months post-HSCT. In this study participants went on to receive a 23-valent PSV (PSV23) booster approximately 6 months after completion of the primary course. Of patients who did not respond to the primary course, almost half responded 1 month after the PSV23 booster. It is important to note that durability of response assessed at 24 months was inferior in the early 3-month group.[38] A follow-on study demonstrated that serotype coverage may be broadened beyond the serotypes included in PCV7 by administration of PSV23.[43] In a study of PCV13, a fourth PCV booster dose administered 6 months after the primary course may boost waning immune response but at the expense of increased rate of local and systemic reactions.[41]

In view of the evidence favoring a 3-dose primary PCV schedule followed by a booster we recommend a modification of the NHS routine vaccination schedule. The 18-month booster time point has been chosen pragmatically to coincide with administration of other vaccines.

(1) *Adult and paediatric recipients of autologous and allogeneic HSCT should receive 3 primary doses of PCV13 (Prevenar 13) from 6 months post-HSCT. Consideration can be given to commencing vaccination from 3 months.*
(2) *A booster dose should be given at 18 months post-HSCT (10 months after last primary dose) with either PCV13 if the recipient has active GvHD, or PSV23 (Pneumovax) if they do not have GvHD.*

Human papillomavirus (HPV)

Current guidelines recommend HPV vaccination from 6 to 12 months post-HSCT following national recommendations.[20] In the NHS routine vaccination schedule all children aged 12–13 years of age are offered 2 doses of the quadrivalent HPV vaccine *Gardasil* administered 6–24 months apart. Where vaccination was missed or the schedule incomplete, patients remain eligible up to 25 years of age. A 3 dose schedule is recommended for immunocompromised patients with 2 doses at a monthly interval and then a third dose 4–6 after the first dose.[63] In the UK HPV infection is very rare before 14 years of age. Prevalence of high-risk HPV (type 16 and 18) which is associated with development of cervical cancer peaks at 40% at age 20–24 years but women remain at risk into their 60 s with a reported prevalence of 6%.[64] In HSCT recipients the cumulative incidence of genital HPV infection is reported at 40.1% at 20 years post-HSCT, with incidence of 67.1% in patient with cGvHD.[65] cGvHD is also a risk factor for development of HPV associated tumours.[66] Three doses of Gardasil were immunogenic in female HSCT recipients aged 18–49. Patients were vaccinated regardless of HPV history and pre-HSCT HPV vaccination, but patients with active HPV disease were excluded.[67] Vaccination may protect against infection with new HPV types in patients previously infected.

In view of national recommendations for immunocompromised patients and the above data, we recommend that all HSCT recipients aged 12 or over are offered 3 doses of HPV vaccine. Pragmatically in order to limit the number of vaccinations given at any one time point to a maximum of 4, we recommend commencing paediatric HPV vaccination from 6 months post-HSCT, and adult HPV vaccination from 18 months. However, consideration can be given to earlier HPV vaccination in selected adult patients considered at higher risk of HPV in the first 18 months post HSCT.

(1) *All HSCT recipients aged 12 or over should be offered a primary course of 3 doses of a quadrivalent HPV (Gardasil). For adults a pragmatic 18, 19 and 24 months post-HSCT schedule is recommended. Paediatric vaccination is recommended at 6,7 and 12 months.*

Seasonal inactivated influenza vaccine (SIIV)

The NHS offers the SIIV annually to high-risk individuals. The live attenuated influenza vaccine (LAIV) is contraindicated in the immunocompromised patients and should not be given to HSCT recipients of any age.[68]

In HSCT populations the SIIV is minimally immunogenic before 6 months and responses are impaired until at least 12 months.[32,34,37,69] However, the seasonal pattern of influenza means that delaying SIIV administration to 12 months or beyond HSCT leaves patients at risk of influenza related morbidity and mortality; patients transplanted during the influenza season are at highest risk of infection, with progression to pneumonia occurring more frequently in the early post-HSCT period and associated with a 30-day mortality rate of up to 28%.[30,70] In the absence of alternative evidence-based strategies, current guidelines recommend annual administration of the SIIV from 6 months post autologous and allogeneic HSCT.

(1) *Adult and paediatric recipients of autologous and allogeneic HSCT should receive one dose of the SIIV annually from 6 months post-HSCT. Consider giving SIIV from 3 months post-HSCT if within a peak influenza transmission period.*
(2) *LAIV should not be administered to HSCT recipients of any age and should not be administered to household contacts of HSCT recipients who should be advised to receive the SIIV.*

SARS-CoV-2

HSCT recipients are in a COVID-19 high-risk group and conferring immunity by vaccination at the earliest effective timepoint is desirable. There are emerging data on the immunogenicity of SARS-CoV-2 vaccines in HSCT recipients, mostly to the Pfizer mRNA BNT162b2 vaccine. Seroconversion following two doses of Pfizer vaccine has been shown to occur in 50 – 84.7% of allogeneic HSCT recipients and 60 – 84% of autologous HSCT recipients,[50,71–74] which was significantly lower than in healthy control participants when included.[50] Similar antibody titres between autologous and allogeneic HSCT recipients have been noted.[75] Several studies have also observed lower antibody induction in individuals within the first 12 months following HSCT and HSCT recipients should receive a 3-dose primary course.[50,72,73] The Green Book recommends that HSCT recipients who were vaccinated pre-HSCT are considered for re-vaccination post-HSCT with a 3-dose primary course and 4th dose as a booster. The optimum SARS-CoV-2 vaccination strategy following HSCT is an active and evolving area of research. Updated position statements on post-HSCT SARS-CoV-2 vaccination are available on the BSBMTCT website (https://bsbmtct.org/bsbmtct-and-covid/). A paediatric formulation of the Pfizer-BioNTech vaccine has been licensed for children aged 5–11.

(1) *Adult recipients of autologous and allogeneic HSCT aged 18 or more should receive a 3-dose primary course of SARS-CoV-2 vaccine from 3 – 6 months following HSCT. The first two doses should be administered at the minimum licensed interval (*e.g. *3 weeks for Pfizer BNT162b2 and Novavax NVX-CoV2373 and 4 weeks for AstraZeneca ChAdOX1-S and Moderna mRNA 1273 vaccines). The 3rd primary dose should be administered at a minimum interval of 8 weeks later, followed by a booster 4th dose no sooner than 3 months after the 3rd dose, both with SARS-CoV-2 mRNA vaccines. If mRNA vaccination is clinically contraindicated, then NVX-CoV-2373 can be used instead for primary and/or booster doses.*
(2) *Following this re-vaccination schedule, recommendations for additional boosters in adult HSCT recipients should follow current national recommendations, including the use of novel multi-valent vaccines.*
(3) *Paediatric recipients of autologous and allogeneic HSCT aged 12 and over should receive a 3-dose primary course of an mRNA SARS-CoV-2 vaccine from 3 – 6 months following HSCT. If mRNA*

vaccines are clinically contraindicated then NVX-CoV-2373 may be used instead.

(4) *Paediatric recipients of autologous and allogeneic HSCT aged 5–11 years should receive a 2-dose primary course of the Pfizer BioNTech paediatric dose mRNA SARS-CoV-2 vaccine from 3 – 6 months following HSCT.*

(5) *Following this revaccination schedule, recommendations for additional boosters in paediatric HSCT recipients should follow national recommendations, including the use of novel multi-valent vaccines.*

Varicella zoster virus (VZV)

The risk of Herpes zoster reactivation increases following HSCT.[59,60] Antiviral prophylaxis is given to reduce this risk, but the required duration of prophylaxis is unclear and the risk of reactivation increases following cessation of antivirals in many individuals. A recombinant zoster vaccine Shingrix is now available which contains the varicella zoster virus glycoprotein E antigen adjuvanted with the $ASO1_B$ system. It is licensed for use in those aged 18 or over. In a phase 3 clinical trial in autologous HSCT recipients aged 18 years or more, two doses of Shingrix given 1 – 2 months apart as early as 50–70 days following HSCT had 68.2% efficacy against the incidence of herpes zoster over a median follow-up of 21 months.[76] Recommendations for use in the UK as detailed in the Green Book are as part of the National Programme in adults aged 70–79 years old. Given the high risk of zoster reactivation in the first 2 – 3 years after HSCT and contraindication to live varicella vaccines until 24 months (see section on live vaccines below), we recommend that all adult HSCT recipients should receive 2 doses of Shingrix at least 2 months apart. Patients who receive Shingrix should have VZV serology performed at 24 months and if antibody negative receive 2 doses of live VZV (Varivax or Varilrix) providing all criteria for administration of live vaccines are met. For paediatric HSCT recipients in whom the vaccine is not licensed, and for adults in whom the recombinant zoster vaccine is contraindicated, see VZV under live vaccines.

(1) *Adult recipients of autologous and allogeneic HSCT aged 18 years or more should receive 2 doses of Shingrix at least 2 months apart, commencing at 6 months following HSCT.*

(2) *VZV serology should be performed at 24 months and if antibody negative then administration of a live attenuated varicella vaccines (LAVV) Varivax or Varilrix should be considered as per VZV section under live vaccines.*

Live vaccines

Live vaccines are contraindicated in patients with certain primary or acquired immunodeficiencies or receiving immunosuppressive medications. These are outlined in detail in chapter 6 of the UK Health Security Agency (UKHSA) Green Book.[77] All current guidelines recommend delay of live vaccines in HSCT recipients until specific criteria are met. Considering the consensus across the guidelines and also the UKHSA Green Book we recommend the following minimum criteria for administration of live vaccines.

(1) *Live vaccines should not be administered to adult or paediatric recipients of autologous or allogeneic HSCT unless all of the following criteria are met: (i) 24 months post HSCT; (ii) No active GvHD; (iii) Remain in remission from underlying disease; (iv) No systemic immunosuppressive therapy for 12 months including monoclonal antibodies; (v) No intravenous immunoglobulin (IVIg) in last 3 months. Many autologous HSCT recipients, such as those with myeloma, may remain on long-term maintenance chemotherapy and live vaccines will be contraindicated long-term.*

(2) *If patients meet the criteria above but remain on post-HSCT therapy targeted at underlying disease, the safety of administration of live vaccines must be considered with reference to the Green Book and relevant summary of product characteristics.*

(3) *The Green Book Chapter 11: The UK Immunisation Schedule should be consulted for current guidance on time interval between administration of live vaccines.*[78]

Measles-mumps-rubella (MMR)

Current guidelines recommend administration of an MMR vaccine from 24 months post-HSCT in measles seronegative patients who meet criteria for administration of live vaccines. We do not consider evaluation of measles serostatus mandatory for paediatric patients, and lack of access to serological testing should not restrict vaccination in adult patients. In the NHS routine vaccination schedule, primary immunisation is with either *VaxPRO* or *Priorix* at 1 year of age, and a booster dose is administered from 3 years 4 months of age. Loss of MMR seropositivity is well documented post-HSCT.[7–9] Two doses of MMR vaccine administered 6 months apart are immunogenic from 12 to 24 months post-HSCT.[79–81]

(1) *Adult recipients of autologous and allogeneic HSCT who are 24 months post procedure, have no active GvHD, have not received systemic IST for 12 months, meet all other criteria for administration of live vaccines, and are measles seronegative should receive 2 primary doses of an MMR vaccines (MMR VaxPro or Priorix) administered 6 months apart. Lack of access to serological testing should not preclude vaccination as long as other criteria are met.*

(2) *Paediatric recipients of autologous and allogeneic HSCT who are 24 months post procedure, have no active GvHD, have not received systemic IST for 12 months, meet all other criteria for administration of live vaccines, should receive 2 primary doses of an MMR vaccines (MMR VaxPro or Priorix) administered 6 months apart. In the setting of a community measles outbreak consider vaccination of paediatric HSCT recipients who are at least 18 months post-HSCT but meet all other criteria.*

Varicella zoster virus (VZV)

Live attenuated Varicella vaccines are administered for two purposes: (i) to reduce the risk of primary infection in seronegative patients; (ii) to reduce risk of reactivation (shingles) in previously infected patients. Low-titre ($\geq$1350 PFU) live attenuated varicella vaccines (LAVV) are indicated for the former, and high-titre (19,400 PFU) live attenuated zoster vaccines (LAZV) for the latter.

The LAVV is not yet part of the NHS childhood routine vaccination schedule but is recommended for non-immune healthcare workers and close contacts of immunocompromised individuals. However, the LAZV Zostavax is routinely administered on the NHS routine vaccination schedule from the age of 70. Given the high viral titre and absence of safety data LAZVs are not recommended for HSCT recipients at any stage post-HSCT. Current guidelines recommend consideration of LAVV in HSCT recipients who are varicella seronegative and meet the criteria for administration of live vaccines.

Data on LAVV in HSCT recipients are limited. Retrospective studies report seroconversion rates of 35–65% after a single LAVV dose in VZV seronegative paediatric patients who were more than 24 months post auto or allogeneic HSCT. Up to 71% of non-responders seroconverted after 2nd or 3rd doses [82,83]. Similar high seroconversion rates were seen in a small prospective study of seronegative paediatric patients[84]. Immunogenicity of two LAVV doses administered 8 weeks apart to VZV seropositive adults within 6 months of autologous HSCT was poor. In these studies small numbers of patients developed possible varicella rash but there were no serious safety concerns. VZV serology should be performed in all patients (including adult patients who received Shingrix at 6 months) and those patients who are antibody negative should receive 2 doses of LAVV (Varivax or Varilrix) providing all criteria for live vaccines are met.

(1) *For paediatric recipients of autologous and allogeneic HSCT who are 24 months post procedure, have no active GvHD, have not received systemic IST for 12 months, meet all other criteria for administration of live vaccines and are VZV seronegative, consider 2 doses of LAVV (Varivax or Varilrix) administered 2 months apart.*
(2) *VZV serology should be performed for all adult recipients of autologous and allogeneic HSCT (including those who received Shingrix) at 24 months and for those who are VZV seronegative, have no active GvHD, have not received systemic IST for 12 months, meet all other criteria for administration of live vaccines, consider 2 doses of LAVV (Varivax or Varilrix) administered 2 months apart.*
(3) *Live attenuated Zoster Vaccines (*e.g. *Zostavax) are contraindicated in HSCT recipients and should not be administered.*

Rotavirus vaccine

The rotavirus vaccine is administered as part of the NHS routine vaccination schedule to infants at eight weeks of age. The rotavirus vaccine may cause severe diarrhoea in immunocompromised patients, and disease incidence is lower after infancy (and the incidence of temporal vaccine linked intussusception increases after infancy) so it is not recommended in HSCT recipients.[85]

Non-routine vaccines

BCG (Bacillus Calmette-Guerin) vaccine

The BCG vaccine is not administered as part of the NHS routine vaccination schedule. However, it is given on the NHS to children and adults considered at increased risk of coming into contact with TB either through area of residence, country of origin, or occupational exposure. There is little data on the safety of BCG vaccines in HSCT recipients and current international guidance is that the vaccine is contraindicated in HSCT recipients and therefore administration is not recommended.

Travel vaccines

HSCT recipients travelling to regions of endemic disease should undergo a risk assessment at a specialist travel clinic. Consideration must be given as to whether vaccines are live attenuated or inactivated with the former generally considered contraindicated in HSCT recipients. There are no data on safety, immunogenicity or efficacy of vaccines against Japanese enchephalitis, rabies, typhoid and cholera. A small number of carefully selected HSCT recipients have received live attenuated yellow fever vaccine without adverse events.[86–88]

Assessing response to vaccines in HSCT recipients

Serological assessment may be undertaken to evaluate response to an initial vaccine course, or for monitoring long-term durability of response. In the absence of evidence to guide assessment of response to vaccines in HSCT recipients, recommendations across current guidelines vary. The IDSA recommends routine assessment of HepB Ab titres post-vaccination. The CCCPG suggests serological testing should be considered post primary vaccine and booster dosing in patients with cGvHD. ASBMT guidelines advocate assessing response to pneumococcal and HepB vaccines, as well as routine long-term monitoring every 4 to 5 years for HepB, measles, tetanus, diphtheria and polio. ECIL guidelines suggest assessment of response to pneumococcal vaccine at 2 years post vaccination, and long-term monitoring of Hib every 5–10 years and DTP every 3–5 years. No groups give recommendations around repeating vaccine doses.

(1) *Routine assessment of vaccine response in HSCT recipients is not recommended. Response assessment may be considered if patients have risk factors for poor response such as cGvHD or long-term immunosuppressive therapy.*
(2) *Scheduled booster doses for DTP and polio are recommended in keeping with the NHS routine vaccination schedule (see section non-live vaccines) and therefore routine long-term monitoring is not recommended.*
(3) *Assessment of response may be considered at any post-vaccination time point in clinical contexts such as breakthrough infections with VPDs, recurrent infections, or other clinical concerns about immune deficiency. However, in the absence of evidence, decisions regarding vaccine booster doses or repeating primary re-vaccination courses must be made on a case-by-case basis.*

Vaccination of household members and close contacts

Adult and paediatric household members and close contacts of HSCT recipient should be vaccinated in accordance with the NHS routine vaccination schedule with the following caveats.

(1) *Household members and close contacts should receive the SIIV annually. Given the theoretical risk of transmission of live attenuated virus, the LAIV should not be administered to household members and close contacts of HSCT recipients who are within 2 months of transplant or have active GvHD.*
(2) *Given the theoretical risk of transmission of live attenuated virus, If an infant household member or close contact receives the rotavirus vaccine, HSCT recipients who are within 2 months of transplant or have active GvHD should avoid contact with the infant's stool for 4 weeks.*
(3) *Household members of adult and paediatric HSCT recipients should be offered SARS-CoV-2 vaccination in keeping with current Greenbook guidance on SARS-CoV-2 vaccination in household contacts of immunosuppressed individuals.*

Quality assurance and audit

In accordance with European Society of Blood and Marrow Transplant (EBMT) – Joint Accreditation Committee (JACIE) standards[89] all units should maintain local Standard Operating Procedures (SOP) for vaccination of HSCT recipients and auditable records of vaccine administration for quality assurance purposes. When re-vaccination is commenced, general practitioners should be provided with a copy of the re-vaccination schedules for paediatrics (Appendix 1) or Adults (Appendix 2) to ensure appropriate vaccine selection and timing of administration. HSCT recipients should be encouraged to hold a vaccine record that is completed by the healthcare practitioner administering each vaccine. The schedules in Appendix 1 and 2 may serve this purpose, or the post-HSCT vaccination record produced by Anthony Nolan may be used for this purpose.

Audit standards

Percentage of HSCT recipients commencing routine re-vaccination at 6 months post-HSCT or for whom a documented decision has been made by an HSCT physician to defer re-vaccination: target 100%

Percentage of HSCT recipients who by 24 months post-HSCT have received all recommended non-live vaccines, or for whom a documented decision has been made by an HSCT physician to defer re-vaccination: target 100%

Percentage of HSCT recipients receiving a live vaccine who do not meet all criteria for administration of live vaccines: target 0%

Contributions

PM, SP, RS, FD, AR, pH, JS, TdS all attended develop meetings.

PM, SP, RS, FD, AR, AK, pH, KO, JS, TdS all contributed substantially to develop and review of guidelines and approved final document.

PM, SP, RS, FD, AR, AK, pH, AC, KO, JS, KJ, TdS all contributed substantially to review and approval of final document.

Declaration of Competing Interest

JS – Honoraria for educational events from Jazz, Gilead, Janssen. Advisory board membership from Medac, and trial IDMC membership from Kiadis Pharma.

Other authors have no conflicts of interest to declare.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jinf.2022.11.005.

References

1. Ljungman P, Wiklund-Hammarsten M, Duraj V, Hammarstrom L, Lonnqvist B, Paulin T, et al. Response to tetanus toxoid immunization after allogeneic bone marrow transplantation. *J Infect Dis* 1990;**162**:496–500.
2. Ljungman P, Duraj V, Magnius L. Response to immunization against polio after allogeneic marrow transplantation. *Bone Marrow Transpl* 1991;**7**:89–93.
3. Engelhard D, Handsher R, Naparstek E, Hardan I, Strauss N, Aker M, et al. Immune response to polio vaccination in bone marrow transplant recipients. *Bone Marrow Transpl* 1991;**8**:295–300.
4. Parkkali T, Stenvik M, Ruutu T, Hovi T, Volin L, Ruutu P. Randomized comparison of early and late vaccination with inactivated poliovirus vaccine after allogeneic BMT. *Bone Marrow Transpl* 1997;**20**:663–8.
5. Winston DJ, Ho WG, Schiffman G, Champlin RE, Feig SA, Gale RP. Pneumococcal vaccination of recipients of bone marrow transplants. *Arch Intern Med* 1983;**143**:1735–7.
6. Giebink GS, Warkentin PI, Ramsay NK, Kersey JH. Titers of antibody to pneumococci in allogeneic bone marrow transplant recipients before and after vaccination with pneumococcal vaccine. *J Infect Dis* 1986;**154**:590–6.
7. Ljungman P, Lewensohn-fuchs I, Hammarstrom V, Aschan J, Brandt L, Bolme P, et al. Long-term immunity to measles, mumps, and rubella after allogeneic bone marrow transplantation. *Blood* 1994;**84**:657–63.
8. Pauksen K, Duraj V, Ljungman P, Sjolin J, Oberg G, Lonnerholm G, et al. Immunity to and immunization against measles, rubella and mumps in patients after autologous bone marrow transplantation. *Bone Marrow Transplant* 1992;**9**:427–32.
9. Ljungman P, Fridell E, Lonnqvist B, Bolme P, Bottiger M, Gahrton G, et al. Efficacy and safety of vaccination of marrow transplant recipients with a live attenuated measles, mumps, and rubella vaccine. *J Infect Dis* 1989;**159**:610–15.
10. Colton H, Greenfield DM, Snowden JA, Miller PDE, Morley NJ, Wright J, et al. Long-term survivors following autologous haematopoetic stem cell transplantation have significant defects in their humoral immunity against vaccine preventable diseases, years on from transplant. *Vaccine* 2021;**39**:4778–83.
11. Styczyński J, Tridello G, Koster L, Iacobelli S, Biezen van A, Werf van der S, et al. Death after hematopoietic stem cell transplantation: changes over calendar year time, infections and associated factors. *Bone Marrow Transplant* 2020;**55**:126–36.
12. Ljungman P, Camara R de L, Perez-Bercoff L, Abecasis M, Campuzano JBN, Cannata-Ortiz MJ, et al. Outcome of pandemic H1N1 infections in hematopoietic stem cell transplant recipients. *Haematologica* 2011;**96**:1231–5.
13. Kumar D, Humar A, Plevneshi A, Siegal D, Franke N, Green K, et al. Invasive pneumococcal disease in adult hematopoietic stem cell transplant recipients: a decade of prospective population-based surveillance. *Bone Marrow Transplant* 2008;**41**:743–7.
14. Kochethu G, Clark FJ, Craddock CF. Pertussis: should we vaccinate post transplant? *Bone Marrow Transplant* 2006;**37**:793–4.
15. Lossos IS, Breuer R, Or R, Strauss N, Elishoov H, Naparstek E, et al. Bacterial pneumonia in recipients of bone marrow transplantation. *Transplantation* 1995;**60**:672–8.
16. Rubin LG, Levin MJ, Ljungman P, Davies EG, Avery R, Tomblyn M, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clin Infect Dis* 2014;**58**:1–57.
17. Tomblyn M, Chiller T, Einsele H, Gress R, Sepkowitz K, Storek J, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. Preface. *Bone Marrow Transplant* 2009;**15**:1143–238.
18. Ljungman P, Cordonnier C, Einsele H, Englund J, Machado CM, Storek J, et al. Vaccination of hematopoietic cell transplant recipients. *Bone Marrow Transplant* 2009;**44**:521–6.
19. Hilgendorf I, Wolff D, Meisel R. Vaccination of allogeneic haematopoietic stem cell transplant recipients: report from the International consensus conference on clinical practice in chronic GVHD. *Vaccine* 2011;**29**:2825–33.
20. Cordonnier C, Einarsdottir S, Cesaro S, Blasi RD, Mikulska M, Rieger C, et al. Vaccination of haemopoietic stem cell transplant recipients: guidelines of the 2017 European conference on infections in Leukaemia (ECIL 7). *Lancet Infect Dis* 2019;**19**:e200–12.
21. Patel S.R., Skinner R., Heath P. Vaccinations for paediatric patients treated with standard-dose chemotherapy and haematopoietic stem cell transplantation (HSCT) recipients.
22. Health RC of P and C. Immunisation of the immunocompromised child. 2002.
23. Gilleece M, Towlson K, Wilson M, Littlewood T, Cook G, Marks D. Vaccination against Infection after Haematopoietic stem cell transplant : a survey of practice in the UK and Ireland. *BBMT* 2007;**21**:S614–708.
24. Miller PDE, de Silva TI, Skinner R, Gilleece M, Peniket A, Hamblin A, et al. Routine vaccination practice after adult and paediatric allogeneic haematopoietic stem cell transplant: a survey of UK NHS programmes. *Bone Marrow Transplant* 2017;**52**:775–7.
25. Dignan FL, Hamblin A, Chong A, Lee J, Kenyon M, Miller P, et al. Survivorship care for allogeneic transplant patients in the UK NHS: changes centre practice, impact of health service policy and JACIE accreditation over 5 years. *Bone Marrow Transplant* 2021;**56**:673–8.
26. Bate J, Patel SR, Chisholm J, Heath PT. CCLG) SCG of the CC and LG. Immunisation practices of paediatric oncology and shared care oncology consultants: a United Kingdom survey. *Pediatr Blood Cancer* 2010;**54**:941–6.
27. Meiring J, Silva de T, Snowden JA. A study of adherence to a vaccination schedule following adult allogeneic haematopoietic stem cell transplants in UK. *Bone Marrow Transplant* 2015:203–4.
28. Miller PDE, Forster AS, de Silva TI, Leonard H, Anthias C, Mayhew M, et al. Sociodemographic and psychological determinants of influenza vaccine intention among recipients of autologous and allogeneic haematopoietic stem cell transplant: a cross-sectional survey of UK transplant recipients using a modified health belief model. *BMJ Open* 2018;**8**:e021222.
29. Hassan IA, Chopra R, Swindell R, Mutton KJ. Respiratory viral infections after bone marrow/peripheral stem-cell transplantation: the Christie hospital experience. *Bone Marrow Transplant* 2003;**32**:73–7.
30. Nichols WG, Guthrie KA, Corey L, Boeckh M. Influenza infections after hematopoietic stem cell transplantation : risk factors, mortality, and the effect of antiviral therapy. *Clin Infect Dis* 2004;**39**:1300–6.
31. Engelhard D, Cordonnier C, Shaw PJ, Parkalli T, Guenther C, Martino R, et al. Early and late invasive pneumococcal infection following stem cell transplantation: a European bone marrow transplantation survey. *Br J Haematol* 2002;**117**:444–50.
32. Engelhard D, Nagler A, Hardan I, Morag A, Aker M, Baciu H, et al. Antibody response to a two-dose regimen of influenza vaccine in allogeneic T cell-depleted and autologous BMT recipients. *Bone Marrow Transplant* 1993;**11**:1–5.
33. Natori Y., Humar A., Lipton J., Kim D., Hoschler K., Ashton P. et al. A pilot randomized controlled trial of Adjuvanted vs. Nonadjuvanted influenza vaccine in adult allogeneic hematopoietic stem cell transplant recipients. In: IDWeek. New Orleans, 2016.
34. Karras N, Weeres M, Sessions W, Xu X, DeFor TE, Young JAAH, et al. A randomized trial of one versus two doses of influenza vaccine after allogeneic transplantation. *Biol Blood Marrow Transplant* 2013;**19**:109–16.
35. Engelhard D, Zakay-Rones Z, Shapira MY, Resnick I, Averbuch D, Grisariu S, et al. The humoral immune response of hematopoietic stem cell transplantation recipients to AS03-adjuvanted A/California/7/2009 (H1N1)v-like virus vaccine during the 2009 pandemic. *Vaccine* 2011;**29**:1777–82.
36. Karras N, Weeres M, Sessions W, Xu X, DeFor TE, Young J-AH, et al. A randomized trial of one Vs. Two doses of influenza vaccine following allogeneic transplantation. *Biol Blood Marrow Transplant* 2013;**19**:109–16.
37. Miller PDE, Silva de T, Leonard H, Anthias C, Hoschler K, Goddard K, et al. A comparison of viral microneutralization and haemagglutination inhibition assays as measures of seasonal inactivated influenza vaccine immunogenicity in the first year after reduced intensity conditioning, lymphocyte depleted allogeneic haematopoietic stem cell transplant. *Vaccine* 2019;**37**:452–7.
38. Cordonnier C, Labopin M, Chesnel V, Ribaud P, Camara RDL, Martino R, et al. Randomized study of early versus late immunization with pneumococcal conjugate vaccine after allogeneic stem cell transplantation. *Clin Infect Dis* 2009;**48**:1392–401.
39. Boles EE, Chiuzan C, Ragucci D, Hudspeth MP. Analysis of factors affecting immune recovery and initial response to tetanus after DTaP vaccination in pediatric allogeneic HSCT patients. *Pediatr Transplant* 2014;**18**:882–8.
40. Parkkali T, Kayhty H, Ruutu T, Volin L, Eskola J, Ruutu P. A comparison of early and late vaccination with Haemophilus influenzae type b conjugate and pneumococcal polysaccharide vaccines after allogeneic BMT. *Bone Marrow Transplant* 1996;**18**:961–7.
41. Cordonnier C, Ljungman P, Juergens C, Maertens J, Selleslag D, Sundaraiyer V, et al. Immunogenicity, safety, and tolerability of 13-valent pneumococcal conjugate vaccine followed by 23-valent pneumococcal polysaccharide vaccine in recipients of allogeneic hematopoietic stem cell transplant aged =2 years: an open-label study. *Clin Infect Dis* 2015;**61**:313–23.
42. Parkkali T, Kayhty H, Hovi T, Olander R-M, Roivainen M, Volin L, et al. A randomized study on donor immunization with tetanus-diphtheria, Haemophilus influenzae type b and inactivated poliovirus vaccines to improve the recipient responses to the same vaccines after allogeneic bone marrow transplantation. *Bone Marrow Transplant* 2007;**39**:179–88.
43. Cordonnier C, Labopin M, Chesnel V, Ribaud P, Camara RDL, Martino R, et al. Immune response to the 23-valent polysaccharide pneumococcal vaccine after the 7-valent conjugate vaccine in allogeneic stem cell transplant recipients: results from the EBMT IDWP01 trial. *Vaccine* 2010;**28**:2730–4.

44. Mahler MB, Taur Y, Jean R, Kernan NA, Prockop SE, Small TN. Safety and immunogenicity of the tetravelent protein-conjugated meningococcal vaccine (MCV4) in recipients of related and unrelated allogeneic stem cell transplantation (alloHSCT). *Biol Blood Marrow Transplant* 2012;**18**:145–9.
45. Barra a, Cordonnier C, Preziosi MP, Intrator L, Hessel L, Fritzell B, et al. Immunogenicity of Haemophilus influenzae type b conjugate vaccine in allogeneic bone marrow recipients. *J Infect Dis* 1992;**166**:1021–8.
46. Avetisyan G, Aschan J, Hassan M, Ljungman P. Evaluation of immune responses to seasonal influenza vaccination in healthy volunteers and in patients after stem cell transplantation. *Transplantation* 2008;**86**:257–63.
47. Mohty B, Bel M, Vukicevic M, Nagy M, Levrat E, Meier S, et al. Graft-versus-host disease is the major determinant of humoral responses to the AS03-adjuvanted influenza A/09/H1N1 vaccine in allogeneic hematopoietic stem cell transplant recipients. *Haematologica* 2011;**96**:896–904.
48. Lavallade de H, Garland P, Sekine T, Hoschler K, Marin D, Stringaris K, et al. Repeated vaccination is required to optimize seroprotection against H1N1 in the immunocompromised host. *Haematologica* 2011;**96**:307–14.
49. Meisel R, Kuypers L, Dirksen U, Schubert R, Gruhn B, Strauss G, et al. Pneumococcal conjugate vaccine provides early protective antibody responses in children after related and unrelated allogeneic hematopoietic stem cell transplantation. *Blood* 2007;**109**:2322–6.
50. Bergman P, Blennow O, Hansson L, Mielke S, Nowak P, Chen P, et al. Safety and efficacy of the mRNA BNT162b2 vaccine against SARS-CoV-2 in five groups of immunocompromised patients and healthy controls in a prospective open-label clinical trial. *EBioMedicine* 2021;**74**:103705.
51. Sharrack B, Saccardi R, Alexander T, Badoglio M, Burman J, Farge D, et al. Autologous haematopoietic stem cell transplantation and other cellular therapy in multiple sclerosis and immune-mediated neurological diseases: updated guidelines and recommendations from the EBMT autoimmune diseases working party (ADWP) and the joint accreditation committee of EBMT and ISCT (JACIE). *Bone Marrow Transplant* 2020;**55**:283–306.
52. Malard F, Genthon A, Brissot E, van de Wyngaert Z, Marjanovic Z, Ikhlef S, et al. COVID-19 outcomes in patients with hematologic disease. *Bone Marrow Transplant* 2020;**55**:2180–4.
53. Kanellopoulos A, Ahmed MZ, Kishore B, Lovell R, Horgan C, Paneesha S, et al. COVID-19 in bone marrow transplant recipients: reflecting on a single centre experience. *Br J Haematol* 2020;**190**:e67–70.
54. Parkkali T, Olander RM, Ruutu T, Vuontela K, Volin L, Eskola J, et al. A randomized comparison between early and late vaccination with tetanus toxoid vaccine after allogeneic BMT. *Bone Marrow Transplant* 1997;**19**:933–8.
55. Papadopoulos EB, Young JW, Kernan NA, Boulad F, Castro-Malaspina HR, O'Reilly RJ, et al. Use of the tetanus toxoid, reduced dose diphtheria and pertussis vaccine (Tdap) in allogeneic transplant (alloHCT) recipients. *Blood* 2008;**112**:2214 –2214.
56. Small TN, Zelenetz AD, Noy A, Rice RD, Trippett TM, Abrey L, et al. Pertussis immunity and response to tetanus-reduced diphtheria-reduced pertussis vaccine (Tdap) after autologous peripheral blood stem cell transplantation. *Biol Blood Marrow Transplant* 2009;**15**:1538–42.
57. Vance E, George S, Guinan EC, Wheeler C, Antin JH, Ambrosino DM, et al. Comparison of multiple immunization schedules for Haemophilus influenzae type b-conjugate and tetanus toxoid vaccines following bone marrow transplantation. *Bone Marrow Transplant* 1998;**22**:735–41.
58. Royal College of Physician of Ireland, Immunisation guidelines for Ireland 2013. 2013.http://www.hse.ie/eng/health/immunisation/hcpinfo/guidelines/.
59. Jaffe D, Papadopoulos EB, Young JW, O'Reilly RJ, Prockop S, Kernan NA, et al. Immunogenicity of recombinant hepatitis B vaccine (rHBV) in recipients of unrelated or related allogeneic hematopoietic cell (HC) transplants. *Blood* 2006;**108**:2470–5.
60. Cheng MP, Pandit A, Antin JH, Walsh SR, Huynh D, Ghobrial IM, et al. Safety and immunogenicity of conjugate quadrivalent meningococcal vaccination after hematopoietic cell transplantation. *Blood Adv* 2018;**2**:1272–6.
61. Hammarstrom V, Pauksen K, Azinge J, Oberg G, Ljungman P. Pneumococcal immunity and response to immunization with pneumococcal vaccine in bone marrow transplant patients: the influence of graft versus host reaction. *Support Care Cancer* 1993;**1**:195–9.
62. Kumar D, Chen MH, Welsh B, Siegal D, Cobos I, Messner H a, et al. A randomized, double-blind trial of pneumococcal vaccination in adult allogeneic stem cell transplant donors and recipients. *Clin Infect Dis* 2007;**45**:1576–82.
63. PublicHealth England, Green Book Human Papillomavirus chapter 18a, PublicHealth England. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1065283/HPV-greenbook-chapter-18a.pdf (accessed 8 May2022).
64. Kitchener HC, Almonte M, Wheeler P, Desai M, Gilham C, Bailey A, et al. HPV testing in routine cervical screening: cross sectional data from the ARTISTIC trial. *Br J Cancer* 2006;**95**:56–61.
65. Shanis D, Anandi P, Grant C, Bachi A, Vyas N, Merideth MA, et al. Risks factors and timing of genital human papillomavirus (HPV) infection in female stem cell transplant survivors: a longitudinal study. *Bone Marrow Transplant* 2018;**53**:78–83.
66. Savani BN, Stratton P, Shenoy A, Kozanas E, Goodman S, Barrett AJ. Increased risk of cervical dysplasia in long-term survivors of allogeneic stem cell transplantation—implications for screening and HPV vaccination. *Biol Blood Marrow Transplant* 2008;**14**:1072–5.
67. Stratton P, Battiwalla M, Tian X, Abdelazim S, Baird K, Barrett AJ, et al. Immune response following quadrivalent human papillomavirus vaccination in women after hematopoietic allogeneic stem cell transplant. *Jama Oncol* 2020;**6**:696–705.
68. Public Health England. *Green Book Chapter 19 - Influenza*. Public Health England; 2020 *https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/931139/Green_book_chapter_19_influenza_V7_OCT_2020.pdf* accessed 11 Apr2021.
69. Pauksen K, Linde A, Hammarstrom V, Sjolin J, Carneskog J, Jonsson G, et al. Granulocyte-macrophage colony-stimulating factor as immunomodulating factor together with influenza vaccination in stem cell transplant patients. *Clin Infect Dis* 2000;**30**:342–8.
70. Whimbey E, Elting LS, Couch RB, Lo W, Williams L, Champlin RE, et al. Influenza A virus infections among hospitalized adult bone marrow transplant recipients. *Bone Marrow Transplant* 1994;**13**:437–40.
71. Dhakal B, Abedin SM, Fenske TS, Chhabra S, Ledeboer N, Hari P, et al. Response to SARS-CoV-2 vaccination in patients after hematopoietic cell transplantation and CAR-T cell therapy. *Blood* 2021;**138**:1278–81.
72. Redjoul R, Bouter AL, Beckerich F, Fourati S, Maury S. Antibody response after second BNT162b2 dose in allogeneic HSCT recipients. *Lancet Lond Engl* 2021;**398**:298–9.
73. Ram R, Hagin D, Kikozashvilli N, Freund T, Amit O, Bar-On Y, et al. Safety and immunogenicity of the BNT162b2 mRNA COVID-19 vaccine in patients after allogeneic HCT or CD19-based CART therapy—a single-center prospective cohort study. *Transplant Cell Ther* 2021;**27**:788–94.
74. Chiarucci M, Paolasini S, Isidori A, Guiducci B, Loscocco F, Capalbo M, et al. Immunological response against SARS-COV-2 after BNT162b2 vaccine administration is impaired in allogeneic but not in autologous stem cell transplant recipients. *Front Oncol* 2021;**11**:737300.
75. Maneikis K, Šablauskas K, Ringelevičiūtė U, Vaitekėnaitė V, Čekauskienė R, Kryžauskaitė L, et al. Immunogenicity of the BNT162b2 COVID-19 mRNA vaccine and early clinical outcomes in patients with haematological malignancies in Lithuania: a national prospective cohort study. *Lancet Haematol* 2021. doi:10.1016/s2352-3026(21)00169-1.
76. Bastidas A, Serna J de L, Idrissi ME, Oostvogels L, Quittet P, López-Jiménez J, et al. Effect of recombinant zoster vaccine on incidence of herpes zoster after autologous stem cell transplantation: a randomized clinical trial. *JAMA* 2019;**322**:123.
77. Public Health England. *Green Book Chapter 6 - Contraindications and Special Considerations*. Public Health England; 2017 *https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/655225/Greenbook_chapter_6.pdf* accessed 9 Apr2021.
78. Public Health England, Green book - Chapter 11 - the UK immunisation schedule, Public Health England. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/855727/Greenbook_chapter_11_UK_Immunisation_schedule.pdf (accessed 19 Jun2021).
79. Olkinuora H, Käyhty H, Davidkin I, Roivainen M, Ölander R, Kantele JM, et al. Immunity after (re)vaccination of paediatric patients following haematopoietic stem cell transplantation. *Acta Paediatr* 2012;**101**:e373–7.
80. Shah GL, Shune L, Purtill D, Devlin S, Lauer E, Lubin M, et al. Robust vaccine responses in adult and pediatric cord blood transplantation recipients treated for hematologic malignancies. *Biol Blood Marrow Transplant* 2015;**21**:2160–6.
81. Patel SR, Ortin M, Cohen BJ, Borrow R, Irving D, Sheldon J, et al. Revaccination with measles, tetanus, poliovirus, Haemophilus influenzae type B, meningococcus C, and pneumococcus vaccines in children after hematopoietic stem cell transplantation. *Clin Infect Dis* 2007;**44**:625–34.
82. Kussmaul SC, Horn BN, Dvorak CC, Abramovitz L, Cowan MJ, Weintrub PS. Safety of the live, attenuated varicella vaccine in pediatric recipients of hematopoietic SCTs. *Bone Marrow Transplant* 2010;**45**:1602–6.
83. Chou J, Kernan NA, Prockop S, Heller G, Scaradavou A, Kobos R, et al. Safety and efficacy of the live attenuated varicella vaccine following T replete or T cell depleted related and unrelated haematopoietic cell transplantation. *Biol Blood Marrow Transplant* 2011;**17**:1708–13.
84. Sasadeusz J, Prince HM, Schwarer A, Szer J, Stork A, Bock HL, et al. Immunogenicity and safety of a two-dose live attenuated varicella vaccine given to adults following autologous hematopoietic stem cell transplantation. *Transplant Infect Dis* 2014;**16**:1024–31.
85. Patel NC, Hertel PM, Estes MK, Morena de la M, Petru AM, Noroski LM, et al. Vaccine-acquired rotavirus in infants with severe combined immunodeficiency. *New Engl J Med* 2010;**362**:314–19.
86. de Fontbrune FS, Arnaud C, Cheminant M, Boulay A, Konopacki J, Lapusan S, et al. Immunogenicity and safety of yellow fever vaccine in allogeneic hematopoietic stem cell transplant recipients after withdrawal of immunosuppressive therapy. *J Infect Dis* 2017;**217**:494–7.
87. Yax JA, Farnon EC, Engleberg NC. Successful immunization of an allogeneic bone marrow transplant recipient with live, attenuated yellow fever vaccine. *J Travel Med* 2009;**16**:365–7.
88. Gowda R, Cartwright K, Bremner JAG, Green ST. Yellow fever vaccine: a successful vaccination of an immunocompromised patient. *Eur J Haematol* 2004;**72**:299–301.
89. Snowden JA, Aljurf M, Hayden P, Orchard KH, McGrath E. *Quality Management and Accreditation in Haematopoietic Stem Cell Transplantation and Cellular Therapy: The JACIE Guide*. Springer; 2021 *https://www.ebmt.org/sites/default/files/2021-03/The-JACIE-Guide.pdf* accessed 6 May2022.