Appendix: Supplementary information

Table 1: Full search terms for Pubmed (MEDLINE) database

1.	exp lymphoma, non-hodgkin/ or exp lymphoma, b-cell/ or exp lymphoma, follicular/ or exp lymphoma, large-cell, immunoblastic/ or lymphoma, mantle-cell/
2.	non hodgkin*.mp.
3.	1 or 2
4.	(chronic lymphocytic leukemia or CLL).mp. or exp Leukemia, Lymphocytic, Chronic, B-Cell/
5.	chronic lymph* leuk?emia*.mp.
6.	4 or 5
7.	(multiple myeloma or plasma cell myeloma).mp. or exp Multiple Myeloma/ or exp Neoplasms, Plasma Cell/
8.	(myeloma or plasma cell neoplasm).mp.
9.	7 or 8
10.	3 or 6 or 9
11.	exp "immunoglobulins, intravenous"/ or exp immunoglobulins/ or exp "immunoglobulin G"/
12.	((intravenous or IV) adj2 (immunoglobulin* or Ig or IgG)).mp.
13.	((Subcut* or SC) adj2 (immunoglobulin* or Ig or IgG)).mp.
14.	SCIG.mp.
15.	IVIG.mp.
16.	11 or 12 or 13 or 14 or 15
17.	exp antibiotic prophylaxis/ or exp Trimethoprim, Sulfamethoxazole Drug Combination/ or exp Doxycycline/ or exp Amoxicillin-Potassium Clavulanate Combination/ or exp Ciprofloxacin/ or exp Ofloxacin/ or exp Clarithromycin/ or antibiotic prophylaxis.mp.
18.	(abactrim or abactrin or alfatrim or "apo sulfatrim" or bactar or bactipront or "bactoreduct forte" or bactramin or bactrim or bactrimel or bethaprim or biseptol or chemotrim or co trimoxazole or co-trimoxazole or comox or comoxol or cotrim cotrimoxazol or cotrimstada or drylin or duobact or duobiocin or duratrimet or eltrianyl or escoprim or espectrin or eusaprim or fectrim or groprim or helveprim or imexim or infectrim or kepinol or lagaprim or lagatrim or linaris or microtrim or neoprim or nopil or oecotrim or omsat or oribact or oriprim or pharmaprim or potesept or resprim or resprin or scanprin or septra or septran or septrim or septrin or septrine or sigaprim or sinersol or soltrim or sulfamethoprim or sulfamethoxazole or sulfaprim or sulfatrim or sulfotrim or sulmeprim or sulprim or sumetrolim or sumetrolin or supracombin or thiocuran or "tms forte" or trib or trigonyl or "trimethoprim plus sulfamethoxazole" or trimethoprim sulfamethoxazole or "trimethoprim sulfamethoxazole colistin maltose medium" or "trimethoprim sulfamethoxazole combination" or trimethoprim sulphamethoxazole or trimethoprimsulfamethoxazole or trimetoprimsulfamethoxazole or trimezol or trimforte or trimosulfa or trimoxazole or trimoxol or "uro ts d" or "uroplus ds" or "uroplus ss").mp.
19.	(amermycin or atrax or azudoxat or bactidox or banndoclin or basedillin or bassado or biocolyn or biodoxi or bronmycin or calcium doxycycline or cloran or cyclidox or dentistar or deoxycycline or deoxymykoin or deoxyoxytetracycline or desoxy oxytetracycline or desoxycycline or doinmycin or dosil or dotur or doxaciclin or doxacycline or doxat or doxatet or doxi-sergo or doxibiotic or doxicycline or doxilin or doximed or doximycin or doxin or doxine or doxocycline or doxsig or doxy or doxybiocin or doxycen or doxycen retard or doxychel or

	doxycin or doxycyclin or doxycycline or doxylag or doxylin or doxymycin or doxypuren or doxytec or doxytrim or dumoxin or duracycline or esdoxin or etidoxina or gewacyclin or "gs 3065" or ibralene or idocyclin or idocyklin or interdoxin or investin or longamycin or lydox or magdrin or medomycin or mespafin or mildox or miraclin or monodox or nordox or oracea or paldomycin or radox or remycin or respidox or roximycin or serodoxy or servidoxine or servidoxyne or siadocin or siclidon or sigadoxin or spanor or supracyclin or supramycina or tenutan or tolexine or tolexine ge or torymycin or tsurupioxin or unidox or veemycin or viadoxin or vibra s or vibrabiotic or vibracina or vibradox or vibramicina or vibramycin or vibramycin-n or vibramycine or vibraveineuse or vibravenos or vibravet or viradoxyl-n or wanmycin or zadorin or zenavod).mp.
20.	(aclam or aktil or ambilan or amocla or amocla duo or amoclan or amoclav or amoksiklav or amolanic or amolanic duo or amometin or "amoxi plus" or "amoxicillin plus clavulanate potassium" or "amoxicillin potassium clavulanate combination" or "amoxicillin-potassium clavulanate combination" or amoxiclav or amoxsiklav or amoxxlin or ancla or auclatin or augamox or augmaxcil or augmentan or augmentin augmentine or augmex or augpen or augucillin or augurcin or ausclav or auspilic or bactiv or bactoclav or bioclavid or "brl 25000" or brl25000 or cavumox or ciblor or clacillin or clamax or clamentin or clamobit or clamonex or clamovid or clamoxin or clamoxyl or clarin-duo or clavamox or clavar or clavinex or clavodar or clavoxil or clavoxilin or clavubactin or clavudale or "clavulanate potassium plus amoxicillin" or "clavulanic acid plus amoxicillin" or clavulin or clavulox duo or clavumox or co amoxiclav or co amoxyclav or co-amoxiclav or coamoxiclav or coamoxyclav or cramon duo or croanan duo dry syrup or curam or danoclav or "darzitil plus" or e-moxclav or enhancin or fleming or fugentin or "fullicilina plus" or gumentin or hibiotic or inciclav or klamonex or kmoxilin or lactamox or lansiclav or moxiclav or moxicle or moxyclav or natravox or nufaclav or palentin or quali-mentin or ranclav or spektramox or stacillin or strenzen or suplentin or synermox or synulox or synulox lc or taromentin or taromentin es or "velamox cl" or vestaclav or viaclav or vulamox or xiclav or "zami 8503").mp.
21.	(acire or alcon cilox or bacquinor or bactiflox or bactiflox lactab or baflox or baycip or bernoflox or c-flox or c-floxacin or cetraxal or ciclodin or cidroxal or ciflo or ciflox or cifloxin or cifran or cilab or ciloquin or ciloxan or ciloxin or cimogal or cinaflox or cipflox or cipide or cipio or ciplox or ciplus or cipocin or ciprecu or ciprinol or cipro or ciprobac or ciprobay or ciprobay uro or ciprobid or ciprobiotic or ciprocan or ciprocep or ciprocin or ciprocinol or ciprodar or ciproflox or ciprofloxacin or ciprogis or ciproglen or ciprok or ciprolet or ciprolin or ciprolkan or ciprolon or cipromycin or ciropharm or ciproquin or ciproquinol or ciproval or ciprox or ciproxacol or ciproxan or ciproxin or ciproxina or ciproxine or ciproxyl or ciriax or cirok or cirokan or cirox or ciroxin or citopcin or cobay or corsacin or cosflox or cycin or cyfloxin or cypral or cyprobay or cysfec or eprocin or fimoflox or flociprin or floroxin or floxager or floxantina or floxbio or gonning or grifociprox or h-next or holdestin or inciflox or iprolan or isotic or jayacin or k-sacin or kenzoflex or kinoves or kipocin or lofucin or loxan or medociprin or mitroken or neofloxin or nivoflox or opthaflox or otiprio or otosec or probiox or procin or proflaxin or profloxin or "proksi 250" or "proksi 500" or proquin or "proquin xr" or proxacin or qilaflox or qinosyn or quilox or quinobiotic or quinolide or quintor or qupron or rigoran or rofcin or rosacin eye drop or sarf or septicide or septocipro or sifloks or siprogut or sophixin ofteno or spitacin or superocin or unex or uniflox or uroxin or zipra or zumaflox).mp.
22.	(akilen or audret or bactocin or bioquil or danoflox or "dl 8280" or dl8280 or "dr 3354" or dr3354 or effexin or eukinoft or exocin or exocine or flobacin or flodemex or flotavid or flovid or floxal or floxedol or floxil or floxin or floxin otic or floxstat or fugacin or gyroflox or "hoe 280" or inoflox or kinflocin or kinoxacin or liflox or loxinter or marfloxacin or medofloxin or medofloxine or mergexin or monoflocet or monoox or novecin or nufafloqo or o-flox

	or obide or occidal or ocuflox or ofcin or oflin or oflocee or oflocet or oflocin or oflodal or oflodex or oflodinex or oflodura or oflogen or oflohexal or oflox or ofloxacin or ofloxacina or ofloxacine or ofloxamed or ofloxin or ofus or onexacin or operan or "orf 18489" or orf18489 or orocin or otonil or ottoflox or oxacid or oxatrex or pharflox or praxin or "pt 01" or pt01 or puiritol or qinolon or qipro or quinofree or quinolon or quotavil or "rg 191" or rg191 or rilox or "ru 43280" or ru43280 or sinflo or surnox or tabrin or taravid or tariflox or tarivid or tarivid eye ear or tarivid otic or taroflox or telbit or trafloxal or tructum or uro tarivid or urotarivid or viotisone or zanocin).mp.
23.	(abbotic or abbotic xl or "abbott 56268" or aeroxina or bactirel or baxin filmtab or biaxin or biclar or bicrolid or binoklar or bremon or c-clarin or carimycin or celex or clacin or clacine or clambiotic or clapharma or clari or claribid or claridar or clarikan or clarimac or claripen or clarith or clarithromycin or claritrol or claroma or clormicin or crixan or cylind or cyllind or dicupal or "er 36469" or er36469 or gervaken or hecobac or heliclar or helitic or klacid or klacid xl or klacina or klaciped or klaribac or klaricid or klaricid paediatric or klaricid pediatric or klaricid xl or klaridex or klaridia or klarin or klerimed or kofron or lagur or macladim or macladin or maclar or macrobiol or mavid or monozeclar or naxy or "te 031" or te031 or veclam or zeclar).mp.
24.	(actira or avalox or avelon or avelox or bacterol or "bay 12 8039" or "bay 128039" or bay128039 or floxamic or floxitrat or izilox or kanavig or lifodrox or megaxin or moksacin or monafox or moxeza or moxeza af or moxif or moxifloxacin or moxivig or octegra or proflox or tamvelier or vamocin or vigamox or xiflodrop).mp.
25.	(antibiotic* adj2 prophyl*).mp.
26.	17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25
27.	exp immunization/ or exp immunization, secondary/ or exp immunotherapy, active/ or exp vaccination/
28.	(vaccin* or immuni?ation).mp.
29.	27 or 28
30.	16 or 26 or 29
31.	10 and 30
32.	(randomized controlled trial or controlled clinical trial).pt.
33.	(random* or trial or placebo).tw. or clinical trial*.mp.
34.	32 or 33
35.	31 and 34
36.	exp animals/ not humans.sh.
37.	35 not 36
38.	limit 37 to english language

Table 2: List of studies excluded at full text screening stage with brief reasons

Title	Journal	First Author, Published Year	Exclusion Reason
Tackling early morbidity and mortality in myeloma: Assessing the benefit of antibiotic prophylaxis and its effect on healthcare associated infections	Haematologica	Drayson 2011	Duplicate
Immunogenicity and safety of an adjuvanted herpes zoster subunit vaccine in adult autologous hematopoietic stem cell transplant recipients: phase 3, randomized, placebo-controlled, ZOEHSCT clinical trial	Bone marrow transplantation	Sullivan 2019	Duplicate
Effect of various doses of intravenous polyclonal IgG on in vivo levels of 12 pneumococcal antibodies in patients with chronic lymphocytic leukaemia and multiple myeloma.	Oncology	Sklenar 1993	Wrong outcomes
Role of gamma globulin for immunoprophylaxis in multiple myeloma.	The New England journal of medicine	Salmon 1967	Wrong route of administration
Levofloxacin prophylaxis in patients with newly diagnosed myeloma (TEAMM): a multicentre, double-blind, placebo-controlled, randomised, phase 3 trial	The Lancet	Drayson 2019	Duplicate
Randomized Trial of Lenalidomide and Dexamethasone Versus Clarythromycin, Lenalidomide and Dexamethasone As First Line Treatment in Patients with Multiple Myeloma Not Candidates for Autologous Stem Cell Transplantation: Results of the GEM-Claridex Clinical Trial	Blood	Puig 2019	Duplicate
Randomized trial of lenalidomide and dexamethasone versus crythromycin, lenalidomide and dexamethasone as first line treatment in patients with multiple myeloma not candidates for autologous stem cell transplantation: results of the GEM-claridex clinical trial	Blood	Puig 2019	Duplicate
Immunogenicity and safety of the adjuvanted recombinant zoster vaccine in adults with haematological malignancies: a phase 3, randomised, clinical trial and post-hoc efficacy analysis	The Lancet	Dagnew 2019	Duplicate
Doses of 13-valent conjugated pneumococcal vaccine (PCV13) for patients with multiple myeloma (MM)	Open Forum Infectious Diseases	Sun 2018	Duplicate
Conjugated pneumococcal vaccine triggers a better immune response than polysaccharide pneumococcal vaccine in patients with chronic lymphocytic leukemia a randomized study by the Swedish CLL group	Haematologica	Svensson 2017	Duplicate
Tandem high-dose influenza vaccination is associated with more durable serologic immunity in patients with plasma cell dyscrasias	Blood Advances	Branagan 2021	Duplicate
Does curative intravenous immunoglobulin therapy improve outcome in the treatment of infections in chronic lymphoid leukemia?	Critical care	Benlabed 2020	Wrong study design
The prosid study: evaluating eicacy and safety of intravenousimmunoglobulin (IVIG) 10% in primary infection prophylaxis inpatients with chronic lymphocytic leukemia-study design	Blood	Cornely 2020	Duplicate
Immunogenicity, safety, and post-hoc efficacy assessment of the adjuvanted recombinant zoster vaccine in adults with hematologic malignancies: a phase 3, randomized clinical trial	Open forum infectious diseases	Dagnew 2018	Duplicate

Oral third-generation cephalosporins vs. levofloxacin for antibacterial prophylaxis in neutropenic patients with hematologic malignancies	Open forum infectious diseases	DeVoe 2019	Wrong patient population
Tackling early morbidity and mortality in myeloma (TEAMM): assessing the benefit of antibiotic prophylaxis and its effect on healthcare associated infections in 977 patients	British journal of cancer	Drayson 2018	Duplicate
Immunoglobulin prophylaxis against cytomegalovirus infection in patients at high risk of infection following allogeneic hematopoietic cell transplantation	Transplantation proceedings	Ichihara 2011	Wrong patient population
The importance of continued follow-up in cancer trials: results from the TEAMM myeloma trial assessing the benefit of 12 weeks levofloxacin prophylaxis on febrile episodes or deaths	Trials	Iqbal 2019	Duplicate
Pneumococcal vaccine responses in B cell malignancies and dysfunctions	Haematologica	Karlsson 2013	Wrong study design
Immunogenicity and safety of an adjuvanted herpes zoster subunit candidate vaccine in adults with hematologic malignancies: a phase III, randomized clinical trial	Open forum infectious diseases	Oostvogels 2017	Wrong outcomes
A randomized prospective study of ceftazidime and ciprofloxacin with or without teicoplanin as an empiric antibiotic regimen for febrile neutropenic patients	British journal of haematology	Lim 1990	Wrong patient population
Lenalidomide and dexamethasone plus or minus clarythromycin in newly diagnosed multiple myeloma patients ineligible for autologous stem cell transplantation: updated results of the gemclaridex trial	Hemasphere	Puig 2020	Duplicate
Doses of 13-valent conjugated pneumococcal vaccine (PCV13) for patients with multiple myeloma (MM)	Open forum infectious diseases	Sun 2018	Wrong outcomes
Conjugated pneumococcal vaccine triggers a better immune response than polysaccharide pneumococcal vaccine in patients with chronic lymphocytic leukemia a randomized study by the Swedish CLL group	Haematologica	Svensson 2017	Wrong outcomes
A randomised trial of two 2-dose influenza vaccination strategies for patients following autologous haematopoietic stem cell transplantation	Hemasphere	Teh 2020	Duplicate
Two dose series of high-dose influenza vaccine is associated with longer duration of serologic immunity in patients with plasma cell disorders	Blood. Conference: 59th Annual Meeting of the American Society of Hematology, ASH	Branagan 2017	Duplicate
Two dose series of high-dose influenza vaccine is associated with longer duration of serologic immunity in patients with plasma cell disorders	Haematologica	Branagan 2018	Wrong outcomes
The prosid study: Evaluating efficacy and safety of intravenous immunoglobulin (IVIG) 10% in primary infection prophylaxis in patients with chronic lymphocytic leukemia-study design	Blood	Cornely 2020	Duplicate
Oral antibiotic prophylaxis of early infection in multiple myeloma: A URCC/ECOG phase III study	Blood Annual Meeting of the American Society of Hematology, ASH	Vesole 2010	Duplicate
Poxvirus vectored cytomegalovirus vaccine to prevent cytomegalovirus viremia in transplant recipients: A phase 2, randomized clinical trial	Annals of Internal Medicine	Aldoss 2020	Wrong patient population
Levofloxacin prophylaxis in newly diagnosed myeloma reduces febrile episodes and death without increasing healthcare associated infections: Results from the teamm trial	HemaSphere	Bowcock 2018	Duplicate

Levofloxacin prophylaxis in newly diagnosed myeloma reduces febrile episodes and death without increasing healthcare associated infections: Results from the teamm trial (tackling early morbidity and mortality in myeloma)	British Journal of Haematology	Bowcock 2018	Duplicate
Immunogenicity, safety, and post-hoc efficacy assessment of the adjuvanted recombinant zoster vaccine in adults with hematologic malignancies: A phase 3, randomized clinical trial	Open Forum Infectious Diseases	Dagnew 2018	Wrong outcomes
Tackling early morbidity and mortality in myeloma (TEAMM): Assessing the benefit of antibiotic prophylaxis and its effect on healthcare associated infections in 977 patients	British Journal of Cancer	Drayson 2018	Duplicate
Clarithromycin and lenalidomide combination: A full oral regimen for relapsed/ refractory malt lymphoma patients. results of the international extranodal lymphoma study group IELSG40/CLEO trial	HemaSphere	Ferreri 2020	Wrong study design
TEAMM Work Saves Lives in Myeloma	HemaSphere	Hallam 2018	Duplicate
Immunogenicity and safety of an adjuvanted herpes zoster subunit candidate vaccine in adults with hematologic malignancies: A phase III, randomized clinical trial	Open Forum Infectious Diseases	Oostvogels 2017	Wrong outcomes;
Lenalidomide and dexamethasone plus or minus clarythromycin in newly diagnosed multiple myeloma patients ineligible for autologous stem cell transplantation: Updated results of the gemclaridex trial	HemaSphere	Puig 2020	Duplicate
A randomised trial of two 2-dose influenza vaccination strategies for patients following autologous haematopoietic stem cell transplantation	HemaSphere	Teh 2020	Duplicate
Low neutralizing antibody responses against SARS-CoV-2 in older patients with myeloma after the first BNT162b2 vaccine dose	Blood	Terpos 2021	Wrong study design
	NIHR Journals Library. Efficacy and Mechanism Evaluation	Chicca 2020	Duplicate
Clinical efficacy of pneumococcal vaccination in multiple myeloma patients on novel agents: Results of a prospective clinical study.	Vaccine	Stoma 2020	Wrong study design
Levofloxacin prophylaxis in patients with myeloma.	The Lancet. Oncology	Albrich 2020	Wrong study design
Levofloxacin prophylaxis in patients with myeloma.	The Lancet. Oncology	Teh 2020	Wrong study design
Levofloxacin prophylaxis in patients with myeloma - Authors' reply.	The Lancet. Oncology	Drayson 2020	Wrong study design
Antibiotic prophylaxis for patients with newly diagnosed multiple myeloma: Systematic review and meta-analysis.	European journal of haematology	Mohyuddin 2020	Wrong study design
Pneumococcal conjugate vaccine triggers a better immune response than pneumococcal polysaccharide vaccine in patients with chronic lymphocytic leukemia A randomized study by the Swedish CLL group.	Vaccine	Svensson 2018	Wrong outcomes
Immunoglobulin replacement in chronic lymphocytic leukaemia.	Nouvelle revue francaise d'hematologie	Bunch 1988	Duplicate
A randomized placebo-controlled phase II study of clarithromycin or placebo combined with VCD induction therapy prior to high-dose melphalan with stem cell support in patients with newly diagnosed multiple myeloma	Blood	Gregersen 2017	Duplicate

Clarithromycin added to the VCD regimen causes reduced health-related quality of life in multiple myeloma patients	HemaSphere	Nielsen 2018	Duplicate
Recent advances in the treatment of chronic lymphocytic leukemia: defining the role of intravenous immunoglobulin.	Seminars in hematology	Besa 1992	Wrong study design;
Randomised trial of intravenous immunoglobulin as prophylaxis against infection in plateau-phase multiple myeloma. The UK Group for Immunoglobulin Replacement Therapy in Multiple Myeloma.	Lancet (London, England)	Chapel 1994	Duplicate
Clarithromycin added to bortezomib-cyclophosphamide-dexamethasone impairs health-related quality of life in multiple myeloma patients.	European journal of haematology	Nielsen 2019	Duplicate
Improved vaccination response during ranitidine treatment, and increased plasma histamine concentrations, in patients with B cell chronic lymphocytic leukemia.	Leukemia	Jurlander 1995	Wrong comparator;
Effect of antimicrobial prophylaxis on hematopoietic recovery following autologous bone marrow transplantation: ciprofloxacin versus co-trimoxazole.	Bone marrow transplantation	Imrie 1995	Wrong study design
Safety and efficacy profiles of clarithromycin monotherapy in 55 patients with extranodal marginal zone lymphoma (EMZL)	Haematologica	Ferreri 2016	Wrong study design
Intravenous immunoglobulin therapy in patients with multiple myeloma.	Immunodeficiency	Chapel 1993	Wrong study design
Prophylactic antibiotics for the prevention of neutropenic fever in patients undergoing autologous stem-cell transplantation: Results of a single institution, randomized phase 2 trial	American Journal of Hematology	Eleutherakis-Papaiakovou 2010	Wrong patient population
Randomized double-blinded comparison of three intravenous immunoglobulin products in bone marrow transplantation	Seminars in Hematology	Peltier 1992	Wrong study design
Antibacterial prophylaxis reduces the incidence of neutropenic fever and the rate of infections in patients with multiple myeloma who undergo an autologous stem cell transplantation	Blood	Eleutherakis-Papaiakovou 2009	Duplicate
Double-blind randomized study of prophylactic trimethoprim/sulfamethoxazole in granulocytopenic patients with hematologic malignancies	American Journal of Medicine	Gualtieri 1983	Wrong patient population
Trimethoprim-sulfa prevents early infection in multiple myeloma	Cancer Research Therapy and Control	Oken 1998	Duplicate
Tackling early morbidity and mortality in myeloma (TEAMM): Assessing the benefit of antibiotic prophylaxis and its effect on healthcare associated infections in 977 patients	British Journal of Cancer	Drayson 2018	Duplicate
Levofloxacin prophylaxis in newly diagnosed myeloma reduces febrile episodes and death without increasing healthcare associated infections: Results from the teamm trial	HemaSphere	Bowcock 2018	Duplicate
Levofloxacin prophylaxis in newly diagnosed myeloma reduces febrile episodes and death without increasing healthcare associated infections: Results from the teamm trial (tackling early morbidity and mortality in myeloma)	British Journal of Haematology	Bowcock 2018	Duplicate
The use of intravenous immune globulin in multiple myeloma.	Clinical and experimental immunology	Chapel 1994	Duplicate
The use of intravenous immune globulin in multiple myeloma	Clinical and Experimental Immunology, Supplement	Chapel 1994	Duplicate
Hypogammaglobulinaemia in low grade B cell tumours; significance and therapy.	Immunological investigations	Chapel 1991	Wrong study design

Protected environment-prophylactic antibiotic program for malignant lymphoma. Randomized trial during chemotherapy to induce remission.	The American journal of medicine	Bodey 1979	Wrong patient population
Human immunoglobulin	Prescrire International	Anonymous 1996	Wrong study design
Phase III randomized, double-blind, placebo controlled trial of North American (NA) ginseng (Panax quinquefolium) extract (CVT-E002) in patients with chronic lymphocytic leukemia: Effect on respiratory infection and antibiotic use	Journal of Clinical Oncology	High 2010	Wrong intervention
Better response with conjugate vaccine than with polysaccaride vaccine 12 months after rituximab treatment in lymphoma patients.	British journal of haematology	Svensson 2012	Wrong outcomes
One-year safety and immunogenicity of two formulations of an adjuvanted varicella-zoster virus (VZV) subunit candidate vaccine in adult autologous hematopoietic cell transplant (HCT) recipients	Biology of Blood and Marrow Transplantation	Stadtmauer 2013	Duplicate
Prophylaxis against infections with intravenous immunoglobulins in multiple myeloma.	British journal of haematology	Musto 1995	Duplicate
Vaccination of patients with haematological malignancies with one or two doses of influenza vaccine: a randomised study.	British journal of haematology	Ljungman 2005	Wrong outcomes
Intravenous immune globulin in chronic lymphocytic leukaemia.	Clinical and experimental immunology	Gamm 1994	Wrong study design
Correlation between immunoglobulin dose and incidence of severe and serious infections in secondary immunodefficiencies	Journal of Clinical Oncology	Ehlers 2017	Wrong study design
Efficacy of different immunoglobulin doses in the prevention of severe and serious infections in patients with secondary immunodeficiencies-results from a multicenter observational study with Privigen	Oncology Research and Treatment	Ehlers 2017	Wrong study design
Rational selection of patients for antibacterial prophylaxis after chemotherapy.	Journal of clinical oncology : official journal of the American Society of Clinical Oncology	Cullen 2007	Wrong study design
Lower rates of influenza infection following two dose series of high dose vaccination in plasma cell disorders: Results of a randomized, double-blind, place bo-assisted clinical trial	Blood	Branagan 2016	Wrong comparator
Use of patient diaries in conjunction with standard reporting methods: Duplication of data or a valuable resource?	Trials	Dunn 2015	Wrong study design
Clinical trials of dendritic cell-based cancer vaccines in hematologic malignancies.	Human vaccines & immunotherapeutics	Pyzer 2014	Wrong intervention
Treatment of high-risk aggressive B-cell non-Hodgkin lymphomas with rituximab, intensive induction and high-dose consolidation: long-term analysis of the R-MegaCHOP-ESHAP-BEAM Trial.	Leukemia & lymphoma	Pytlik 2015	Wrong intervention
Lack of response to vaccination in MGUS and stable myeloma	Blood	Prabhala 2009	Wrong outcomes
Lenalidomide-induced immunomodulation in multiple myeloma: impact on vaccines and antitumor responses.	Clinical cancer research : an official journal of the American Association for Cancer Research	Noonan 2012	Wrong outcomes
Effect of meropenem with or without immunoglobulin as second-line therapy for pediatric febrile neutropenia	Pediatrics International	Kobayashi 2014	Wrong patient population
A phase 2 study of lenalidomide to repair immune synapse response and humoral immunity in early-	Blood	Jones 2016	Wrong comparator

stage, asymptomatic chronic llmphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) with high-risk genomic features			
Immunogenicity and safety of high-dose trivalent inactivated influenza vaccine compared to standard-dose vaccine in children and young adults with cancer or HIV infection.	Vaccine	Hakim 2016	Wrong patient population
Clinical and Serologic Responses After a Two-dose Series of High-dose Influenza Vaccine in Plasma Cell Disorders: A Prospective, Single-arm Trial.	Clinical lymphoma, myeloma & leukemia	Branagan 2017	Wrong study design
Antibody response to pneumococcal conjugate vaccine (PCV13) in chronic lymphocytic leukemia patients receiving ibrutinib	Blood	Andrick 2016	Wrong comparator
Prevention of infection in cancer patients	Cancer Treatment and Research	Pomakova 2014	Wrong study design
Immunoglobulin prophylaxis in hematological malignancies and hematopoietic stem cell transplantation.	The Cochrane database of systematic reviews	Raanani 2008	Wrong study design
Immunoglobulin prophylaxis in chronic lymphocytic leukemia and multiple myeloma: systematic review and meta-analysis.	Leukemia & lymphoma	Raanani 2009	Wrong study design
Vaccine therapy and chronic lymphocytic leukaemia	Best Practice and Research: Clinical Haematology	Ramsay 2008	Wrong study design
A review of supportive care and recommended preventive approaches for patients with chronic lymphocytic leukemia	Expert Review of Hematology	Randhawa 2016	Wrong study design
Influenza vaccine in chronic lymphoproliferative disorders and multiple myeloma	European Journal of Haematology	Rapezzi 2003	Wrong study design
Immunoglobulin G treatment of secondary immunodeficiencies in the era of novel therapies	Clinical and Experimental Immunology	Seppanen 2014	Wrong study design
Seasonal Influenza Vaccination in Patients With Chronic Lymphocytic Leukemia Treated With Ibrutinib.	JAMA oncology	Sun 2016	Wrong study design
European myeloma network guidelines for the management of multiple myeloma-related complications	Haematologica	Terpos 2015	Wrong study design
Vaccinations in patients with hematological malignancies	Blood Reviews	Tsigrelis 2016	Wrong study design
Fluoroquinolone prophylaxis for the prevention of central line-associated bloodstream infection in autologous stem cell transplant	Journal of Clinical Oncology	Ziegler 2017	Wrong study design
Cost effectiveness of prophylactic intravenous immune globulin in chronic lymphocytic leukemia.	The New England journal of medicine	Weeks 1991	Wrong study design
Anti-infective prophylaxis with aciclovir and cotrimoxazole to reduce the rate of infections and therapy-associated deaths in elderly patients with DLBCL undergoing R-CHOP immunochemotherapy	Journal of Clinical Oncology	Murawski 2017	Wrong study design
Infectious complications in patients with chronic lymphocytic leukemia: Pathogenesis, spectrum of infection, and approaches to prophylaxis	Clinical Lymphoma and Myeloma	Morrison 2009	Wrong study design
History of infections and vaccinations and risk of lymphoid neoplasms: Does influenza immunization reduce the risk? [18]	Leukemia	Monnereau 2007	Wrong study design
Part II: Vaccines for haematological malignant disorders	Lancet Oncology	Mocellin 2004	Wrong study design
Management of infectious complications in chronic lymphocytic leukemia	European journal of Clinical and Medical Oncology	Matutes 2010	Wrong study design
Levofloxacin prophylaxis for multiple myeloma patients undergoing autologous transplant	Biology of Blood and Marrow Transplantation	Lamprecht 2015	Wrong study design

A Canadian perspective on the use of immunoglobulin therapy to reduce infectious complications in chronic lymphocytic leukemia	Current Oncology	Lachance 2016	Wrong study design
Impact of a change in antibacterial prophylaxis on bacteremia and hospitalization rates following outpatient autologous peripheral blood stem cell transplantation for multiple myeloma	Transplant Infectious Disease	Kim 2014	Wrong study design
Effect of levofloxacin prophylaxis for prevention of severe infections in multiple myeloma patients receiving bortezomib-containing regimens.	International journal of hematology	Jung 2014	Wrong study design
Antibody responses to pneumococcal and haemophilus vaccinations in patients with B-cell chronic lymphocytic leukaemia.	Vaccine	Hartkamp 2001	Wrong study design
The immunodeficiency of chronic lymphocytic leukaemia	British Medical Bulletin	Hamblin 2008	Wrong study design
Intravenous immunoglobulin treatment in hematological diseases	European Journal of Haematology	Otten 1998	Wrong study design
Lenalidomide augments immune responses to prevnar vaccination in relapsed myeloma patients: Implications for cancer and infectious vaccines	Blood	Noonan 2009	Wrong study design
Anti-infective prophylaxis with aciclovir and cotrimoxazole significantly reduces the rate of infections and therapyassociated deaths in elderly patients with DLBCL undergoing R-CHOP immunochemotherapy	Oncology Research and Treatment	Murawski 2017	Wrong study design
Antibody response to polysaccharide anti-Streptococcus pneumoniae vaccine in relation to the selected immunological parameters of patients with chronic lymphocytic leukaemia	Clinical Microbiology and Infection	Grywalska 2012	Wrong study design
Influenza virus vaccine in B-cell chronic lymphocytic leukaemia patients.	Acta haematologica	Gribabis 1994	Wrong study design
Six-month oral clarithromycin regimen is safe and active in extranodal marginal zone B-cell lymphomas: final results of a single-centre phase II trial.	British journal of haematology	Govi 2010	Wrong study design
Ciprofloxacin prophylaxis in high risk neutropenic patients: Effects on outcomes, antimicrobial therapy and resistance	BMC Infectious Diseases	Garnica 2013	Wrong study design
Bendamustine associated immune suppression and infections during therapy of hematological malignancies.	Leukemia & lymphoma	Gafter-Gvili 2016	Wrong study design
High-dose clarithromycin is an active monotherapy for patients with relapsed/refractory extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT): the HD-K phase II trial.	Annals of oncology : official journal of the European Society for Medical Oncology	Ferreri 2015	Wrong study design
Management of infections in patients with chronic lymphocytic leukemia treated with alemtuzumab	Annals of Hematology	Elter 2009	Wrong study design
Low circulating mannan-binding lectin levels correlate with increased frequency and severity of febrile episodes in myeloma patients who undergo ASCT and do not receive antibiotic prophylaxis	Bone Marrow Transplantation	Eleutherakis-Papaiakovou 2017	Wrong study design
Development of a predictive model to identify patients with multiple myeloma not eligible for autologous transplant at risk for severe infections using data from the first trial	Haematologica	Dumontet 2016	Wrong study design
Antibody deficiency secondary to chronic lymphocytic leukemia: Should patients be treated with prophylactic replacement immunoglobulin?	Journal of Clinical Immunology	Dhalla 2014	Wrong study design
Vaccines for prophylaxis of viral infections in patients with hematological malignancies.	The Cochrane database of systematic reviews	Cheuk 2011	Wrong study design
Safety and efficacy of clarithromycin monotherapy in patients (pts) with extranodal marginal zone lymphoma (EMZL)	Annals of Oncology	Cecchetti 2016	Wrong study design

Immunological response to influenza virus vaccine in B-cell chronic lymphocytic leukaemia patients [1]	Acta Haematologica	Bucalossi 1995	Wrong study design
Humoral response to hemagglutinin components of influenza vaccine in patients with non-Hodgkin malignant lymphoma	Vaccine	Brydak 2006	Wrong study design
Randomized trial of the addition of gram-positive prophylaxis to standard antimicrobial prophylaxis for patients undergoing autologous bone marrow transplantation	Antimicrobial Agents and Chemotherapy	Broun 1994	Wrong patient population
Practical review of immunizations in adult patients with cancer	Human Vaccines and Immunotherapeutics	Ariza-Heredia 2015	Wrong study design

Supplementary Information

Clinically documented infections

From the trials evaluating Ig, three trials (Boughton 1995, Chapel 1994, Cooperative CLL 1988) evaluating IVIg and one trial (Vacca 2018) evaluating SCIg reported the number of episodes of CDIs.(9, 12, 30) In one study (Boughton 1995), the overall number of CDIs were reported but not by treatment arm.(9) We were unable to pool these outcomes in a meta-analysis as no standard deviation were provided for the RCTs evaluating IVIg; and in the RCT evaluating SCIg, the outcomes were reported per person-time but time was not provided in the denominator and there were varying follow-up times. Results are reported narratively. In Boughton 1995, 122 infections occurred in 18 of the 42 study patients.(9) In Chapel 1994, 19 serious infections occurred in 449 patient-months in the Ig arm, compared to 38 in 470 patient-months in the placebo arm.(30) In Cooperative CLL 1988, 66 infections occurred in 41 patients receiving Ig compared to 81 infections in 42 patients on placebo.(12) In Vacca, 85 infections (16 major, 69 minor) occurred in 24 patients receiving Ig vs. 333 infections (190 major, 143 minor) in 22 patients in the control arm.(16)

From the trials evaluating antibiotics, two trials reported the number of CDIs. However, as no standard deviation was provided, we were unable to pool these outcomes in a meta-analysis. Results are reported narratively. In Drayson 2019, the number of CDIs was 257 in antibiotic arm vs. 329 in control arm. In Oken, the number of CDIs were 5 in antibiotic arm vs. 16 in control arm.

Microbiologically documented infections

From the trials evaluating Ig, the proportion of patients with one or more bacterial infections was used in the meta-analysis from one of these trials (Cooperative CLL 1988). Two trials (Boughton 1995, Chapel 1994) reported the number of MDIs in each arm.(9, 30) However, as no standard deviation was provided, we were unable to pool these outcomes in a meta-analysis. Results are reported narratively. In Boughton 1995, 19 (from a total of 122) infections had bacterial pathogens isolated.(9) In Chapel 1994, infections in patients on Ig arm were classified into 23 bacterial, 40 viral and 3 fungal vs 42 bacterial, 37 viral and 2 fungal infections in patients on the control arm.(30)

From the trials evaluating antibiotics, one trial reported on the numbers of MDIs. From 977 patients, the number of MDIs was 44 in the antibiotic arm vs. 68 in the control arm (Drayson 2019).(17)

From the trials evaluating VZV vaccinations, four studies were not included in the meta-analysis – one study used clinical criteria for diagnosis of herpes zoster infection,(23) three studies (Winston 2018, Stadtmauer 2014, Stadtmauer 2021) confirmed CDIs by a combination of PCR testing or on the basis of blinded adjudication and we were unable to ascertain from these numbers, the proportion of patients with VZV confirmation by PCR testing alone.(25, 26, 28) Microbiological testing was not specified in the trial evaluating influenza vaccination.(24)

Hospitalisations due to infection

One study (Vacca 2018) evaluating SCIg reported on the duration of hospitalisation due to severe infections.(16) Mean days/year of hospitalisation due to severe infections were 8 in the SCIg arm vs. 121 in the control arm ($p<0.001$). One study (Drayson 2019) evaluating prophylactic oral antibiotics reported on the number of hospitalisations and intensive care admissions.(17) The number of hospitalisations for infection was 88 (from 489 patients) in the antibiotic arm vs 114 (from 488 patients) in control arm, and the number of intensive care admissions was 3 (from 489 patients) in the antibiotic arm vs. 5 (from 488 patients) in the control arm. None of the other studies reported on hospitalisations or intensive care admissions due to infection.

Adverse events

From the trials evaluating Ig, Ig prophylaxis significantly increased the risk of adverse events, RR 2.23 (95% CI 1.67 to 2.99). From the Chapel 1994 study, we included the proportion of patients with adverse events of at least moderate severity in this meta-analysis

as the number of all-grade adverse events was reported by total events, rather than by proportion of patients. In the study evaluating SCIg, adverse events were reported in the treatment arm only, which were predominantly mild and comprised of local injection site reactions.(16)

From the trials evaluating antibiotics, we did not include the Drayson study in our meta-analysis as the authors reported the number of adverse events as event outcomes (instead of proportion of patients).(17) They reported a total of 308 serious adverse events from 489 patients in the intervention arm vs. 289 serious adverse events from 488 patients in the control group. The majority of serious adverse events were reported as unlikely or unrelated to study drug. From 308 serious adverse events in the intervention group, events thought related to study drug included tendonitis (in five patients), confusion (one patient). Other mild adverse events included nausea, diarrhoea, chills/fever, rash and musculoskeletal pains.

From the trials evaluating VZV vaccinations, one study reported adverse events leading to treatment discontinuation, which were similar between arms.(28) From the trials evaluating influenza vaccination, there were no reported adverse events leading to treatment discontinuation.

Crossover studies evaluating prophylactic immunoglobulin

Three studies had a crossover study design and were not included in the meta-analysis as data for first randomisation was not available. Importantly, no washout period was reported in these trials so carry-over effect is not excluded. More details are provided in the appendix (Supplementary information).

The first trial (Griffiths 1989) reported on 12 patients (8 with CLL and 4 with low-grade NHL) with hypogammaglobulinaemia or a recent history of recurrent infections.(13) Patients were randomised to receive either IVIg 0.4g/kg or saline infusion every 3 weeks for 12 months, and were then switched to the alternative preparation for another 12 months. A total of 41 CDIs occurred in 143 patient-months during the IVIg period compared with 68 CDIs in 121 patient-months during the standard care (saline infusion) period. Serious infections, defined as life-threatening infections requiring hospitalisation and intravenous therapy (major infections) or anti-bacterial therapy (moderate infections), were also reported, and 18 serious infections occurred in 143 patient-months during the IVIg period compared with 46 CDIs in 121 patient-months during the standard care (saline infusion) period.

The second trial (Musto 1995) reported on 25 patients with multiple myeloma with hypogammaglobulinaemia or a recent history of recurrent infections.(15) These patients were randomised to receive either IVIg 0.3g/kg every 4 weeks or no therapy (observation) for 6 months, switched to the alternative arm for 12 months, then switched again to the original arm for another 6 months. A total of 33 CDIs (of which 10 were serious infections) occurred in 261 patient-months during the IVIg period compared with 57 CDIs (of which 30 were serious infections) in 250 patient-months during the standard care (observation) period. Serious infections were not specifically defined in this study.

The third trial (Molica 1996) reported on 42 patients with CLL with hypogammaglobulinaemia or a history of at least one infection during the previous six months.(14) Patients were randomised to receive either IVIg 0.3g/kg every 4 weeks or no therapy for 6 months, switched to the alternative arm for 12 months, then switched again to the original arm for another 6 months. A total of 41 CDIs (of which 5 were serious infections) occurred in 376 patient-months during the IVIg period compared with 62 CDIs (of which 8 were serious infections) in 368 patient-months during the standard care (observation) period.

Prophylactic immunoglobulin comparing different doses

One study compared different doses of prophylactic Ig with results reported in two publications.(12, 31) The authors (Chapel 1994 and Gamm 1994) reported on reported on 36 patients with haematological malignancies (34 patients with CLL and 2 with NHL)

and hypogammaglobulinaemia or a recent history of one or more serious infections. Patients were randomised to receive either IVIg 0.5g/kg or 0.25g/kg every 4 weeks for 12 months.

Four CLL patients died, two patients in each treatment group; one death in the low-dose treatment group was due to infection. A total of 23 CDIs (of which 6 were serious infections) occurred in 180 patient-months in the high-dose IVIg group compared with 22 (of which 11 were serious infections) CDIs in 223 patient-months in the low-dose IVIg group. Thirteen MDIs occurred in 180 patient-months in the high-dose IVIg group compared with 19 in 223 patient-months in the low-dose IVIg group. Treatment-related adverse events were reported in two of 16 CLL patients in the high-dose IVIg group compared to eight of 18 CLL patients in the low-dose IVIg group.(31)

Prophylactic vaccinations comparing differing doses of vaccinations

Two trials compared differing doses of VZV(25) and influenza vaccination.(27) One study compared three doses of VZV glycoprotein E (gE) vaccine adjuvanted with AS01B vs. three doses of gE adjuvanted with AS01E vs. two doses of gE/AS01B vs. placebo.(25) In this comparison, we evaluated outcomes in patients receiving three vs. two doses of gE/ASO1B vaccine. One study compared high-dose (HD) inactivated influenza vaccine followed by standard dose (SD) vaccine (HD-SD arm) or 2 SD vaccines (SD-SD arm) in patients with myeloma or lymphoma post autologous stem cell transplant.(27) There was no difference in CDIs or adverse events in both studies (Appendix 17, 18, 19).

Supplementary Forest Plots

Figure 1: Prophylactic immunoglobulin versus standard care, Outcome: All-cause mortality

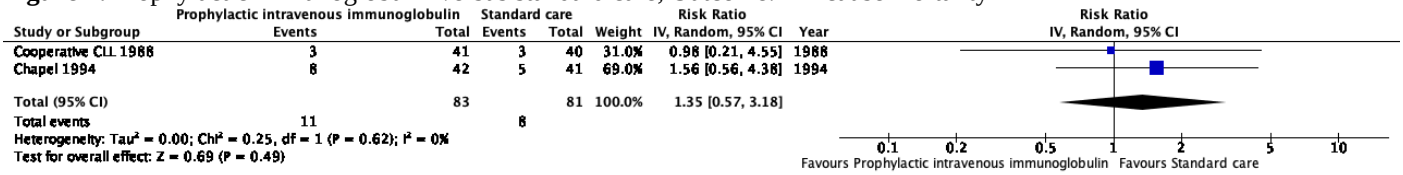

Figure 2: Prophylactic immunoglobulin versus standard care, Outcome: Infection-related mortality

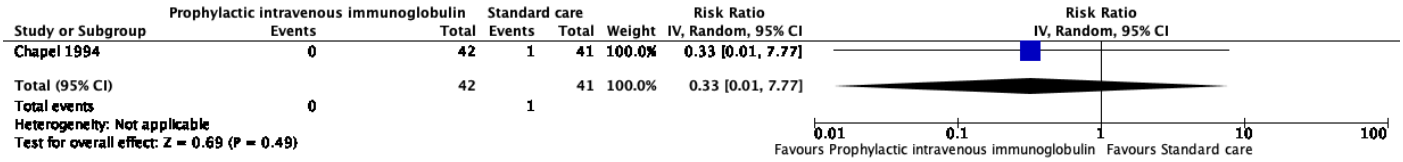

Figure 3: Prophylactic immunoglobulin versus standard care, Outcome: Patients with three or more clinically documented infections

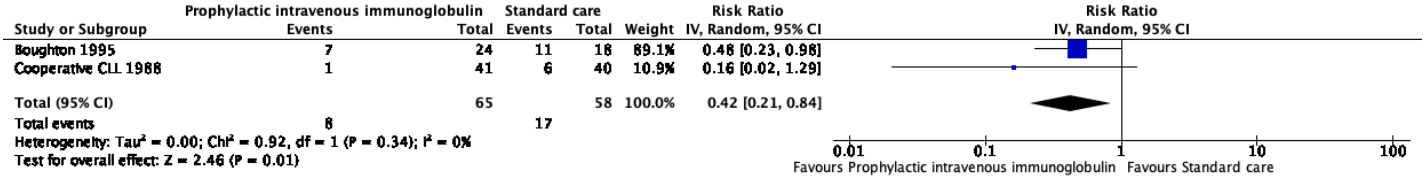

Figure 4: Prophylactic immunoglobulin versus standard care, Outcome: Patients with three or more serious infections

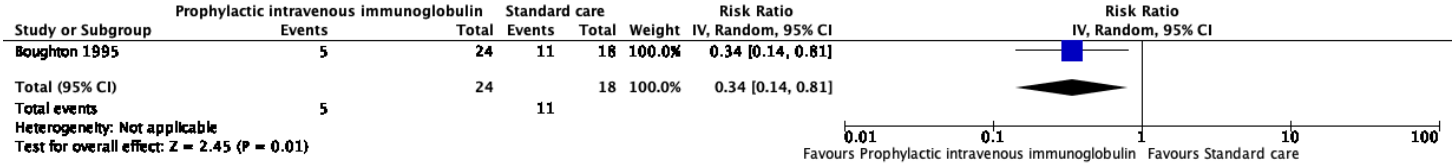

Figure 5: Prophylactic immunoglobulin versus standard care, Outcome: Patients with one or more microbiologically documented infections

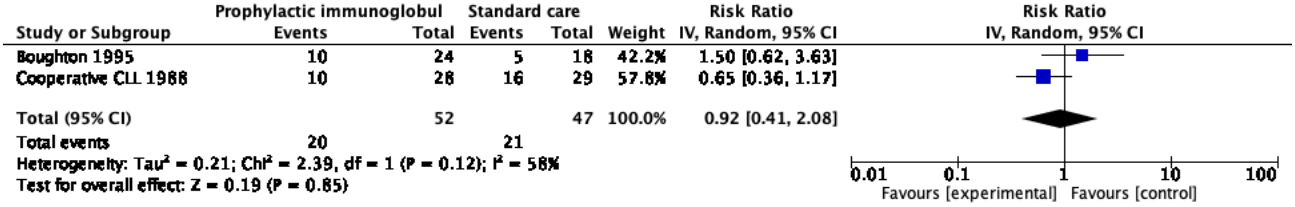

Figure 6: Prophylactic immunoglobulin versus standard care, Outcome: Adverse events

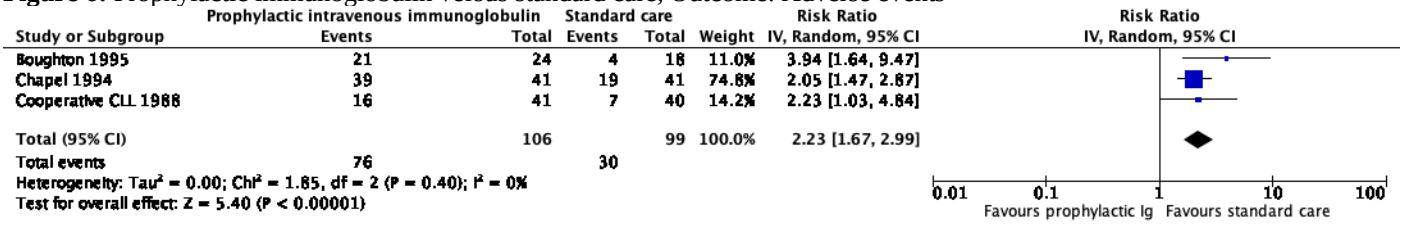

Figure 7: Prophylactic immunoglobulin versus standard care, Outcome: Adverse events leading to treatment discontinuation

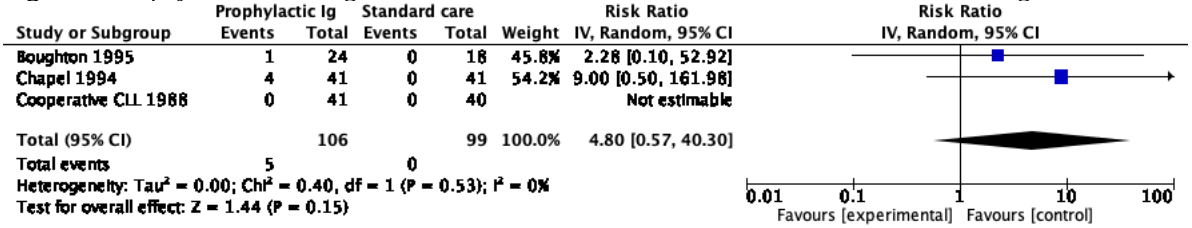

Figure 8: Prophylactic antibiotics versus standard care, Outcome: All-cause mortality

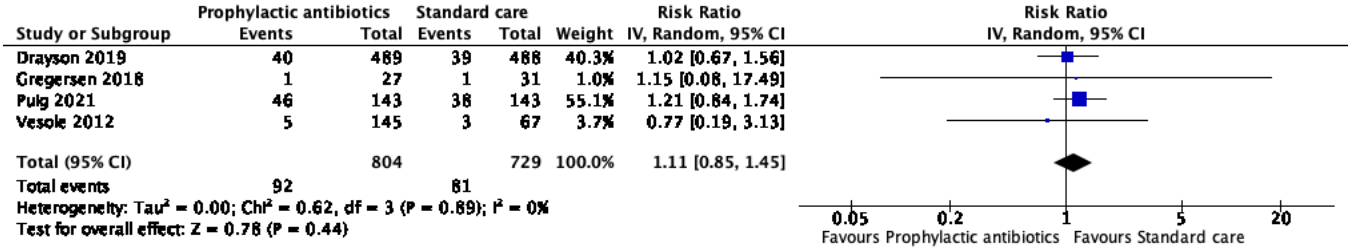

Figure 9: Prophylactic antibiotics versus standard care, Outcome: Infection-related mortality

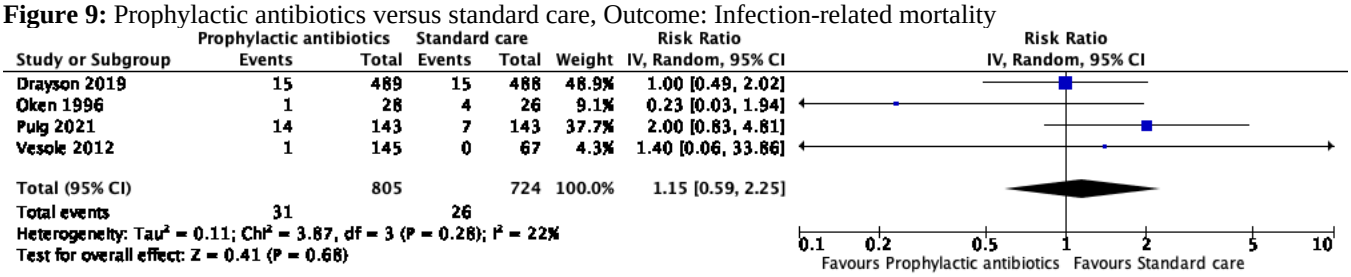

Figure 10: Prophylactic antibiotics versus standard care, Outcome: Patients with one or more serious infections

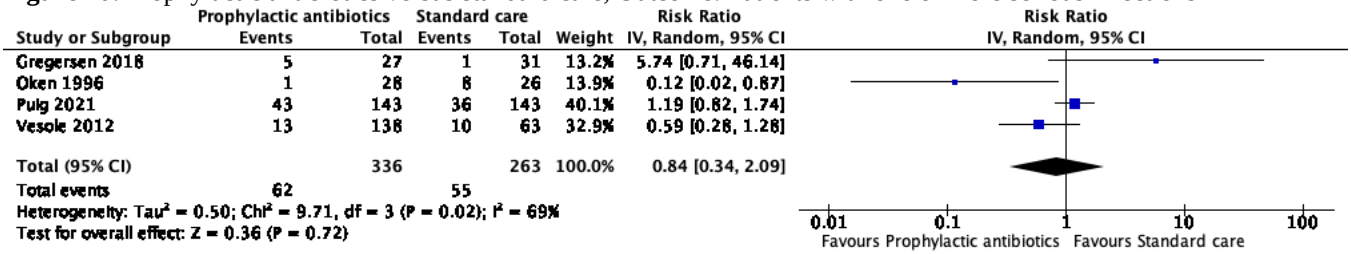

Figure 11: Prophylactic antibiotics versus standard care, Outcome: Patients with one or more microbiologically documented infections

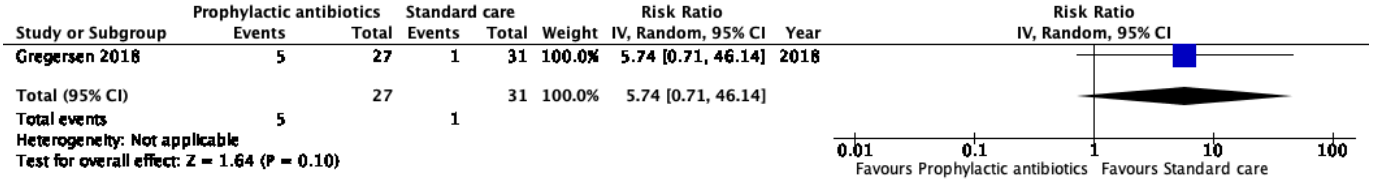

Figure 12: Prophylactic antibiotics versus standard care, Outcome: Adverse events

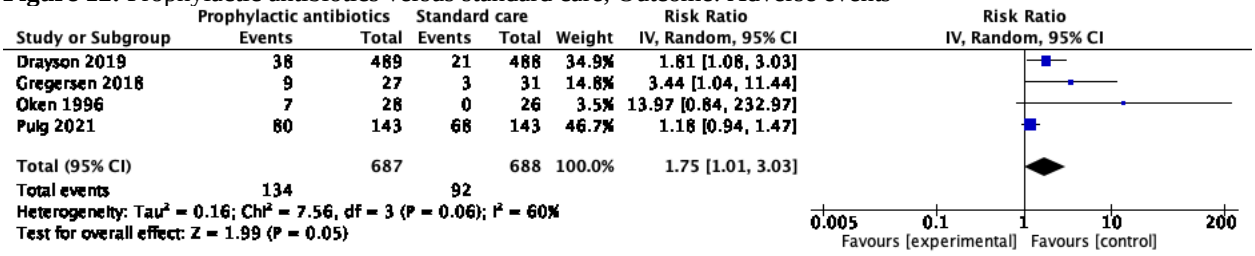

Figure 13: Prophylactic antibiotics by subgroup (publications after 2000), Outcome: Patients with one or more clinically documented infections

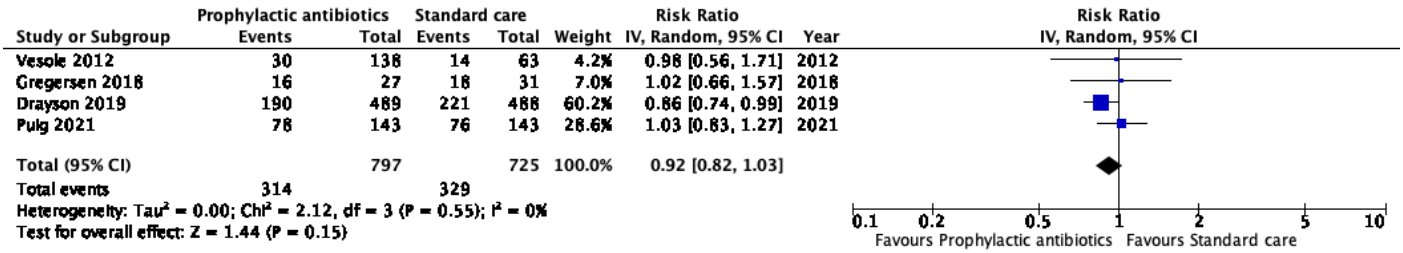

Figure 14: Prophylactic vaccinations versus standard care, Outcome: All-cause mortality

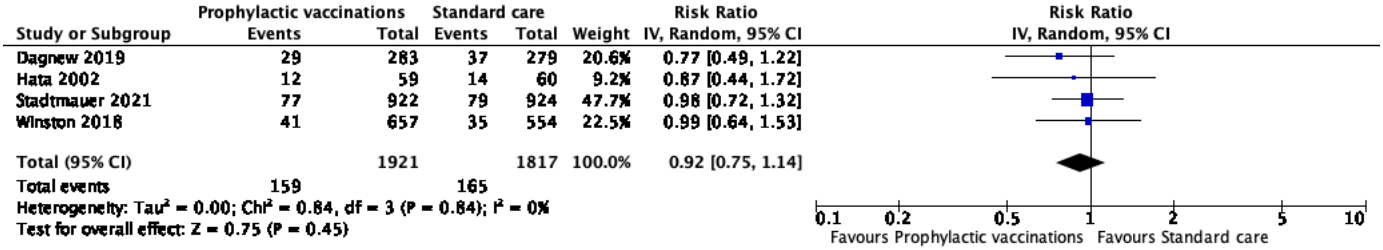

Figure 15: Prophylactic vaccinations versus standard care, Outcome: Infection-related mortality

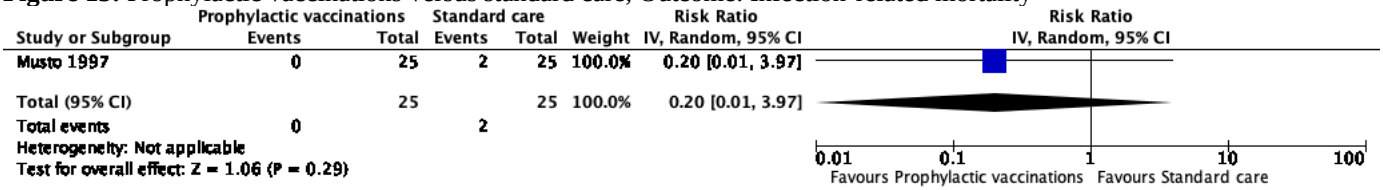

Figure 16: Prophylactic vaccinations versus standard care, Outcome: Patients with one or more microbiologically documented infections

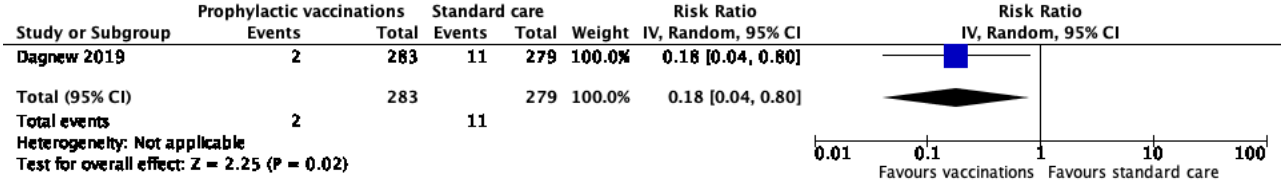

Figure 17: Prophylactic vaccinations versus standard care, Outcome: Adverse events

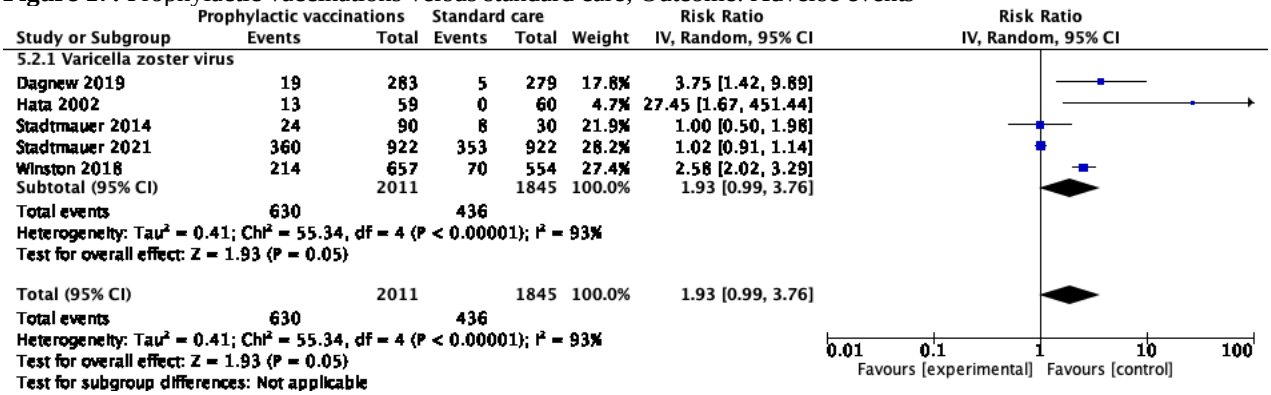

Figure 18: Prophylactic vaccinations comparing differing doses of vaccinations, Outcome: Patients with one or more clinically documented infections

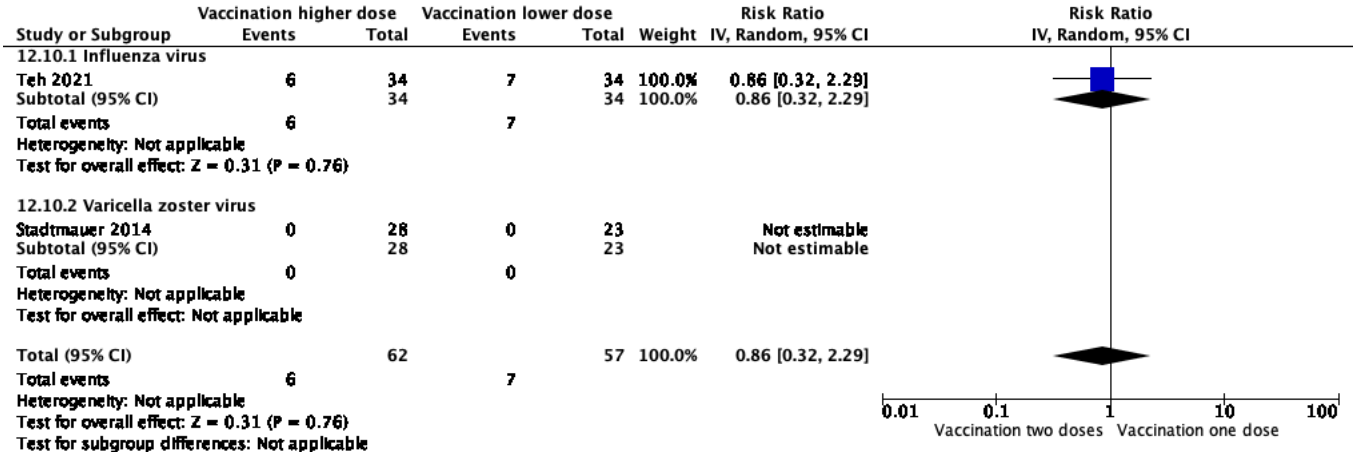

Figure 19: Prophylactic vaccinations comparing differing doses of vaccinations, Outcome: Patients with one or more microbiologically documented infections

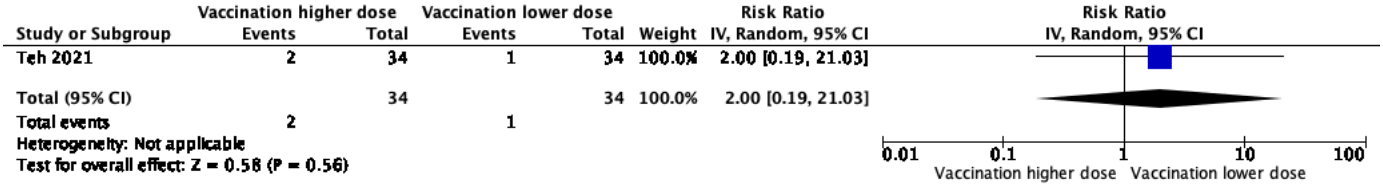

Figure 20: Prophylactic vaccinations comparing differing doses of vaccinations, Outcome: Adverse events