# **SUPPLEMENTARY MATERIAL**

Supplementary Table 1. Search strategies

1. Embase search strategy performed March 29, 2021. Limits: February 1, 2019 – March 29, 2021

| Search No. | Search Terms | Results |
| --- | --- | --- |
| **Interventions** |
| #1 | subcuvia:ti,ab,de OR cuvitru:ti,ab,de OR ig20gly:ti,ab,de OR i.g.-20GLY:ti,ab,de OR ig20-gly:ti,ab,de OR i.g.-20-gly:ti,ab,de OR Hizentra:ti,ab,de OR HizentraR:ti,ab,de OR IgPro20:ti,ab,de OR Ig-Pro20:ti,ab,de OR Ig-Pro-20:ti,ab,de OR IgPro-20:ti,ab,de | 286 |
| #2 | 'immunoglobulin'/dd\_sc OR 'immunoglobulin G'/dd\_sc OR 'human immunoglobulin’/dd\_sc | 1,102 |
| #3 | scig:ti,ab,de OR scigs:ti,ab,de OR scgg:ti,ab,de OR scggs:ti,ab,de OR igsc:ti,ab,de OR igscs:ti,ab,de OR sqig:ti,ab,de OR sqigs:ti,ab,de OR sc-i.g.:ti,ab,de OR sc-igs:ti,ab,de OR sc-gg:ti,ab,de OR sc-ggs:ti,ab,de OR i.g.-sc:ti,ab,de OR i.g.-scs:ti,ab,de | 979 |
| #4 | ((subcutaneous OR "for subcutaneous" OR subcutaneous-infusion OR subcutaneously OR sc OR "s.c." OR subq OR “sub q” OR hypodermoclysis) NEAR/2 (immunoglobulin\* OR immuneglobulin\* OR immune-globulin\* OR gammaglobulin\* OR gamma-globulin\* OR Gammagard OR kiovig OR “igg” OR “iggs” OR scig OR “i.g.” OR "igs" OR igsc OR scgg OR sqig OR sc-i.g., OR sc-gg OR i.g.-sc OR "Polyclonal-antibodies" OR "Polyvalent antibodies" OR "igrt" OR "igrts" OR "HNIG" OR "HNIGs")):ti,ab,de | 1,465 |
| #5 | HyQvia:ti,ab,de OR "ighy":ti,ab,de OR i.g.-hy:ti,ab,de OR "fscig":ti,ab,de OR "fscigs":ti,ab,de | 142 |
| #6 | ((rHuPH20 OR Hylenex OR r-huph20 OR RHU-PH20 OR RHUPH-20 OR r-hu-ph-20 OR rHuPH20 OR rHuPH2O OR r-huph2O OR RHU-PH2O OR RHUPH-2O OR r-hu-ph-2O OR rHuPH2O OR Enhanze OR hyaluronidase OR hyaluronoglucosidas OR Hyaluronoglucosaminidase OR PH20 OR ph-20 OR huph20 OR huph-20 OR PH2O OR ph-2O OR rhuph2O OR huph2O OR huph-2O) NEAR/3 (immunoglobulin\* OR immuneglobulin\* OR immune-globulin\* OR gammaglobulin\* OR gamma-globulin\* OR Gammagard OR kiovig OR “igg” OR “iggs” OR scig OR “i.g.” OR "igs" OR igsc OR scgg OR sqig OR sc-i.g., OR sc-gg OR i.g.-sc OR "Polyclonal-antibodies" OR "Polyvalent antibodies" OR "igrt" OR "igrts" OR "HNIG" OR "HNIGs”)):ti,ab,de | 93 |
| #7 | (Facilitated NEXT/3 (immunoglobulin\* OR immuneglobulin\* OR immune-globulin\* OR gammaglobulin\* OR gamma-globulin\* OR Gammagard OR kiovig OR igg OR iggs OR scig OR “i.g.” OR "igs" OR igsc OR scgg OR sqig OR sc-i.g., OR sc-gg OR i.g.-sc OR "Polyclonal-antibodies" OR "Polyvalent antibodies" OR "igrt" OR "igrts" OR "HNIG" OR "HNIGs")):ti,ab,de | 86 |
| #8 | #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 | 2,414 |
| **Population** |
| #9 | ("immune deficiency":de OR dysgammaglobulinemia:de OR "cellular immunodeficiency":de OR “immunoglobulin deficiency":de OR “immunoglobulin G deficiency":de OR "granulocytopenia":de OR "humoral immune deficiency":de OR agammaglobulinemia:de) AND (Primary:ti,ab OR Pri-mary:ti,ab OR Hereditary:ti,ab OR Congenital:ti,ab OR Inborn:ti,ab OR Familial:ti,ab OR Genetic:ti,ab OR Autosomal:ti,ab OR heterozygous:ti,ab OR homozygous:ti,ab OR recessive:ti,ab) | 31,457 |
| #10 | (((Primary OR pri-mary OR Hereditary OR Congenital OR Inborn OR Familial OR Genetic OR Autosomal OR heterozygous OR homozygous OR recessive) NEAR/1 (Immune-Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno-Deficien\* OR Immunedeficien\* OR Immune-Deficien\* OR Immune-Disorder\* OR Immunedisorder\* OR Immune-Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficien\*”))):ti,ab,de | 12,060 |
| #11 | ((PID:ti,ab OR PIDs:ti,ab OR PIDD:ti,ab OR PIDDs:ti,ab) AND (Immune-Disease\*:ti,ab OR Immunedisease\*:ti,ab OR Immunodeficien\*:ti,ab OR Immuno-Deficien\*:ti,ab OR Immunedeficien\*:ti,ab OR Immune-Deficien\*:ti,ab OR Immune-Disorder\*:ti,ab OR Immunedisorder\*:ti,ab OR Immune-Syndrome\*:ti,ab OR Agammaglobulin\*:ti,ab OR hypogammaglobulin\*:ti,ab OR dysgammaglobulin\*:ti,ab OR “antibody deficiency”:ti,ab OR "Antibody deficiencies":ti,ab)) | 2,844 |
| #12 | #10 OR #11 | 12,228 |
| #13 | "common variable immunodeficiency":de OR "CVID":ti,ab OR (("common variable" NEAR/1 (Immune-Disease OR Immune-Diseases OR Immunedisease\* OR Immunodeficien\* OR Immuno-Deficien\* OR Immunedeficien\* OR Immune-Deficien\* OR Immune-Disorder\* OR Immunedisorder\* OR Immune-Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency” OR "Antibody deficiencies")):ti,ab) | 6,323 |
| #14 | ("autosomal recessive severe combined immunodeficiency":de OR ‘severe combined immunodeficiency’:de OR "combined immunodeficiency":de OR "Omenn syndrome":de OR "bare lymphocyte syndrome":de) OR (SCID:ti,ab AND (Severe-Combined:ti,ab OR Immune-Disease\*:ti,ab OR Immunedisease\*:ti,ab OR Immunodeficien\*:ti,ab OR Immuno-Deficien\*:ti,ab OR Immunedeficien\*:ti,ab OR Immune-Deficien\*:ti,ab OR Immune-Disorder\*:ti,ab OR Immunedisorder\*:ti,ab OR Immune-Syndrome\*:ti,ab OR Agammaglobulin\*:ti,ab OR hypogammaglobulin\*:ti,ab OR dysgammaglobulin\*:ti,ab OR “antibody deficiency”:ti,ab OR "Antibody deficiencies":ti,ab))  | 16,946 |
| #15 | ((“Severe Combined”) NEAR/1 (Immune-Disease OR Immune-Diseases OR Immunedisease\* OR Immunodeficien\* OR Immuno-Deficien\* OR Immunedeficien\* OR Immune-Deficien\* OR Immune-Disorder\* OR Immunedisorder\* OR Immune-Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency” OR "Antibody deficiencies")):ti,ab | 11,121 |
| #16 | #14 OR #15 | 19,615 |
| #17 | “purine nucleoside phosphorylase deficiency”:de OR “Purine Nucleoside Phosphorylase deficien\*”:ti,ab | 268 |
| #18 | "complement disorder":de OR "complement deficiency":de OR (“complement disorder”:ti,ab AND (Immune-Disease\*:ti,ab OR Immunedisease\*:ti,ab OR Immunodeficien\*:ti,ab OR Immuno-Deficien\*:ti,ab OR Immunedeficien\*:ti,ab OR Immune-Deficien\*:ti,ab OR Immune-Disorder\*:ti,ab OR Immunedisorder\*:ti,ab OR Immune-Syndrome\*:ti,ab OR Agammaglobulin\*:ti,ab OR hypogammaglobulin\*:ti,ab OR dysgammaglobulin\*:ti,ab OR “antibody deficiency”:ti,ab OR "Antibody deficiencies":ti,ab)) | 2,798 |
| #19 | "phagocyte dysfunction":de OR "Chediak Higashi syndrome":de OR "chronic granulomatous disease":de OR (((“Chediak Higashi” OR “Chronic Granulomatous”) NEAR/1 (deficien\* OR disorder OR disease OR syndrome OR patient OR Immune-Disease OR Immunedisease\* OR Immunodeficien\* OR Immuno-Deficien\* OR Immunedeficien\* OR Immune-Deficien\* OR Immune-Disorder\* OR Immunedisorder\* OR Immune-Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency” OR "Antibody deficiencies")):ti,ab) | 9,046 |
| #20 | "DiGeorge syndrome":de OR ((DiGeorge NEAR/1 (deficien\* OR disorder OR disease OR syndrome OR patient OR Immune-Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno-Deficien\* OR Immunedeficien\* OR Immune-Deficien\* OR Immune-Disorder\* OR Immunedisorder\* OR Immune-Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency” OR "Antibody deficiencies")):ti,ab) | 3,859 |
| #21 | “JAK3 deficiency":de OR ((JAK3 deficien\*:ti,ab OR JAK 3 deficien\*:ti,ab OR “janus kinase 3”:ti,ab) AND (Immune-Disease\*:ti,ab OR Immunedisease\*:ti,ab OR Immunodeficien\*:ti,ab OR Immuno-Deficien\*:ti,ab OR Immunedeficien\*:ti,ab OR Immune-Deficien\*:ti,ab OR Immune-Disorder\*:ti,ab OR Immunedisorder\*:ti,ab OR Immune-Syndrome\*:ti,ab OR Agammaglobulin\*:ti,ab OR hypogammaglobulin\*:ti,ab OR dysgammaglobulin\*:ti,ab OR “antibody deficiency”:ti,ab OR "Antibody deficiencies":ti,ab)) | 294 |
| #22 | "immunoglobulin A deficiency":de OR SigAD:ti,ab OR ((("Selective IgA" OR immunoglobulin-A OR Immune-globulin-A OR gammaglobulin-A) NEAR/1 (deficien\* OR disorder OR disease OR syndrome OR patient)):ti,ab) | 3,751 |
| #23 | "X linked severe combined immunodeficiency":de OR “X linked agammaglobulinemia":de OR ((("X linked") NEAR/1 (Immune-Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno-Deficien\* OR Immunedeficien\* OR Immune-Deficien\* OR Immune-Disorder\* OR Immunedisorder\* OR Immune-Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency” OR "Antibody deficiencies")):ti,ab) OR XLA:ti,ab | 3,210 |
| #24 | "adenosine deaminase deficiency":de OR “Adenosine deaminase deficiency”:ti,ab | 1,312 |
| #25 | "ataxia telangiectasia":de OR ataxia-telangiectasia:ti,ab | 9,610 |
| #26 | "transient hypogammaglobulinemia of infancy":de OR “Transient Hypogammaglobulin\* of Infancy”:ti,ab OR “Transient agammaglobulin\* of Infancy”:ti,ab | 183 |
| #27 | "severe congenital neutropenia":de OR “Severe Congenital Neutropenia”:ti,ab | 1,151 |
| #28 | "congenital disorder of glycosylation type 2c":de OR "leukocyte adhesion deficiency":de OR “Leukocyte Adhesion Deficiency”:ti,ab OR "congenital disorder of glycosylation type 2c":ti,ab OR "congenital disorder of glycosylation type IIc":ti,ab OR "Leukocyte-Adhesion Deficiency Syndrome":ti,ab | 1,189 |
| #29 | “immunoglobulin M deficiency":de OR (((IG-M OR IGM OR immunoglobulin-M OR Immune-globulin-M OR gammaglobulin-M) NEAR/1 (deficien\* OR disorder OR disease OR syndrome OR patient OR Immune-Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno-Deficien\* OR Immunedeficien\* OR Immune-Deficien\* OR Immune-Disorder\* OR Immunedisorder\* OR Immune-Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency” OR "Antibody deficiencies")):ti,ab) | 1,442 |
| #30 | ("Wiskott Aldrich syndrome":de) OR ((Wiskott-Aldrich) NEAR/1 (disease OR syndrome OR disorder OR patient)):ti,ab | 5,808 |
| #31 | "hyper IgE syndrome":de OR ((("Hyper IgE” OR "hyper Immunoglobulin E" OR “Hyper Immune globulin E”) NEAR/1 (deficien\* OR disorder OR disease OR syndrome OR patient OR Immune-Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno-Deficien\* OR Immunedeficien\* OR Immune-Deficien\* OR Immune-Disorder\* OR Immunedisorder\* OR Immune-Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency” OR "Antibody deficiencies")):ti,ab) | 2,099 |
| #32 | "Nijmegen breakage syndrome":ti,ab OR ((("Nijmegen Breakage") NEAR/1 (disease OR syndrome OR disorder OR patient)):ti,ab) | 719 |
| #33 | "immunoglobulin G4 related disease":de OR (((IgG-subclass OR immunoglobulin-G1 OR gammaglobulin-G1 OR Immune-globulin-G1 OR IgG1 OR IgG-1 OR immunoglobulin-G2 OR gammaglobulin-G2 OR Immune-globulin-G2 OR IgG2 OR IgG-2 OR immunoglobulin-G3 OR gammaglobulin-G3 OR Immune-globulin-G3 OR IgG3 OR IgG-3 OR immunoglobulin-G4 OR gammaglobulin-G4 OR Immune-globulin-G4 OR IgG4 OR IgG-4) NEAR/1 (deficien\* OR disorder OR disease OR syndrome OR patient OR Immune-Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno-Deficien\* OR Immunedeficien\* OR Immune-Deficien\* OR Immune-Disorder\* OR Immunedisorder\* OR Immune-Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency” OR "Antibody deficiencies")):ti,ab) | 5,126 |
| #34 | #9 OR #12 OR #13 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 | 93,940 |
| #35 | #8 AND #34 | 1,225 |
| #36 | #35 AND ([article]/lim OR [article in press]/lim OR [erratum]/lim OR [review]/lim) AND [1-2-2019]/sd NOT [30-3-2021]/sd | 110 |
| #37 | #35 AND ([conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim) AND [1-2-2019]/sd NOT [30-3-2021]/sd | 101 |
| **All relevant studies** |
| #38 | #36 OR #37 | **211** |

IG = immunoglobulin; PID = primary immunodeficiency.

1. MEDLINE search strategy performed March 29, 2021. Limits: February 1, 2019 – March 29, 2021

| Search No. | Search Terms | Results |
| --- | --- | --- |
| Interventions |
| #1 | Subcuvia[Text Word] OR cuvitru[Text Word] OR ig20gly[Text Word] OR i.g.-20GLY[Text Word] OR ig20-gly[Text Word] OR i.g.-20-gly[Text Word] OR Hizentra[Text Word] or HizentraR[Text Word] or IgPro20[Text Word] OR Ig-Pro20[Text Word] OR Ig-Pro-20[Text Word] OR IgPro-20[Text Word] | 74 |
| #2 | ("Immunoglobulins/administration and dosage"[MeSH:NoExp] OR "Immunoglobulins/adverse effects"[MeSH:NoExp] OR "Immunoglobulins/poisoning"[MeSH:NoExp] OR "Immunoglobulins/therapeutic use"[MeSH:NoExp] OR "Immunoglobulins/toxicity"[MeSH:NoExp]) AND ("Infusions, Subcutaneous"[MeSH] OR "Injections, Subcutaneous"[MeSH]) | 178 |
| #3 | scig[Text Word] OR scigs[Text Word] OR scgg[Text Word] OR scggs[Text Word] OR igsc[Text Word] OR igscs[Text Word] OR sqig[Text Word] OR sqigs[Text Word] OR sc-i.g.[Text Word] OR sc-igs[Text Word] OR sc-gg[Text Word] OR sc-ggs[Text Word] OR i.g.-sc[Text Word] OR i.g.-scs[Text Word] | 393 |
| #4 | HyQvia[Text Word] OR "ighy"[Text Word] OR i.g.-hy[Text Word] OR "fscig"[Text Word] OR "fscigs"[Text Word] | 33 |
| #5 | (rHuPH20[Text Word] OR Hylenex[Text Word] OR r-huph20[Text Word] OR RHU-PH20[Text Word] OR RHUPH-20[Text Word] OR r-hu-ph-20[Text Word] OR rHuPH20[Text Word] OR rHuPH2O[TEXT Word] OR r-huph2O[Text Word] OR RHU-PH2O[Text Word] OR RHUPH-2O[Text Word] OR r-hu-ph-2O[Text Word] OR rHuPH2O[Text Word] OR Enhanze[Text Word] OR hyaluronidase[Text Word] OR hyaluronoglucosidas[Text Word] OR Hyaluronoglucosaminidase[Text Word] OR PH20[Text Word] OR ph-20[Text Word] OR huph20[Text Word] OR huph-20[Text Word] OR PH2O[Text Word] OR ph-2O[Text Word] OR rhuph2O[Text Word] OR huph2O[Text Word] OR huph-2O[Text Word]) AND (immunoglobulin\*[Text Word] OR immuneglobulin\*[Text Word] OR immune-globulin\*[Text Word] OR gammaglobulin\*[Text Word] OR gamma-globulin\*[Text Word] OR Gammagard[Text Word] OR kiovig[Text Word] OR igg[Text Word] OR “iggs”[Text Word] OR scig[Text Word] OR i.g.[Text Word] OR "igs"[Text Word] OR igsc[Text Word] OR scgg[Text Word] OR sqig[Text Word] OR sc-i.g.[Text Word] OR sc-gg[Text Word] OR i.g.-sc[Text Word] OR "Polyclonal-antibodies"[Text Word] OR "Polyvalent antibodies"[Text Word] OR "igrt"[Text Word] OR "igrts"[Text Word] OR "HNIG"[Text Word] OR "HNIGs"[Text Word]) | 299 |
| #6 | Facilitated[Text Word] AND (immunoglobulin\*[Text Word] OR immuneglobulin\*[Text Word] OR immune-globulin\*[Text Word] OR gammaglobulin\*[Text Word] OR gamma-globulin\*[Text Word] OR Gammagard[Text Word] OR kiovig[Text word] OR igg[Text Word] OR iggs[Text Word] OR scig[Text Word] OR i.g.[Text Word] OR "igs"[Text Word] OR igsc[Text Word] OR scgg[Text Word] OR sqig[Text Word] OR sc-i.g.[Text Word] OR sc-gg[Text Word] OR i.g.-sc[Text Word] OR "Polyclonal-antibodies"[Text Word] OR "Polyvalent antibodies"[Text Word] OR "igrt"[Text Word] OR "igrts"[Text Word] OR "HNIG"[Text Word] OR "HNIGs"[Text Word]) | 1,409 |
| #7 | #1 OR #2 OR #3 OR #4 OR #5 OR #6 | 2,187 |
| **Population** |
| #8 | ("Immunologic Deficiency Syndromes"[MeSH:NoExp] OR "IgG Deficiency"[MeSH:NoExp] OR "Agammaglobulinemia"[MeSH:No Exp] OR "T-Lymphocytopenia, Idiopathic CD4-Positive"[MeSH:No Exp] OR "Dysgammaglobulinemia"[MeSH:NoExp] OR "Agranulocytosis"[MeSH:NoExp] OR "Granulocytopenia with Immunoglobulin Abnormality" [Supplementary Concept] OR "Immune Deficiency Disease" [Supplementary Concept]) AND (Primary[Title/Abstract] OR Pri-mary[Title/Abstract] OR Hereditary[Title/Abstract] OR Congenital[Title/Abstract] OR Inborn[Title/Abstract] OR Familial[Title/Abstract] OR Genetic[Title/Abstract] OR Autosomal[Title/Abstract] OR heterozygous[Title/Abstract] OR homozygous[Title/Abstract] OR recessive[Title/Abstract]) | 6,817 |
| #9 | (Primary[Title/Abstract] OR pri-mary[Title/Abstract] OR Hereditary[Title/Abstract] OR Congenital[Title/Abstract] OR Inborn[Title/Abstract] OR Familial[Title/Abstract] OR Genetic[Title/Abstract] OR Autosomal[Title/Abstract] OR heterozygous[Title/Abstract] OR homozygous[Title/Abstract] OR recessive[Title/Abstract] OR PID[Title/Abstract] OR “PIDs”[Title/Abstract] OR “PIDD”[Title/Abstract] OR “PIDDs”[Title/Abstract]) AND (Immune-Disease\*[Title/Abstract] OR Immunedisease\*[Title/Abstract] OR Immunodeficien\*[Title/Abstract] OR Immuno-Deficien\*[Title/Abstract] OR Immunedeficien\*[Title/Abstract] OR Immune-Deficien\*[Title/Abstract] OR Immune-Disorder\*[Title/Abstract] OR Immunedisorder[Title/Abstract] OR Immunedisorders[Title/Abstract] OR Immune-Syndrome[Title/Abstract] OR Immune-Syndromes[Title/Abstract] OR Agammaglobulin\*[Title/Abstract] OR hypogammaglobulin\*[Title/Abstract] OR dysgammaglobulin\*[Title/Abstract] OR antibody deficien\*[Title/Abstract]) | 32,720 |
| #10 | #8 OR #9 | 34,353 |
| #11 | "Common Variable Immunodeficiency"[MeSH:NoExp] OR “CVID”[Title/Abstract] OR ("common variable"[Title/Abstract] AND (Immune-Disease\*[Title/Abstract] OR Immunedisease\*[Title/Abstract] OR Immunodeficien\*[Title/Abstract] OR Immuno-Deficien\*[Title/Abstract] OR Immunedeficien\*[Title/Abstract] OR Immune-Deficien\*[Title/Abstract] OR Immune-Disorder\*[Title/Abstract] OR Immunedisorder\*[Title/Abstract] OR Immune-Syndrome\*[Title/Abstract] OR Agammaglobulin\*[Title/Abstract] OR hypogammaglobulin\*[Title/Abstract] OR dysgammaglobulin\*[Title/Abstract] OR “antibody deficiency”[Title/Abstract] OR "Antibody deficiencies"[Title/Abstract])) | 3,656 |
| #12 | "Severe Combined Immunodeficiency"[MeSH:NoExp] OR "Bare Lymphocyte Syndrome, Type II, Complementation Group A" [Supplementary Concept] OR "Bare lymphocyte syndrome 2" [Supplementary Concept] OR "Bare Lymphocyte Syndrome, Type I" [Supplementary Concept] OR “SCID”[Title/Abstract] OR ((Severe-Combined[Title/Abstract] OR “Severe Combined”[Title/Abstract]) AND (Immune-Disease\*[Title/Abstract] OR Immunedisease\*[Title/Abstract] OR Immunodeficien\*[Title/Abstract] OR Immuno-Deficien\*[Title/Abstract] OR Immunedeficien\*[Title/Abstract] OR Immune-Deficien\*[Title/Abstract] OR Immune-Disorder\*[Title/Abstract] OR Immunedisorder\*[Title/Abstract] OR Immune-Syndrome\*[Title/Abstract] OR Agammaglobulin\*[Title/Abstract] OR hypogammaglobulin\*[Title/Abstract] OR dysgammaglobulin\*[Title/Abstract] OR “antibody deficiency” [Title/Abstract] OR "Antibody deficiencies"[Title/Abstract])) OR ("SCID"[Title/Abstract) AND (Severe-Combined[Title/Abstract] OR “Severe Combined”[Title/Abstract] OR Immune-Disease\*[Title/Abstract] OR Immunedisease\*[Title/Abstract] OR Immunodeficien\*[Title/Abstract] OR Immuno-Deficien\*[Title/Abstract] OR Immunedeficien\*[Title/Abstract] OR Immune-Deficien\*[Title/Abstract] OR Immune-Disorder\*[Title/Abstract] OR Immunedisorder\*[Title/Abstract] OR Immune-Syndrome\*[Title/Abstract] OR Agammaglobulin\*[Title/Abstract] OR hypogammaglobulin\*[Title/Abstract] OR dysgammaglobulin\*[Title/Abstract] OR “antibody deficiency” [Title/Abstract] OR "Antibody deficiencies"[Title/Abstract]) | 11,213 |
| #13 | "Purine Nucleoside Phosphorylase Deficiency" [Supplementary Concept] OR "Purine-Nucleoside Phosphorylase/deficiency"[MeSH:NoExp] OR Purine Nucleoside Phosphorylase deficien\*[Title/Abstract] | 377 |
| #14 | complement disorder\*[Title/Abstract] OR complement deficien\*[Title/Abstract] OR (complement disease\*[Title/Abstract]) AND (Immune-Disease\*[Title/Abstract] OR Immunedisease\*[Title/Abstract] OR Immunodeficien\*[Title/Abstract] OR Immuno-Deficien\*[Title/Abstract] OR Immunedeficien\*[Title/Abstract] OR Immune- [Title/Abstract] OR Immune-Disorder\*[Title/Abstract] OR Immunedisorder\*[Title/Abstract] OR Immune-Syndrome\*[Title/Abstract] OR Agammaglobulin\*[Title/Abstract] OR hypogammaglobulin\*[Title/Abstract] OR dysgammaglobulin\*[Title/Abstract] OR “antibody deficiency”[Title/Abstract] OR "Antibody deficiencies"[Title/Abstract]) | 9,982 |
| #15 | "Phagocyte Bactericidal Dysfunction"[MeSH:NoExp] OR "Chediak-Higashi Syndrome"[MeSH:NoExp] OR "Granulomatous Disease, Chronic"[MeSH:NoExp] OR ((“Chediak Higashi”[Title/Abstract] OR “Chronic Granulomatous” [Title/Abstract]) AND (deficien\*[Title/Abstract] OR disorder[Title/Abstract] OR disease[Title/Abstract] OR syndrome[Title/Abstract] OR patient[Title/Abstract] OR Immune-Disease\*[Title/Abstract] OR Immunedisease\*[Title/Abstract] OR Immunodeficien\*[Title/Abstract] OR Immuno-Deficien\*[Title/Abstract] OR Immunedeficien\*[Title/Abstract] OR Immune-Deficien\*[Title/Abstract] OR Immune-Disorder[Title/Abstract] OR Immune-Disorders[Title/Abstract] OR Immunedisorder\*[Title/Abstract] OR Immune-Syndrome\*[Title/Abstract] OR Agammaglobulin\*[Title/Abstract] OR hypogammaglobulin\*[Title/Abstract] OR dysgammaglobulin\*[Title/Abstract] OR “antibody deficiency”[Title/Abstract] OR "Antibody deficiencies"[Title/Abstract])) | 7,005 |
| #16 | "DiGeorge Syndrome"[MeSH:NoExp] OR "22q11 Deletion Syndrome"[MeSH:NoExp] OR (DiGeorge[Title/Abstract] AND (deficien\*[Title/Abstract] OR disorder[Title/Abstract] OR disease[Title/Abstract] OR syndrome[Title/Abstract] OR patient[Title/Abstract] OR Immune-Disease\*[Title/Abstract] OR Immunedisease\*[Title/Abstract] OR Immunodeficien\*[Title/Abstract] OR Immuno-Deficien\*[Title/Abstract] OR Immunedeficien\*[Title/Abstract] OR Immune-Deficien\*[Title/Abstract] OR Immune-Disorder\*[Title/Abstract] OR Immunedisorder\*[Title/Abstract] OR Immune-Syndrome\*[Title/Abstract] OR Agammaglobulin\*[Title/Abstract] OR hypogammaglobulin\*[Title/Abstract] OR dysgammaglobulin\*[Title/Abstract] OR “antibody deficiency”[Title/Abstract] OR "Antibody deficiencies"[Title/Abstract])) | 3,194 |
| #17 | "Janus Kinase 3/deficiency"[MeSH:NoExp] OR ((JAK3 deficien\*[Title/Abstract] OR JAK 3 deficien\*[Title/Abstract] OR “janus kinase 3”[Title/Abstract]) AND (Immune-Disease\*[Title/Abstract] OR Immunedisease\*[Title/Abstract] OR Immunodeficien\*[Title/Abstract] OR Immuno-Deficien\*[Title/Abstract] OR Immunedeficien\*[Title/Abstract] OR Immune-Deficien\*[Title/Abstract] OR Immune-Disorder\*[Title/Abstract] OR Immunedisorder\*[Title/Abstract] OR Immune-Syndrome\*[Title/Abstract] OR Agammaglobulin\*[Title/Abstract] OR hypogammaglobulin\*[Title/Abstract] OR dysgammaglobulin\*[Title/Abstract] OR “antibody deficiency”[Title/Abstract] OR "Antibody deficiencies"[Title/Abstract])) | 99 |
| #18 | "IgA Deficiency"[MeSH:NoExp] OR (("Selective IgA"[Title/Abstract] OR “immunoglobulin-A”[Title/Abstract] OR “Immune-globulin-A”[Title/Abstract] OR “gammaglobulin-A”[Title/Abstract]) AND (deficien\*[Title/Abstract] OR disorder[Title/Abstract] OR disease[Title/Abstract] OR syndrome[Title/Abstract] OR patient[Title/Abstract])) OR "SigAD"[Title/Abstract] | 5,309 |
| #19 | "X-Linked Combined Immunodeficiency Diseases"[MeSH] OR XLA[Title/Abstract] OR (("X linked"[Title/Abstract] OR X-linked[Title/Abstract]) AND (Immune-Disease\*[Title/Abstract] OR Immunedisease\*[Title/Abstract] OR Immunodeficien\*[Title/Abstract] OR Immuno-Deficien\*[Title/Abstract] OR Immunedeficien\*[Title/Abstract] OR Immune-Deficien\*[Title/Abstract] OR Immune-Disorder\*[Title/Abstract] OR Immunedisorder\*[Title/Abstract] OR Immune-Syndrome\*[Title/Abstract] OR Agammaglobulin\*[Title/Abstract] OR hypogammaglobulin\*[Title/Abstract] OR dysgammaglobulin\*[Title/Abstract] OR “antibody deficiency” [Title/Abstract] OR "Antibody deficiencies"[Title/Abstract])) | 3,294 |
| #20 | "Adenosine Deaminase/deficiency"[MeSH:NoExp] OR “Adenosine deaminase deficiency”[Title/Abstract] OR “Adenosine deaminase deficiencies”[Title/Abstract] | 1,201 |
| #21 | "Ataxia Telangiectasia"[MeSH:NoExp] OR ataxia-telangiectasia[Title/Abstract] | 7,474 |
| #22 | (Transient Hypogammaglobulin\*[Text Word] OR Transient agammaglobuli\*[Text Word]) AND (Infancy[Text Word] OR Infant[Text Word]) | 123 |
| #23 | “Severe Congenital Neutropenia”[Text word] | 538 |
| #24 | "Leukocyte-Adhesion Deficiency Syndrome"[MeSH:NoExp] OR "Congenital disorder of glycosylation, type 2C" [Supplementary Concept] OR “Leukocyte Adhesion Deficiency”[Title/Abstract] OR "congenital disorder of glycosylation type 2c"[Title/Abstract] OR "congenital disorder of glycosylation type IIc"[Title/Abstract] OR "Leukocyte-Adhesion Deficiency Syndrome"[Title/Abstract] | 730 |
| #25 | "Immunoglobulin M/deficiency"[MeSH] OR ((“IG-M”[Title/Abstract] OR “IGM”[Title/Abstract] OR “immunoglobulin-M”[Title/Abstract] OR “Immune-globulin-M”[Title/Abstract] OR “gammaglobulin-M”[Title/Abstract]) AND (deficien\*[Title/Abstract] OR disorder[Title/Abstract] OR disease[Title/Abstract] OR syndrome[Title/Abstract] OR patient[Title/Abstract] OR Immune-Disease\*[Title/Abstract] OR Immunedisease\*[Title/Abstract] OR Immunodeficien\*[Title/Abstract] OR Immuno-Deficien\*[Title/Abstract] OR Immunedeficien\*[Title/Abstract] OR Immune-Deficien\*[Title/Abstract] OR Immune-Disorder\*[Title/Abstract] OR Immunedisorder\*[Title/Abstract] OR Immune-Syndrome\*[Title/Abstract] OR Agammaglobulin\*[Title/Abstract] OR hypogammaglobulin\*[Title/Abstract] OR dysgammaglobulin\*[Title/Abstract] OR “antibody deficiency” [Title/Abstract] OR "Antibody deficiencies"[Title/Abstract])) | 29,691 |
| #26 | "Wiskott-Aldrich Syndrome"[MeSH:NoExp] OR (Wiskott-Aldrich[Title/Abstract] AND (disease[Title/Abstract] OR syndrome[Title/Abstract] OR disorder[Title/Abstract] OR patient[Title/Abstract])) | 2,696 |
| #27 | "Job Syndrome"[MeSH:NoExp] OR (("Hyper IgE"[Title/Abstract] OR "hyper Immunoglobulin E"[Title/Abstract] OR “Hyper Immune globulin E”[Title/Abstract]) AND (deficien\*[Title/Abstract] OR disorder[Title/Abstract] OR disease[Title/Abstract] OR syndrome[Title/Abstract] OR patient[Title/Abstract] OR Immune-Disease\*[Title/Abstract] OR Immunedisease\*[Title/Abstract] OR Immunodeficien\*[Title/Abstract] OR Immuno-Deficien\*[Title/Abstract] OR Immunedeficien\*[Title/Abstract] OR Immune-Deficien\*[Title/Abstract] OR Immune-Disorder\*[Title/Abstract] OR Immunedisorder\*[Title/Abstract] OR Immune-Syndrome\*[Title/Abstract] OR Agammaglobulin\*[Title/Abstract] OR hypogammaglobulin\*[Title/Abstract] OR dysgammaglobulin\*[Title/Abstract] OR “antibody deficiency”[Title/Abstract] OR "Antibody deficiencies"[Title/Abstract])) | 1,140 |
| #28 | "Nijmegen Breakage Syndrome"[MeSH] OR ("Nijmegen Breakage"[Title/Abstract] AND (disease[Title/Abstract] OR syndrome[Title/Abstract] OR disorder[Title/Abstract] OR patient[Title/Abstract])) | 588 |
| #29 | "Immunoglobulin G4-Related Disease"[MeSH:NoExp] OR ((IgG-subclass[Title/Abstract] OR immunoglobulin-G1[Title/Abstract] OR gammaglobulin-G1[Title/Abstract] OR Immune-globulin-G1[Title/Abstract] OR IgG1[Title/Abstract] OR IgG-1[Title/Abstract] OR immunoglobulin-G2[Title/Abstract] OR gammaglobulin-G2[Title/Abstract] OR Immune-globulin-G2[Title/Abstract] OR IgG2[Title/Abstract] OR IgG-2[Title/Abstract] OR immunoglobulin-G3[Title/Abstract] OR gammaglobulin-G3[Title/Abstract] OR Immune-globulin-G3[Title/Abstract] OR IgG3[Title/Abstract] OR IgG-3[Title/Abstract] OR immunoglobulin-G4[Title/Abstract] OR gammaglobulin-G4[Title/Abstract] OR Immune-globulin-G4[Title/Abstract] OR IgG4[Title/Abstract] OR IgG-4[Title/Abstract]) AND (deficien\*[Title/Abstract] OR disorder[Title/Abstract] OR disease[Title/Abstract] OR syndrome[Title/Abstract] OR patient[Title/Abstract] OR Immune-Disease\*[Title/Abstract] OR Immunedisease\*[Title/Abstract] OR Immunodeficien\*[Title/Abstract] OR Immuno-Deficien\*[Title/Abstract] OR Immunedeficien\*[Title/Abstract] OR Immune-Deficien\*[Title/Abstract] OR Immune-Disorder\*[Title/Abstract] OR Immunedisorder\*[Title/Abstract] OR Immune-Syndrome\*[Title/Abstract] OR Agammaglobulin\*[Title/Abstract] OR hypogammaglobulin\*[Title/Abstract] OR dysgammaglobulin\*[Title/Abstract] OR “antibody deficiency”[Title/Abstract] OR "Antibody deficiencies"[Title/Abstract])) | 13,347 |
| #30 | #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 | 117,741 |
| **All relevant studies** |
| #31 | #7 AND #30 | **350** |
| #32 | #31 AND ("2019/02/01"[Date - Publication] : "2021/03/29"[Date - Publication]) OR ("2019/02/01"[Date - Entry] : "2021/03/29"[Date - Entry])) | **68** |

IG = immunoglobulin; MeSH = Medical Subject Heading; PID = primary immunodeficiency.

1. Cochrane Library search strategy performed March 29, 2021. Limits: February 1, 2019 – March 29, 2021

| Search No. | Search Terms | Results |
| --- | --- | --- |
| Interventions |
| #1 | (Subcuvia OR cuvitru OR "ig20gly" OR "i.g. 20GLY" OR "ig20 gly" OR "i.g. 20 gly" OR Hizentra OR "HizentraR" OR "IgPro20" OR "Ig Pro20" OR "Ig Pro 20" OR "IgPro 20"):ti,ab,kw | 61 |
| #2 | MeSH descriptor: [Immunoglobulins] this term only | 1,302 |
| #3 | (“scig” OR “scigs” OR “scgg” OR “scggs” OR “igsc” OR “igscs” OR “sqig” OR “sqigs” OR “sc i.g.” OR “sc igs” OR “sc gg” OR “sc ggs” OR “i.g. sc” OR “i.g. scs”) (Word variations have been searched) | 88 |
| #4 | (HyQvia OR "ighy" OR “i.g. hy” OR "fscig" OR "fscigs") | 16 |
| #5 | (rHuPH20 OR Hylenex OR “r huph20” OR “RHU PH20” OR “RHUPH 20” OR “r hu ph 20” OR rHuPH20 OR rHuPH2O OR “r huph2O” OR “RHU PH2O” OR “RHUPH 2O” OR “r hu ph 2O” OR rHuPH2O OR Enhanze OR hyaluronidase OR hyaluronoglucosidas OR Hyaluronoglucosaminidase OR PH20 OR “ph 20” OR huph20 OR “huph 20” OR PH2O OR “ph 2O” OR rhuph2O OR huph2O OR “huph 2O”) AND (immunoglobulin\* OR immuneglobulin\* OR immune globulin\* OR gammaglobulin\* OR gamma globulin\* OR Gammagard OR kiovig OR igg OR iggs OR scig OR “i.g.,” OR igs OR igsc OR scgg OR sqig OR “sc i.g.,” OR “sc gg” OR “i.g. sc” OR "Polyclonal antibodies" OR "Polyvalent antibodies" OR "igrt" OR "igrts" OR "HNIG" OR "HNIGs") | 46 |
| #6 | Facilitated AND (immunoglobulin\* OR immuneglobulin\* OR immune globulin\* OR gammaglobulin\* OR gamma globulin\* OR Gammagard OR kiovig OR igg OR iggs OR scig OR “i.g.,” OR igs OR igsc OR scgg OR sqig OR “sc i.g.,” OR “sc gg” OR “i.g. sc” OR "Polyclonal antibodies" OR "Polyvalent antibodies" OR igrt OR igrts OR "HNIG" OR "HNIGs") | 82 |
| #7 | #1 OR #2 OR #3 OR #4 OR #5 OR #6 | 1,499 |
| **Population** |
| #8 | MeSH descriptor: [Immunologic Deficiency Syndromes] this term only | 575 |
| #9 | MeSH descriptor: [IgG Deficiency] this term only | 8 |
| #10 | MeSH descriptor: [Agammaglobulinemia] this term only | 44 |
| #11 | MeSH descriptor: [T-Lymphocytopenia, Idiopathic CD4-Positive] this term only | 3 |
| #12 | MeSH descriptor: [Dysgammaglobulinemia] this term only | 3 |
| #13 | MeSH descriptor: [Agranulocytosis] this term only | 314 |
| #14 | #8 OR #9 OR #10 OR #11 OR #12 OR #13 | 937 |
| #15 | (Primary OR “Pri mary” OR Hereditary OR Congenital OR Inborn OR Familial OR Genetic OR Autosomal OR heterozygous OR homozygous OR recessive):ti,ab | 424,613 |
| #16 | #14 AND #15 | 173 |
| #17 | (Primary:ti,ab OR “pri mary”:ti,ab OR Hereditary:ti,ab OR Congenital:ti,ab OR Inborn:ti,ab OR Familial:ti,ab OR Genetic:ti,ab OR Autosomal:ti,ab OR heterozygous:ti,ab OR homozygous:ti,ab OR recessive:ti,ab OR PID:ti,ab OR “PIDs”:ti,ab OR “PIDD”:ti,ab OR “PIDDs”:ti,ab) AND (Immune-Disease\*:ti,ab OR Immunedisease\*:ti,ab OR Immunodeficien\*:ti,ab OR Immuno-Deficien\*:ti,ab OR Immunedeficien\*:ti,ab OR Immune-Deficien\*:ti,ab OR Immune-Disorder\*:ti,ab OR Immunedisorder:ti,ab OR Immunedisorders:ti,ab OR “Immune Syndrome”:ti,ab OR “Immune Syndromes”:ti,ab OR Agammaglobulin\*:ti,ab OR hypogammaglobulin\*:ti,ab OR dysgammaglobulin\*:ti,ab OR antibody deficien\*:ti,ab) | 2,321 |
| #18 | #16 OR #17 | 2,435 |
| #19 | MeSH descriptor: [Common Variable Immunodeficiency] this term only | 23 |
| #20 | “CVID”:ti,ab | 22 |
| #21 | ("common variable":ti,ab) AND (Immune-Disease\*:ti,ab OR Immunedisease\*:ti,ab OR Immunodeficien\*:ti,ab OR Immuno-Deficien\*:ti,ab OR Immunedeficien\*:ti,ab OR Immune-Deficien\*:ti,ab OR Immune-Disorder\*:ti,ab OR Immunedisorder\*:ti,ab OR Immune-Syndrome\*:ti,ab OR Agammaglobulin\*:ti,ab OR hypogammaglobulin\*:ti,ab OR dysgammaglobulin\*:ti,ab OR “antibody deficiency”:ti,ab OR “Antibody deficiencies”:ti,ab) | 41 |
| #22 | #19 OR #20 OR #21 | 55 |
| #23 | MeSH descriptor: [Severe Combined Immunodeficiency] this term only | 5 |
| #24 | “SCID”:ti,ab | 890 |
| #25 | (Severe-Combined:ti,ab OR “Severe Combined”:ti,ab) AND (Immune-Disease\*:ti,ab OR Immunedisease\*:ti,ab OR Immunodeficien\*:ti,ab OR Immuno-Deficien\*:ti,ab OR Immunedeficien\*:ti,ab OR Immune-Deficien\*:ti,ab OR Immune-Disorder\*:ti,ab OR Immunedisorder\*:ti,ab OR Immune-Syndrome\*:ti,ab OR Agammaglobulin\*:ti,ab OR hypogammaglobulin\*:ti,ab OR dysgammaglobulin\*:ti,ab OR “antibody deficiency”:ti,ab OR "Antibody deficiencies":ti,ab) | 16 |
| #26 | "SCID":ti,ab AND (Severe-Combined:ti,ab OR “Severe Combined”:ti,ab OR Immune-Disease\*:ti,ab OR Immunedisease\*:ti,ab OR Immunodeficien\*:ti,ab OR Immuno-Deficien\*:ti,ab OR Immunedeficien\*:ti,ab OR Immune-Deficien\*:ti,ab OR Immune-Disorder\*:ti,ab OR Immunedisorder\*:ti,ab OR Immune-Syndrome\*:ti,ab OR Agammaglobulin\*:ti,ab OR hypogammaglobulin\*:ti,ab OR dysgammaglobulin\*:ti,ab OR “antibody deficiency”:ti,ab OR "Antibody deficiencies":ti,ab) | 15 |
| #27 | #23 OR #24 OR #25 OR #26 | 898 |
| #28 | Purine Nucleoside Phosphorylase deficien\*:ti,ab | 3 |
| #29 | complement disorder\*:ti,ab OR complement deficien\*:ti,ab | 800 |
| #30 | complement disease\*:ti,ab | 1,573 |
| #31 | (Immune-Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno-Deficien\* OR Immunedeficien\* OR Immune-Deficien\* OR Immune-Disorder\* OR Immunedisorder\* OR Immune-Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency” OR “Antibody deficiencies”):ti,ab | 5,943 |
| #32 | #30 AND #31 | 15 |
| #33 | #28 OR #29 OR #32 | 810 |
| #34 | MeSH descriptor: [Phagocyte Bactericidal Dysfunction] this term only | 1 |
| #35 | MeSH descriptor: [Chediak-Higashi Syndrome] this term only | 2 |
| #36 | MeSH descriptor: [Granulomatous Disease, Chronic] this term only | 19 |
| #37 | (((“Chediak Higashi” OR “Chronic Granulomatous”) AND (deficien\* OR disorder OR disease OR syndrome OR patient OR Immune-Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno-Deficien\* OR Immunedeficien\* OR Immune-Deficien\* OR Immune-Disorder OR Immune-Disorders OR Immunedisorder\* OR Immune-Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency” OR “antibody deficiencies”))):ti,ab | 49 |
| #38 | #34 OR #35 OR #36 OR #37 | 54 |
| #39 | MeSH descriptor: [DiGeorge Syndrome] this term only | 10 |
| #40 | MeSH descriptor: [22q11 Deletion Syndrome] this term only | 1 |
| #41 | ((DiGeorge AND (deficien\* OR disorder OR disease OR syndrome OR patient OR Immune-Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno-Deficien\* OR Immunedeficien\* OR Immune-Deficien\* OR Immune-Disorder\* OR Immunedisorder\* OR Immune-Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency” OR “Antibody deficiencies”))):ti,ab | 6 |
| #42 | #39 OR #40 OR #41 | 16 |
| #43 | MeSH descriptor: [Janus Kinase 3] this term only | 27 |
| #44 | (JAK3:ti,ab NEXT deficien\*:ti,ab OR “JAK 3”:ti,ab NEXT deficien\*:ti,ab OR “janus kinase 3”:ti,ab) AND (Immune-Disease\*:ti,ab OR Immunedisease\*:ti,ab OR Immunodeficien\*:ti,ab OR Immuno-Deficien\*:ti,ab OR Immunedeficien\*:ti,ab OR Immune-Deficien\*:ti,ab OR Immune-Disorder\*:ti,ab OR Immunedisorder\*:ti,ab OR Immune-Syndrome\*:ti,ab OR Agammaglobulin\*:ti,ab OR hypogammaglobulin\*:ti,ab OR dysgammaglobulin\*:ti,ab OR “antibody deficiency”:ti,ab OR "Antibody deficiencies":ti,ab) | 0 |
| #45 | #43 OR #44 | 27 |
| #46 | ((JAK3:ti,ab NEXT deficien\*:ti,ab) OR (“JAK 3”:ti,ab NEXT deficien\*:ti,ab) OR “janus kinase 3”:ti,ab) AND (Immune-Disease\*:ti,ab OR Immunedisease\*:ti,ab OR Immunodeficien\*:ti,ab OR Immuno-Deficien\*:ti,ab OR Immunedeficien\*:ti,ab OR Immune-Deficien\*:ti,ab OR Immune-Disorder\*:ti,ab OR Immunedisorder\*:ti,ab OR Immune-Syndrome\*:ti,ab OR Agammaglobulin\*:ti,ab OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency”:ti,ab OR “antibody deficiencies”:ti,ab) | 0 |
| #47 | MeSH descriptor: [IgA Deficiency] this term only | 7 |
| #48 | ("Selective IgA":ti,ab OR “immunoglobulin A”:ti,ab OR “Immune globulin A”:ti,ab OR “gammaglobulin A”:ti,ab) AND (deficien\*:ti,ab OR disorder:ti,ab OR disease:ti,ab OR syndrome:ti,ab OR patient:ti,ab) | 189 |
| #49 | “SigAD”:ti,ab | 1 |
| #50 | #47 OR #48 OR #49 | 195 |
| #51 | MeSH descriptor: [X-Linked Combined Immunodeficiency Diseases] explode all trees | 0 |
| #52 | XLA:ti,ab | 15 |
| #53 | “X linked”:ti,ab AND (Immune-Disease\*:ti,ab OR Immunedisease\*:ti,ab OR Immunodeficien\*:ti,ab OR Immuno-Deficien\*:ti,ab OR Immunedeficien\*:ti,ab OR Immune-Deficien\*:ti,ab OR Immune-Disorder\*:ti,ab OR Immunedisorder\*:ti,ab OR Immune-Syndrome\*:ti,ab OR Agammaglobulin\*:ti,ab OR hypogammaglobulin\*:ti,ab OR dysgammaglobulin\*:ti,ab OR “antibody deficiency”:ti,ab OR “Antibody deficiencies”:ti,ab) | 25 |
| #54 | #51 OR #52 OR #53 | 36 |
| #55 | MeSH descriptor: [Adenosine Deaminase] explode all trees | 21 |
| #56 | “Adenosine deaminase deficiency”:ti,ab OR “Adenosine deaminase deficiencies”:ti,ab | 2 |
| #57 | #55 OR #56 | 23 |
| #58 | MeSH descriptor: [Ataxia Telangiectasia] explode all trees | 7 |
| #59 | “ataxia telangiectasia”:ti,ab | 49 |
| #60 | #58 OR #59 | 49 |
| #61 | (Transient Hypogammaglobulin\* OR Transient agammaglobuli\*) AND (Infancy OR Infant) | 5 |
| #62 | “Severe Congenital Neutropenia” | 5 |
| #63 | MeSH descriptor: [Leukocyte-Adhesion Deficiency Syndrome] explode all trees | 0 |
| #64 | “Leukocyte Adhesion Deficiency”:ti,ab OR "congenital disorder of glycosylation type 2c":ti,ab OR "congenital disorder of glycosylation type IIc":ti,ab OR "Leukocyte-Adhesion Deficiency Syndrome":ti,ab | 2 |
| #65 | #63 OR #64 | 2 |
| #66 | MeSH descriptor: [Immunoglobulin M] this term only | 549 |
| #67 | (“IG M”:ti,ab OR “IGM”:ti,ab OR “immunoglobulin M”:ti,ab OR “Immune globulin M”:ti,ab OR “gammaglobulin M”:ti,ab) AND (deficien\*:ti,ab OR disorder:ti,ab OR disease:ti,ab OR syndrome:ti,ab OR patient:ti,ab OR Immune-Disease\*:ti,ab OR Immunedisease\*:ti,ab OR Immunodeficien\*:ti,ab OR Immuno-Deficien\*:ti,ab OR Immunedeficien\*:ti,ab OR Immune-Deficien\*:ti,ab OR Immune-Disorder\*:ti,ab OR Immunedisorder\*:ti,ab OR Immune-Syndrome\*:ti,ab OR Agammaglobulin\*:ti,ab OR hypogammaglobulin\*:ti,ab OR dysgammaglobulin\*:ti,ab OR “antibody deficiency”:ti,ab OR “Antibody deficiencies”:ti,ab) | 1,020 |
| #68 | #66 OR #67 | 1,434 |
| #69 | MeSH descriptor: [Wiskott-Aldrich Syndrome] explode all trees | 7 |
| #70 | (“Wiskott Aldrich” AND (disease OR syndrome OR disorder OR patient)):ti,ab | 15 |
| #71 | #69 OR #70 | 18 |
| #72 | MeSH descriptor: [Job Syndrome] this term only | 2 |
| #73 | (("Hyper IgE" OR "hyper Immunoglobulin E" OR “Hyper Immune globulin E”) AND (deficien\* OR disorder OR disease OR syndrome OR patient OR Immune-Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno-Deficien\* OR Immunedeficien\* OR Immune-Deficien\* OR Immune-Disorder\* OR Immunedisorder\* OR Immune-Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency” OR “Antibody deficiencies”)):ti,ab | 2 |
| #74 | #72 OR #73 | 3 |
| #75 | MeSH descriptor: [Nijmegen Breakage Syndrome] explode all trees | 0 |
| #76 | (“Nijmegen Breakage” AND (disease OR syndrome OR disorder OR patient)):ti,ab | 1 |
| #77 | #75 OR #76 | 1 |
| #78 | MeSH descriptor: [Immunoglobulin G4-Related Disease] explode all trees | 6 |
| #79 | ((“IgG subclass” OR “immunoglobulin G1” OR “gammaglobulin G1” OR “Immune globulin G1” OR “IgG1” OR “IgG 1” OR “immunoglobulin G2” OR “gammaglobulin G2” OR “Immune globulin G2” OR “IgG2” OR “IgG 2” OR “immunoglobulin G3” OR “gammaglobulin G3” OR “Immune globulin G3” OR “IgG3” OR “IgG 3” OR “immunoglobulin G4” OR “gammaglobulin G4” OR “Immune globulin G4” OR IgG4 OR “IgG 4”) AND (deficien\* OR disorder OR disease OR syndrome OR patient OR Immune-Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno-Deficien\* OR Immunedeficien\* OR Immune-Deficien\* OR Immune-Disorder\* OR Immunedisorder\* OR Immune-Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency” OR “Antibody deficiencies”)):ti,ab | 1,164 |
| #80 | #78 OR #79 | 1,167 |
| #81 | #18 OR #22 OR #27 OR #33 OR #38 OR #42 OR #45 OR #46 OR #50 OR #54 OR #57 OR #60 OR #61 OR #62 OR #65 OR #68 OR #71 OR #74 OR #77 OR #80 | 6,937 |
| **All relevant studies** |
| #82 | #7 AND #81 | **136** |
| #83 | CDSR Cochrane Publication date from 01/02/2019 to present | **0** |
| #84 | TRIALS Cochrane Publication date from 01/02/2019 to present | **26** |

IG = immunoglobulin; MeSH = Medical Subject Heading; PID = primary immunodeficiency.

1. BIOSIS search strategy (ProQuest Dialog Platform) performed March 30, 2021. Limits: February 1, 2019 – March 30, 2021

| Search No. | Search Terms | Results |
| --- | --- | --- |
| Interventions |
| #1 | ti,ab,su(Subcuvia OR cuvitru OR ig20gly OR "i.g.-20GLY" OR "ig20-gly" OR "i.g.-20-gly" OR Hizentra OR HizentraR OR IgPro20 OR "Ig-Pro20" OR "Ig-Pro-20" OR "IgPro-20") | 81 |
| #2 | su(Immunoglobulins P/0 "administration and dosage" OR Immunoglobulins P/0 "adverse effects" OR Immunoglobulins P/0 poisoning OR Immunoglobulins P/0 "therapeutic use" OR Immunoglobulins P/0 toxicity) AND su("Infusions Subcutaneous" OR "Injections Subcutaneous") | 0 |
| #3 | ti,ab,su(scig OR scigs OR scgg OR scggs OR igsc OR igscs OR sqig OR sqigs OR "sc-i.g." OR "sc-igs" OR "sc-gg" OR "sc-ggs" OR "i.g.-sc" OR "i.g.-scs") | 287 |
| #4 | ti,ab,su(subcutaneous P/0 immunoglobulin\* OR subcutaneous P/0 immuneglobulin\* OR "subcutaneous immune" P/0 globulin\* OR subcutaneous P/0 Gammaglobulin\* OR "subcutaneous gamma" P/0 globulin\* OR (("sc" OR "s.c." OR subcutaneously OR "subcutaneous-infusion" OR Subq OR "sub q" OR hypodermoclysis) AND (immunoglobulin\* OR immuneglobulin\* OR immune P/0 globulin\* OR Gammaglobulin\* OR gamma P/0 globulin\* OR Gammagard OR kiovig OR "igg" OR iggs OR scig OR "i.g." OR "igs" OR igsc OR scgg OR sqig OR "sc-i.g." OR "sc-gg" OR "i.g.-sc" OR "Polyclonal-antibodies" OR "Polyvalent antibodies" OR "igrt" OR "igrts" OR "HNIG" OR "HNIGs"))) | 3,455 |
| #5 | ti,ab,su(HyQvia OR "ighy" OR "i.g.-hy" OR "fscig" OR "fscigs") | 39 |
| #6 | ti,ab,su((rHuPH20 OR Hylenex OR "r-huph20" OR "RHU-PH20" OR "RHUPH-20" OR "r-hu-ph-20" OR rHuPH20 OR rHuPH2O OR "r-huph2O" OR "RHU-PH2O" OR "RHUPH-2O" OR "r-hu-ph-2O" OR rHuPH2O OR Enhanze OR hyaluronidase OR hyaluronoglucosidas OR Hyaluronoglucosaminidase OR PH20 OR "ph-20" OR huph20 OR "huph-20" OR PH2O OR "ph-2O" OR rhuph2O OR huph2O OR "huph-2O") AND (immunoglobulin\* OR immuneglobulin\* OR immune P/0 globulin\* OR gammaglobulin\* OR gamma P/0 globulin\* OR Gammagard OR kiovig OR "igg" OR "iggs" OR "scig" OR "i.g." OR "igs" OR igsc OR scgg OR sqig OR "sc-i.g." OR "sc-gg" OR "i.g.-sc" OR "Polyclonal-antibodies" OR "Polyvalent antibodies" OR "igrt" OR "igrts" OR "HNIG" OR "HNIGs")) | 202 |
| #7 | ti,ab,su(Facilitated AND (immunoglobulin\* OR immuneglobulin\* OR immune P/0 globulin\* OR gammaglobulin\* OR gamma P/0 globulin\* OR Gammagard OR kiovig OR "igg" OR iggs OR scig OR "i.g." OR "igs" OR igsc OR scgg OR sqig OR "sc-i.g." OR "sc-gg" OR "i.g.-sc" OR "Polyclonal-antibodies" OR "Polyvalent antibodies" OR "igrt" OR "igrts" OR "HNIG" OR "HNIGs")) | 816 |
| #8 | #1 OR #2 OR #3 OR #5 OR #6 OR #7 | 1,314 |
| **Population** |
| #9 | su("Immunologic Deficiency Syndromes" OR "IgG Deficiency" OR Agammaglobulinemia OR "T-Lymphocytopenia Idiopathic CD4-Positive" OR Dysgammaglobulinemia OR Agranulocytosis OR "Granulocytopenia with Immunoglobulin Abnormality" OR "Immune Deficiency Disease") AND ti,ab(Primary OR "Pri-mary" OR Hereditary OR Congenital OR Inborn OR Familial OR Genetic OR Autosomal OR heterozygous OR homozygous OR recessive) | 1,191 |
| #10 | ti,ab(Primary OR "pri-mary" OR Hereditary OR Congenital OR Inborn OR Familial OR Genetic OR Autosomal OR heterozygous OR homozygous OR recessive OR "PID" OR "PIDs" OR "PIDD" OR "PIDDs") AND ti,ab(Immune P/0 Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno P/0 Deficien\* OR Immunedeficien\* OR Immune P/0 Deficien\* OR Immune P/0 Disorder\* OR Immunedisorder OR Immunedisorders OR Immune P/0 Syndrome OR Immune P/0 Syndromes OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR antibody P/0 deficien\*) | 23,607 |
| #11 | #9 OR #10 | 23,871 |
| #12 | su("Common Variable Immunodeficiency") OR ti,ab(CVID OR ("common variable" AND (Immune P/0 Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno P/0 Deficien\* OR Immunedeficien\* OR Immune P/0 Deficien\* OR Immune P/0 Disorder\* OR Immunedisorder\* OR Immune P/0 Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency” OR "Antibody deficiencies"))) | 2,798 |
| #13 | su("Severe Combined Immunodeficiency" OR "Bare Lymphocyte Syndrome Type II Complementation Group A" OR "Bare lymphocyte syndrome 2" OR "Bare Lymphocyte Syndrome Type I") OR ti,ab("SCID") OR ti,ab(("Severe-Combined" OR "Severe Combined") AND (Immune P/0 Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno P/0 Deficien\* OR Immunedeficien\* OR Immune P/0 Deficien\* OR Immune P/0 Disorder\* OR Immunedisorder\* OR Immune P/0 Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR "antibody deficiency" OR "Antibody deficiencies")) OR ti,ab("SCID" AND ("Severe-Combined" OR "Severe Combined" OR Immune P/0 Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno P/0 Deficien\* OR Immunedeficien\* OR Immune P/0 Deficien\* OR Immune P/0 Disorder\* OR Immunedisorder\* OR Immune P/0 Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR "antibody deficiency" OR "Antibody deficiencies")) | 26,458 |
| #14 | su("Purine Nucleoside Phosphorylase Deficiency" OR "Purine-Nucleoside Phosphorylase" P/0 deficiency) OR ti,ab("Purine Nucleoside Phosphorylase" P/0 deficien\*) | 194 |
| #15 | ti,ab(complement P/0 disorder\* OR complement P/0 deficien\* OR (complement P/0 disease\* AND (Immune P/0 Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno P/0 Deficien\* OR Immunedeficien\* OR Immune P/0 Disorder\* OR Immunedisorder\* OR Immune P/0 Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency” OR "Antibody deficiencies"))) | 710 |
| #16 | su("Phagocyte Bactericidal Dysfunction" OR "Chediak-Higashi Syndrome" OR "Granulomatous Disease Chronic") OR ti,ab((“Chediak Higashi” OR “Chronic Granulomatous”) AND (deficien\* OR disorder OR disease OR syndrome OR patient OR Immune P/0 Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno P/0 Deficien\* OR Immunedeficien\* OR Immune P/0 Deficien\* OR Immune P/0 Disorder OR Immune P/0 Disorders OR Immunedisorder\* OR Immune P/0 Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency” OR "Antibody deficiencies")) | 4,903 |
| #17 | su("DiGeorge Syndrome" OR "22q11 Deletion Syndrome") OR ti,ab(DiGeorge AND (deficien\* OR disorder OR disease OR syndrome OR patient OR Immune P/0 Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno P/0 Deficien\* OR Immunedeficien\* OR Immune P/0 Deficien\* OR Immune P/0 Disorder\* OR Immunedisorder\* OR Immune P/0 Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency” OR "Antibody deficiencies")) | 2,019 |
| #18 | su("Janus Kinase 3" P/0 deficiency) OR ti,ab((JAK3 P/0 deficien\* OR "JAK 3" P/0 deficien\* OR “janus kinase 3”) AND (Immune P/0 Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno P/0 Deficien\* OR Immunedeficien\* OR Immune P/0 Deficien\* OR Immune P/0 Disorder\* OR Immunedisorder\* OR Immune P/0 Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency” OR "Antibody deficiencies")) | 57 |
| #19 | su("IgA Deficiency") OR ti,ab((("Selective IgA" OR “immunoglobulin-A” OR “Immune-globulin-A” OR “gammaglobulin-A”) AND (deficien\* OR disorder OR disease OR syndrome OR patient)) OR "SigAD") | 3,961 |
| #20 | su("X-Linked Combined Immunodeficiency Diseases") OR ti,ab(XLA OR (("X linked" OR X-linked) AND (Immune P/0 Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno P/0 Deficien\* OR Immunedeficien\* OR Immune P/0 Deficien\* OR Immune P/0 Disorder\* OR Immunedisorder\* OR Immune P/0 Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency” OR "Antibody deficiencies"))) | 2,642 |
| #21 | su("Adenosine Deaminase" P/0 deficiency) OR ti,ab(“Adenosine deaminase deficiency” OR “Adenosine deaminase deficiencies”) | 690 |
| #22 | su("Ataxia Telangiectasia") OR ti,ab("ataxia-telangiectasia") | 7,548 |
| #23 | ti,ab,su(Transient P/0 Hypogammaglobulin\* OR Transient P/0 agammaglobuli\*) AND ti,ab,su(Infancy OR Infant) | 81 |
| #24 | ti,ab,su(“Severe Congenital Neutropenia”) | 719 |
| #25 | su("Leukocyte-Adhesion Deficiency Syndrome" OR "Congenital disorder of glycosylation type 2C") OR ti,ab (“Leukocyte Adhesion Deficiency” OR "congenital disorder of glycosylation type 2c" OR "congenital disorder of glycosylation type IIc" OR "Leukocyte-Adhesion Deficiency Syndrome") | 358 |
| #26 | su("Immunoglobulin M/deficiency") OR ti,ab((“IG-M” OR “IGM” OR “immunoglobulin-M” OR “Immune-globulin-M” OR “gammaglobulin-M”) AND (deficien\* OR disorder OR disease OR syndrome OR patient OR Immune P/0 Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno P/0 Deficien\* OR Immunedeficien\* OR Immune P/0 Deficien\* OR Immune P/0 Disorder\* OR Immunedisorder\* OR Immune P/0 Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency” OR "Antibody deficiencies")) | 32,122 |
| #27 | su("Wiskott-Aldrich Syndrome") OR ti,ab("Wiskott-Aldrich" AND (disease OR syndrome OR disorder OR patient)) | 2,531 |
| #28 | su("Job Syndrome") OR ti,ab(("Hyper IgE" OR "hyper Immunoglobulin E" OR “Hyper Immune globulin E”) AND (deficien\* OR disorder OR disease OR syndrome OR patient OR Immune P/0 Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno P/0 Deficien\* OR Immunedeficien\* OR Immune P/0 Deficien\* OR Immune P/0 Disorder\* OR Immunedisorder\* OR Immune P/0 Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR “antibody deficiency” OR "Antibody deficiencies")) | 628 |
| #29 | su("Nijmegen Breakage Syndrome") OR (ti,ab("Nijmegen Breakage" AND (disease OR syndrome OR disorder OR patient))) | 690 |
| #30 | su("Immunoglobulin G4-Related Disease") OR ti,ab(("IgG-subclass" OR "immunoglobulin-G1" OR "gammaglobulin-G1" OR "Immune-globulin-G1" OR "IgG1" OR "IgG-1" OR "immunoglobulin-G2" OR "gammaglobulin-G2" OR "Immune-globulin-G2" OR "IgG2" OR "IgG-2" OR "immunoglobulin-G3" OR "gammaglobulin-G3" OR "Immune-globulin-G3" OR "IgG3" OR "IgG-3" OR "immunoglobulin-G4" OR "gammaglobulin-G4" OR "Immune-globulin-G4" OR "IgG4" OR "IgG-4") AND (deficien\* OR disorder OR disease OR syndrome OR patient OR Immune P/0 Disease\* OR Immunedisease\* OR Immunodeficien\* OR Immuno P/0 Deficien\* OR Immunedeficien\* OR Immune P/0 Deficien\* OR Immune P/0 Disorder\* OR Immunedisorder\* OR Immune P/0 Syndrome\* OR Agammaglobulin\* OR hypogammaglobulin\* OR dysgammaglobulin\* OR "antibody deficiency" OR "Antibody deficiencies")) | 13,582 |
| #31 | #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 | 113,918 |
| All relevant studies |
| #32 | #8 AND #31 Limited by: Date: From February 01 2019 to 2021 | **41** |

BIOSIS = BioSciences Information Service of Biological Abstracts; IG = immunoglobulin; PID = primary immunodeficiency.

1. Search Results, by Database: Supplementary Searches; Search performed on March 29, 2021. Limits: February 2, 2019 to present

| Database |  | Search Terms | Number of Hits |
| --- | --- | --- | --- |
| Embase (Embase.com platform) | #1 | (((subcutaneous:ti,ab,de OR subcutaneously:ti,ab) AND immunoglobulin:ti,ab,de) OR Sigatoka) AND therapy:ti,ab,de | 4,695 |
| #2 | (immunodeficienc\*:ti,ab,de OR 'immune deficiency':ti,ab,de)  | 625,287 |
| #3 | #1 AND #2 AND [1-2-2019]/sd NOT [31-3-2021]/sd | 169 |
| MEDLINE and MEDLINE In-Process (PubMed platform) | #1 | (((subcutaneous[All Fields] OR subcutaneously[Title/Abstract]) AND immunoglobulin[All Fields]) OR SCIG[Title/Abstract]) AND therapy[All Fields] | 11,385 |
| #2 | immunodeficienc\*[All Fields] OR “immune deficiency”[All Fields] | 216,117 |
| #3 | (#1 AND #2) AND (("2019/02/01"[Date - Publication] : "2021/03/29"[Date - Publication]) OR ("2019/02/01"[Date - Entry] : "2021/03/29"[Date - Entry])) | 68 |
| **Totals** | Number of references from Embase and PubMed = 237Number of references after removing duplicates from Embase and PubMed = 180Number of references after removing duplicates from the systematic searches = 67Number of references after removing duplicates from previous library = 57 |

1. Results of registry searches; March 29, 2021

| Web Site/Database/Register Searched (Name, Address) | Date of Search | Search Terms Used | Details/Limits | Number of Records | Number of Potentially Relevant Articles |
| --- | --- | --- | --- | --- | --- |
| Clinicaltrials.gov<https://clinicaltrials.gov>  | 29/03/2021 | Primary immune-deficiency, immune globulin  | Condition or disease and intervention/treatment searched | 111 |  |
| International Clinical Trials Registry Platform<http://www.who.int/ictrp/en/>  | 29/03/2021 | Primary immune-deficiency  | search function, no limitations | 64 |  |
| **Total**  | **175 (106 unique)** |  |

Supplementary Table 2. COMPLETED PRISMA CHECKLIST

| **Section and Topic**  | **Item #** | **Checklist item**  | **Location where item is reported** |
| --- | --- | --- | --- |
| **TITLE**  |  |
| Title  | 1 | Identify the report as a systematic review. | Page 1 |
| **ABSTRACT**  |  |
| Abstract  | 2 | See the PRISMA 2020 for Abstracts checklist. | Page 2 |
| **INTRODUCTION**  |  |
| Rationale  | 3 | Describe the rationale for the review in the context of existing knowledge. | Page 3 |
| Objectives  | 4 | Provide an explicit statement of the objective(s) or question(s) the review addresses. | Pages 3–4 |
| **METHODS**  |  |
| Eligibility criteria  | 5 | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | Pages 4–5 |
| Information sources  | 6 | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | Page 4 |
| Search strategy | 7 | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | Pages 4–5, 34–56 |
| Selection process | 8 | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | Pages 4–5 |
| Data collection process  | 9 | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | Pages 4–5 |
| Data items  | 10a | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | Pages 4,19 |
| 10b | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | Pages 4, 19 |
| Study risk of bias assessment | 11 | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | Pages 5, 61–62 |
| Effect measures  | 12 | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. | Page 19 |
| Synthesis methods | 13a | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)). | N/A |
| 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | N/A |
| 13c | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | N/A |
| 13d | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. | N/A |
| 13e | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | N/A |
| 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | N/A |
| Reporting bias assessment | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | N/A |
| Certainty assessment | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | N/A |
| **RESULTS**  |  |
| Study selection  | 16a | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | Pages 5, 32 |
| 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | Pages 5, 32 |
| Study characteristics  | 17 | Cite each included study and present its characteristics. | Pages 6, 20-23 |
| Risk of bias in studies  | 18 | Present assessments of risk of bias for each included study. | Pages 10–11, 61–62 |
| Results of individual studies  | 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. | Pages 6–11 |
| Results of syntheses | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | N/A |
| 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | N/A |
| 20c | Present results of all investigations of possible causes of heterogeneity among study results. | N/A |
| 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | N/A |
| Reporting biases | 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | N/A |
| Certainty of evidence  | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | Pages 10–11, 61–62 |
| **DISCUSSION**  |  |
| Discussion  | 23a | Provide a general interpretation of the results in the context of other evidence. | Page 11 |
| 23b | Discuss any limitations of the evidence included in the review. | Page 13 |
| 23c | Discuss any limitations of the review processes used. | Page 13 |
| 23d | Discuss implications of the results for practice, policy, and future research. | Page 14 |
| **OTHER INFORMATION** |  |
| Registration and protocol | 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | Page 5 |
| 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | Page 5 |
| 24c | Describe and explain any amendments to information provided at registration or in the protocol. | Page 5 |
| Support | 25 | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | Page 15 |
| Competing interests | 26 | Declare any competing interests of review authors. | Page 15 |
| Availability of data, code and other materials | 27 | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | Page 16 |

*From:*  Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

Supplementary Table 3. Details of SCIG-dosing regimens or patient health and treatment pathways in IG-naïve patients

| Author (Year) | Information on SCIG-dosing Regimens or Patient Health and Treatment Pathways |
| --- | --- |
| Borte et al., (2011) | **Planned treatment**Loading phase (performed at the hospital):* SCIG 100 mg/kg (Vivaglobin) administered for 5 consecutive days; intensive training in self-administration with a portable infusion pump

Maintenance phase:* Patients self-infused SCIG at home
* Recommended dose was 100 mg/kg as a single weekly infusion or divided into 2 infusions per week; administered SCIG as often as twice weekly and not < 3 times a month
* Maximum volume per injection site = 15 mL; recommended infusion rate = up to 22 mL/h per site (depending on tolerability); use of several infusion sites was permitted provided maximum volume was not exceeded
* Dose adjustments permitted in patients who did not achieve an IgG trough level of ≥ 5 g/L on day 12; if trough IgG level did not reach 5 g/L by day 26, the patient was considered a nonresponder and withdrawn from the study
* Weekly dose could be reduced at the discretion of the investigator if IgG trough level was > 10 g/L on day 26

**Treatment received*** All patients received the planned 5 SCIG infusions during the loading phase
* Mean daily SCIG dose was 100.6 mg/kg (mean of individual medians) (median = 100.0 mg/kg, range 91.8‑110.3 mg/kg)
* Median infusion rate was 1.10 mg/kg/min (range 0.4–1.7 mg/kg/min)
* Median duration of infusion was 1.66 hours (range 0.9‑7.8 hours)
* In the maintenance phase, the mean weekly dose was 89.8 mg/kg (mean of individual medians; median = 99.3 mg/kg, range 53.3–106.7 mg/kg); the corresponding mean monthly dose was 359.2 mg/kg
* Dose adjustment was not required in any patient
* The decrease in the mean IgG dose during the maintenance phase was because of the withdrawal of 1 patient
* Median infusion rate was 1.00 mg/kg/min (range 0.6–2.3 mg/kg/min)
* Median infusion duration was 1.38 hours (range 0.4–14.0 hours)
* Extreme infusion duration values were observed in a few patients only, as evident from the 25% and 75% quantile values in both study phases (loading phase, 1.13 hours and 2.37 hours, respectively; maintenance phase, 1.08 hours and 1.75 hours, respectively)
 |
| Cinetto et al., (2021) | Note: this information relates to all primary antibody deficiency patients in the study, not just those who were IG naïve. * SCIG was initiated at a dose of 280.14 ± 84.38 mg/kg/month. The dose was then adjusted to reach a trough level of at least 500 mg/dL or higher if a substantial infectious burden was still present
* Mean duration of SCIG treatment was 73.8 ± 42.4 months (range 12–157 months)
* Mean SCIG dose at steady state was 309.31 ± 95.33 mg/kg per month (range 154.94–640.00 mg/kg)
* Mean interval between infusions was 7.48 ± 1.74 days (range 3–15 days). Facilitated SCIG was administered every 21 days

Of the 102 patients, 45 (44.1%) received 20% SCIG, 43 (42.1%) 16% or 16.5% SCIG, and 14 (13.7%) received 10% facilitated SCIG. |
| Duff and Leiding, (2017), [Abstract only] | * 3 patients required dose adjustments during the 3–4 months of therapy
* 11 patients had therapeutic IgG levels after 12 weeks of therapy and no dose adjustment was necessary
* SCIG brand name not reported
 |
| Gardulf et al., (1993) | * At the time of initiating SCIG (brand name not reported), 15 were receiving ongoing IMIG or IVIG, and 10 were previously untreated with IG
* Patients received SCIG self-infusions once a week (100 mg/kg per week)
* After an introductory period at the hospital (2–6 months), the infusions were taken at home
 |
| Gardulf et al., (1995) | Note: this information relates to all patients in the study, not just those who were previously unsubstituted.* All infusions were given in the abdominal wall, thigh, and/or buttocks (buttocks in Gothenburg only) using portable syringe drivers combined with infusion sets with 0-3 to 0-6 mm butterfly needles
* All patients in Stockholm, Copenhagen, Oslo, and 1 patient in Gothenburg self-infused IG at home (n = 125); remaining patients in Gothenburg received infusions in the hospital outpatient clinic
* Duration of SCIG replacement therapy ranged from 5 months to 9 years 8 months (median = 3 years)

Information on IG therapy for all patients (IG naïve and experienced)* Patients in Stockholm (n = 59) received Gammaglobulin Kabi 165 mg/mL or Gammabulin 160 mg/mL
* Mean mg/kg months (minimum–maximum) = 400 (210–730); dose of 400 mg/kg/month was given to 54/59 (92%) patients
* Infusion rate (mL/h/syringe driver) = 20 (2 syringe drivers were used simultaneously during hospital practice = 40 mL/h)
* mL/infusion site (maximum) = 10 (18)
* Infusion interval = once per week
* Patients in Gothenburg (n = 40) received Gammaglobulin Kabi 165 mg/mL
* Mean mg/kg months (minimum–maximum) = 325 (80–800)
* Infusion rate (mL/h/syringe driver) = 20; 4 syringe drivers were used simultaneously during hospital practice (= 80 mL/h)
* mL/infusion site (maximum) = 10
* Infusion interval = Once per week or once every 2 weeks
* Patients in Copenhagen (n = 20) received Nordimmun 150 mg/mL
* Mean mg/kg months (minimum–maximum) = 465 (310–765)
* Infusion rate (mL/h/syringe driver) = 4–8
* mL/infusion site (maximum) = 20
* Infusion interval = 1–4 times per week
* Patients in Oslo (n = 46) received Gammaglobulin Kabi 165 mg/mL
* Mean mg/kg months (minimum–maximum) = 220 (140–480)
* Infusion rate (mL/h/syringe driver) = 5
* mL/infusion site (maximum) = 20 (40)
* Infusion interval = 1–3 times per week
 |
| Gaspar et al., (1998) | **Information on treatment dosing and administration:*** All patients received mercury free, 16% normal human IG licensed for IM use (Gammabulin) using a portable infusion pump
* Mean dosage = 160 mg/kg/week (range 70–260)
* Lower dosages were used in children with mild immunodeficiency and higher doses in those with severe panhypogammaglobulinemia
* Convenient infusion regimens were set on an individual basis:
* 25 patients received 2 infusions simultaneously (twice each week in 5 patients; once a week in 13 patients; once every 10th day in 7 patients)
* One older patient preferred a single infusion 5 times each week
* Infusions usually given into SC tissue in the thigh; buttocks and abdomen were used successfully in 2 children but were unpopular with the other patients
* A fine 25 G butterfly needle attached to a 10 mL syringe was inserted at a 45° angle
* 8 patients had 10 mL injected at each site; 10 children could tolerate 7.5 mL; and 8 children received 5 mL at each site
* No more than 2 simultaneous infusions per patient were given; the first infusion was given at 10 mL/h and most subsequent infusions at 20 mL/h
* 24 patients were established on home treatment; 1 preferred to attend hospital; and 1 received infusions at their general practitioner’s surgery
 |
| Samaan et al., (2014) | **Interventions:*** IVIG (brand name not reported) administered in the day treatment center every 4 weeks
* SCIG (brand name not reported) patients received 3 weekly 2‑hour sessions with a clinical nurse and then administered SCIG independently at home
* Starting IG doses for all new patients were calculated on the basis of 400 mg/kg/4 weeks
* SCIG doses were measured 3 months after the initiation of the treatment and then at every 4 months with the same objective

**Treatment pathways in the “new” cohort (n = 92**)* 44/92 initially chose SCIG with an additional 35/48 later switching from IVIG to SCIG after an average of 6.8 months
* At the time of analysis, 74 patients (80%) were on SCIG after an average follow-up of 33.2 months (range 7.9–66.3 months)
* Of the 44 patients who initially chose SCIG, 42 (95%) stayed on it and 2 (5%) switched to IVIG
 |
| Sharma et al., (2019) | * Mean dose of SCIG was 437 mg/kg
* Mean dose of facilitated SCIG was 441 mg/kg

Study reports the dose and frequency of treatment for individual patients receiving IVIG, SCIG and facilitated SCIG |
| Walter et al., (2020a), | * 8 of 62 patients discontinued after at least 12 months of push SCIG therapy, 4 were IG-naïve and 4 were IG-experienced. Of these patients, 7 switched to IVIG and 1 discontinued IG replacement therapy. At the end of the study, of the 7 patients who switched to IVIG, 5 remained on IVIG and 2 had switched back to SCIG

Reasons for discontinuation included inconvenience of IgG replacement in general (n = 1), inconvenience of SCIG (n = 1), infection perceived by the patient to be SCIG-related (n = 1), pregnancy (n = 1), infusion pain related to prior surgical scars at infusion site (n = 1), fatigue perceived to be related to infusion (n = 2), and no reason (n = 2).  |
| Westh et al., (2017) | * Medical records of patients 15 years and older were reviewed to characterize them according to the EUROclass classification and clinical presentation
* 170 (95.0%) patients were on IG replacement therapy
* Initially, the chosen route was SC for 97 (57.1%) and IV for 62 (36.5%) patients; 11 (6.5%) patients had unavailable data
* At the time of analysis, the distribution had changed; 129/167 (77.2%) patients were treated with SCIG (brand name not reported); 36/167 (21.6%) were treated with IVIG (brand name not reported); and 2/167 (1.2%) had no data about administration method. A further 3 patients had stopped treatment
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IG, immunoglobulin; IgG, immunoglobulin G; IM, intramuscular; IMIG, intramuscular immunoglobulin; IV, intravenous; IVIG, intravenous immunoglobulin; SC, subcutaneous; SCIG, subcutaneous immunoglobulin.

Supplementary Table 4. Information on Loading Regimens From the Available Studies

| Author (year), country | Average dose used | SCIG loading dose for IG-naïve patients  |
| --- | --- | --- |
| Altook et al. (2019),a Canada [abstract only] | NR  | NR |
| Anterasian et al. (2019), US | NR | NR |
| Borte et al. (2011), Canada, Germany, Italy, and Spain | Maintenance phase:* Mean daily SCIG dose was 100.6 mg/kg (range: 91.8–110.3 mg/kg) as a single weekly infusion or divided into 2 infusions per week
* Administered SCIG as often as twice weekly and not < 3 times a month
 | 100 mg/kg administered for 5 consecutive days |
| Cinetto et al. (2021), Italy | * The mean SCIG monthly dosage for PAD was 309.31 ± 95.33 mg/kg, (range: 154.94–640.00 mg/kg) and mean between-infusions interval was 7.48 ± 1.74 days (range: 3–15 days)
* All facilitated SCIG patients received IG administration every 21 days
 | 280.14 ± 84.38 mg/kg/month and then adjusted to reach a trough level of ≥500 mg/dL if a significant infectious burden was still present |
| Duff and Leiding (2017), US [abstract only] | Received 20% SCIG therapy. No dosing information reported. | No loading dose |
| Gardulf et al. (1995), Sweden, Denmark, and Norway | Mean monthly dosage ranged from 220 mg/kg to 465 mg/kg depending on the study site | NR |
| Gardulf et al. (1993), Sweden | NR | NR |
| Gaspar et al. (1998), UK | Mean dosage was 160 mg/kg/week (range: 70–260)  | NR |
| Kearns et al. (2017), US | NR | NR |
| Noone et al. (2017), US [abstract only] | NR | Patients receiving an SC treatment could receive up to 2 IV loading doses as per treatment guidelines |
| Ritchey et al. (2020), US [abstract only] | * Of 17,961 patients on IG, 2269 received 20% SCIG and 395 received facilitated SCIG
* No dosing information reported
 | NR |
| Samaan et al. (2014), Canada | Titrated based on serum IgG trough levels | * Starting doses for new patients were calculated based on 400 mg/kg/4 weeks, with the objective of avoiding trough levels below 700 mg/dL for SCIG and IVIG doses
* SCIG doses were measured 3 months after the initiation of the treatment and then at every 4 months
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| Sharma et al. (2019), US | * Mean SCIG dose was 437 mg/kg
* 5 patients (7%) received facilitated SCIG replacement; the mean dose was 441 mg/kg
 | NR  |
| Walter et al. (2020a),a Canada | SCIG dose [g/kg/week] in IVIG-naïve patients = 0.14 (range: 0.06–0.29) | NR |
| Walter et al. (2020b),a Canada [abstract only] | NR | NR |
| Westh et al. (2017), Denmark | NR | NR |

aIt could not be confirmed whether these publications were from the same study.

IG, immunoglobulin; IgG, immunoglobulin G; IV, intravenous; IVIG, intravenous immunoglobulin; NR, not reported; PAD, primary antibody deficiencies; SC, subcutaneous; SCIG, subcutaneous immunoglobulin.

Supplementary Table 5. Summary of Quality of Included Studies

| Author (Year) | Did the study address a clearly focused issue? | Was the cohort recruited in an acceptable way? | Was the exposure accurately measured to minimize bias? | Was the outcome accurately measured to minimize bias? | Have the authors identified all important confounding factors? | Have they taken account of the confounding factors in the design and/or analysis? | Was the follow-up of subjects complete enough? | Was the follow-up of subjects long enough? | How precise are the results? | Do you believe the results? | Can the results be applied to the local population? | Do the results of this study fit with other available evidence? |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Altook et al., (2019) | No | Yes  | Not clear  | Yes  | Not clear  | Not clear  | NA | NA | Not clear  | Not clear  | Not clear  | Not clear  |
| Anterasian et al., (2019) | Yes | Not clear | Not clear | No | No | No | Not clear | Not clear | - | Yes | Not clear | Yes  |
| Borte et al., (2011) | Yes | Not clear | Yes  | Yes | NA | NA | Yes | Yes | - | Yes | Not clear  | Yes  |
| Cinetto et al., (2021)  | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes  | - | Yes | Not clear | Yes  |
| Duff and Leiding, (2017) [Abstract only] | Not clear  | Not clear  | Not clear  | Not clear  | Not clear  | Not clear  | Not clear  | Not clear  | Not clear  | Not clear  | Not clear  | Yes |
| Gardulf et al., (1995) | No | Not clear | Yes  | Not clear  | Not clear  | Not clear  | Not clear  | Not clear  | Not clear  | Not clear  | No | Yes |
| Gardulf et al., (1993) | Yes | Yesa | Yes | NA | - | No | NA | NA | Not clearb | Yes | Not clear  | No |
| Gaspar et al., (1998) | No | Not clear  | Yes | Yes  | Not clear  | Not clear  | Yes  | Yes  | Not clear  | Yes | Not clear  | Yes |
| Kearns et al., (2017) | Yes  | Yes  | Yes  | No  | Not clear  | Not clear  | No | Not clear  | Not clear  | Yes | No | No |
| Noone et al., (2017), [Abstract only] | Yes  | Yes | No  | Yes  | Yes  | Yes  | NA | NA |  | Yes | Yes | Yes |
| Ritchey et al., (2020) [Abstract only] | Yes | Yes | Not clear | Not clear | No | No | Not clear | Not clear | - | Yes | Yes | Yes  |
| Sharma et al., (2019) | Yes | Yes | Yes | Not clear  | No | No | Yes | Not clear | - | Yes | Not clear | Yes |
| Walter et al., (2020a) | Yes | Yes | Yes | Not clear | Yes | No | Yes | Yes | - | Yes | Not clear | Yes |
| Walter et al., (2020b) [Abstract only] | No | Yes | Not clear | Not clear | Not clear | Not clear | Not clear | Yes | - | No | Not clear | Yes |

aThis study was a case-control study. The question “was the cohort recruited in an acceptable way?” relates to “were the cases recruited in an acceptable way”.

bThis study was a case-control study. The question “how precise are the results?” relates to “how precise was the estimate of the treatment effect”.