Supplementary Material

Systematic literature review on the incidence of herpes zoster in populations with reduced immunity due to disease or medication in the EU/EEA, Switzerland and UK

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Supplemental file 1. PubMed Search string

#1 Herpes Zoster	"Herpes Zoster"[Mesh] OR zoster[tiab] OR shingle*[tiab]
#2 Incidence	"Incidence"[Mesh] OR inciden*[tiab]
#3 IC populations	immunocompromised[tiab] OR diabet*[tiab] OR **"Diabetes Mellitus"[MeSH] OR** "Pulmonary Disease, Chronic Obstructive"[Mesh] OR COPD[tiab] OR "chronic obstructive pulmonary disease"[tiab] OR COAD[tiab] OR "chronic obstructive airway disease"[tiab] OR "chronic obstructive lung disease"[tiab] OR "chronic bronchitis"[tiab] OR emphysema[tiab] OR "chronic airflow obstruction"[tiab] OR "Asthma"[Mesh] OR asthma*[tiab] OR "bronchial asthma"[tiab] OR wheez*[tiab] OR depression[Mesh] OR depressi*[tiab] OR auto-immun*[tiab] OR autoimmun*[tiab] OR "rheumatoid arthritis"[tiab] OR **"arthritis, rheumatoid"[MeSH]** OR "multiple sclerosis"[tiab] **OR "Multiple Sclerosis"[MeSH]** OR "inflammatory bowel disease*"[tiab] **OR "Inflammatory Bowel Diseases"[MeSH]** OR "crohn disease"[tiab] OR "crohns disease"[tiab] OR "crohn's disease"[tiab] OR "ulcerative colitis"[tiab] OR psoriasis[tiab] **OR "Psoriasis"[MeSH]** OR lupus[tiab] **OR "lupus erythematosus, systemic"[MeSH]** OR immunodeficiency[tiab] OR HIV[tiab] OR **"HIV"[MeSH] OR** transplant*[tiab] **OR "Organ Transplantation"[MeSH]** OR tumor[tiab] OR tumors[tiab] OR tumour*[tiab] OR malignan*[tiab] OR cancer*[tiab] OR "hematologic malignancy"[tiab] OR "hematologic malignancies"[tiab] OR "hematological malignancy"[tiab] OR "hematological malignancies"[tiab] **OR "Hematologic Neoplasms"[MeSH]** OR "hematopoietic stem cell transplantation"[tiab] OR HSCT[tiab] **OR "Hematopoietic Stem Cell Transplantation"[MeSH]**
#4 Countries	Europe[MeSH] OR Europe*[tw] OR Scandinavia*[tw] or Scandinavia*[ad] OR Mediterranean[tw] OR Mediterranean[ad] OR Europe*[ad] OR Baltic[tw] OR Baltic[ad] OR UK[ad] OR "United Kingdom"[ad] OR England[ad] OR Engl*[ad] OR British[ad] OR UK[tw] OR "United Kingdom"[tw] OR England[tw] OR Engl*[tw] OR British[tw] OR Italy[ad] OR Italian[ad] OR Italy[tw] OR Italian[tw] OR Spain[ad] OR Spanish[ad] OR Spain[tw] OR Spanish[tw] OR Germany[ad] OR German*[ad] OR Germany[tw] OR German*[tw] OR France[ad] OR French[ad] OR France[tw] OR French[tw] OR Belgium[ad] OR Belgian[ad] OR Belgium[tw] OR Belgian[tw] OR Austria*[tw] OR Austria*[ad] OR Denmark[tw] OR Denmark[ad] OR Danish[tw] OR Danish[ad] OR Finland[tw] OR Finland[ad] OR Finnish[tw] OR Finnish[ad] OR Ireland*[tw] OR Irish*[tw] OR Ireland*[ad] OR Irish*[ad] OR Netherlands[tw] OR Netherlands[ad] OR Dutch[tw] OR Dutch[ad] OR Portugal[tw] OR Portugal[ad] OR Portuguese[ad] OR Portuguese[tw] OR Sweden[tw] OR Sweden[ad] OR Swedish[tw] OR Swedish[ad] OR Switzerland[tw] OR Switzerland[ad] OR Swiss[tw] OR Swiss[ad] OR Bulgaria*[tw] OR Bulgaria*[ad] OR Croat*[tw] OR Croat*[ad] OR Cyprus[tw] OR Cyprus[ad] OR Cypriot*[ad] OR Cypriot*[tw] OR Czech[tw] OR Czech[ad] OR Estonia*[tw] OR Estonia*[ad] OR Greece[tw] OR Greece[ad] OR Greek[tw] OR Greek[ad] OR Hungar*[tw] OR Hungar*[ad] OR Iceland*[tw] OR Iceland*[ad] OR Latvi*[tw] OR Latvi*[ad] OR Liechtenstein*[tw] OR Liechtenstein*[ad] OR Lithuania*[tw] OR Lithuania*[ad] OR Luxembourg*[tw] OR Luxembourg*[ad] OR Malta[tw] OR Malta[ad] OR Maltese[tw] OR Maltese[ad] OR Norway[ad] OR Norway[tw] OR Norwegian*[ad] OR Norwegian*[tw] or Svalbard*[tw] OR Svalbard*[ad] OR Poland*[tw] OR Polish*[tw] OR Poland*[ad] OR Polish*[ad] OR Romania*[tw] OR Romania*[ad] OR Roumania*[tw] OR Roumania*[ad] OR Rumania*[tw] OR Rumania*[ad] OR Slovak*[tw] OR Slovak*[ad] OR Slovenia*[tw] OR Slovenia*[ad]
Limits	Publication date: 19-04-2002 to 01-01-2022.
	Languages: English, German, Dutch, French, Spanish and Italian
#1 AND #2 AND #3 AND #4 including limits	311 hits

Supplemental file 2. Quality Assessment tool

Are the individuals captured in the study setting likely to be representative of the target population?

- Yes: Study is representative of a broad population (e.g., regional vs country level, age groups, health care setting, socio demographic status). Representative healthcare setting:
    - General practice-based records
    - Health insurance database
- No: Study sample is not representative of a broad population. No representative healthcare setting:
    - Hospital-based records
    - Population-based screening
    - Pharmacy database
    - Reports from clinical practice (this is when they just report what they think they remember seeing but do not get all cases from general practice-based records)

Is there a valid case definition for the diagnosis of herpes zoster patients?

- Yes: A valid method was used to define a case of HZ within the study.
    - ICD codes with chart/laboratory review confirmation
    - ICD codes only
    - Clinical diagnosis but with PCR confirmation
- No: Unclear or no valid method was used to define HZ.
    - ICD codes AND antiviral prescriptions
    - ICD codes OR antiviral prescriptions
    - Antiviral prescriptions only
    - Self-reported diagnosis
    - Clinical diagnosis, without stating this comes from medical records
    - No clear description of case definition

The denominator is properly defined to calculate HZ incidence?

- Yes: Denominator to calculate HZ incidence (per person-time at risk or per study population at risk) calculated appropriately.
- No: Denominator either not clearly defined or calculated inaccurately.

Supplemental file 3. Excluded articles by reason for exclusion

Country (partly) outside the scope	
1.	Chakravarty et al. Lupus. 2013;22(3):238-44.
2.	Georges et al. Biol Blood Marrow Tr 2020;26(2):407-12.
3.	Gupta et al. Clin Gastroenterol Hepatol. 2006;4(12):1483-90.
4.	Humar et al. Liver Transplant. 2007;13(10):1422-7.
5.	Nacher et al. PLoS One. 2013;8(11):e80187.
6.	Peng et al. Expert Opin Drug Saf. 2020;19(11):1505-11.
7.	Razonable et al. J Infect Dis. 2005;192(8):1331-9.
8.	Ritchlin et al. BMC Rheumatol. 2019;3 :52.
9.	Shalom et al. J Dermatolog Treat. 2019;30(6):534-9.
10.	Sun et al. Leuk Lymphoma. 2015;56(2):407-14.
11.	Xue et al. Clin Infect Dis. 2021;72(8):1350-7.
12.	Yenikomshian et al. BMC Infect Dis. 2015;15:106.
Data outside the scope of the review	
1.	Aziz et al. Int J STD AIDS. 2013;24(6):433-9.
2.	Damery et al. Br J Gen Pract. 2013;63(611):e370-7.
3.	Demitrovicova et al. Neoplasma. 2017;64(3):474-81.
4.	Gómez et al. Transplant Proc. 2005;37(9):3760-3.
5.	González et al. Reumatol Clin. 2021; 18(9): 523-30.
6.	Kandus et al. Transplant Proc 2006;38(9):2853-5.
7.	Leon et al. Clin Exp Rheumatol. 2018;36(1):29-35.
8.	Osthoff et al. Haematologica. 2010;95(8):1389-96.
9.	Polverelli et al. Hematol Oncol. 2018;36(3):561-9.
10.	Šimkovič et al. Eur J Clin Invest. 2021;51(4):e13421.
11.	Styczyński et al. Acta Haematol Pol 2019;50(3):167-73.
12.	Wisniewski et al. United Eur Gastroenterol J. 2020;8(3):303-13.
Insufficient description of the methods	
1.	Bender et al. J Am Acad Dermatol. 2020;82(5):1117-23.
2.	Busch et al. Langenbecks Arch Surg. 2018;403(4):509-19.
3.	Failla et al. Dermatology. 2012;224(3):251-6.
4.	Gawrońska et al. Curr Issues Pharm Med Sci. 2012;25(4):392-5.
5.	Grimaldi et al. Transplant Proc. 2005;37(6):2502-3.
6.	Kinder et al. Rheumatology (Oxford). 2005;44(1):61-6.
7.	Saadatian-Elahi et al. Diabetes Res Clin Pract. 2020;159:107983.
8.	Schrezenmeier et al. Transplant Proc. 2017;49(10):2269-73.
9.	Vögelin et al. PLoS One. 2016;11(5):e0155218.
Insufficient description of results	
1.	König et al. Ann Hematol. 2014;93(3):479-84.
Letter to editor	
1.	Crodel et al. Leukemia. 2020;34(7):1949-53.
Narrative review	
1.	Bacigalupo et al. Expert Rev Hematol. 2020;13(11):1235-51.
2.	Schmidt-Hieber et al. Notfall und Rettungsmedizin. 2017;20(3):206-15.
No IC-population of interest	
1.	Fardet et al. Arch Dermatol. 2009;145(8):889-93.
2.	Ratnam et al. Clin Infect Dis. 2006;42(3):418-27.
3.	Schmidt et al. Vaccine. 2017;35(42):5589-96.
Not all IC population of interest (no stratified results per disease)	
1.	García-Doval et al. Ann Rheum Dis. 2010;69(10):1751-5.
2.	Gulín Dávila et al. Farm Hosp. 2013;37(5):351-7.
3.	Hillebrand et al. J Infect. 2015;70(2):178-86.
4.	Schiffner-Rohe et al. MMW Fortschr Med. 2010;151 Suppl 4:193-7.
No representative study population	
1.	Frère et al. Eur J Haematol. 2006;76(2):102-8.
Systematic literature review/meta-analysis	
1.	Che et al. Jt Bone Spine. 2014;81(3):215-21.
2.	Downey et al. Int J Rheum Dis. 2016;19(6):536-50.
3.	Furer et al. RMD Open. 2019;5(2):e001041.
4.	Low et al. Clin Infect Dis. 2016;62(12):1595-603.
5.	Mareque et al. Public Health. 2019;167:136-46.
6.	Marra et al. Open Forum Infect Dis. 2020;7(1):ofaa005.
7.	Müller et al. Lancet Infect Dis. 2010;10(4):251-61.
8.	Olivera et al. Gastroenterology. 2020;158(6):1554-73.e12.
9.	Salliot et al. Ann Rheum Dis. 2009;68(7):1100-4.
10.	Sepriano et al. Ann Rheum Dis. 2020;79(6):760-70.
11.	Taxonera et al. Inflamm Bowel Dis. 2022 ; 28(1):32-40.
Small sample size (n<30)	
1.	Dauby et al. J Int AIDS Soc. 2011;14:16.
2.	Garnier et al. J Rheumatol. 2018;45(11):1541-8.
Too specific population	
1.	Gagnière et al. Aliment Pharmacol Ther. 2018;48(7):713-22.

Unclear description of infection (VZV infection without specifying HZ/chickenpox)	
1.	Aberg et al. Am J Transplant. 2011;11(2):287-95.
2.	Czyżewski et al. Ann Hematol. 2019;98(9):2197-211.
3.	Imperatore et al. J of Gastroenterol and Hepatol (Australia). 2021;36(7):1859-68.
4.	Martin-Gandul et al. Am J Transplant. 2017;17(7):1813-22.
5.	Matłosz et al. Adv. Clin. Exp. Med.. 2008;17(2):201-6.
6.	Pérez-Sola et al. Med Clin (Barc). 2011;137(12):533-40.

HZ: herpes zoster; **IC:** immunocompromised; **VZV:** varicella zoster virus

Supplemental file 4. Study results

Table S1. Baseline characteristics of included studies

Author	Country	Study design	Study period	Setting	IC population Sample size	IC definition	Age (years)	Case definition	Patient type	Stratification	QAT: target population	QAT: case definition	QAT: Denominator
Barraco, 2020[1]	Austria, France, Germany, Italy, Netherlands, Switzerland and United Kingdom	Prospective other comparative study	NR-5 July 2018	NR	Primary/secondary myelofibrosis patients treated with ruxolitinib N=462	Primary: WHO criteria; secondary: The International Working Group for Myelofibrosis Research and Treatment criteria	NR	NR	Outpatient	Type of ruxolitinib users	No	No	Yes
Batram, 2012[2]	Germany	Retrospective matched cohort study	2007–2018	Statutory health insurance BARMER	Asthma COPD T1DM T2DM RA Depression N=NR	ICD codes	≥18	ICD codes	In- and outpatient	IC disease Year	No	No	Yes
Bloechliger, 2018[3]	United Kingdom	Retrospective unmatched cohort study	January 2000–December 2015	Clinical Practice Research Datalink (CPRD)	Asthma N=262,847	Read codes	≥18	Incident Read codes	Outpatient	Corticosteroid use	Yes	Yes	Yes
Bollaerts, 2019[4]	United Kingdom	Retrospective other comparative study	2013–2016	Clinical Practice Research Datalink (CRPD-GOLD) linked with the Hospital Episode Statistics Admitted Patient Care data	Asthma Immunocompromised Immunosuppressed N=NR	Read codes	NR	Incident Read codes or ICD codes	In- and outpatient	IC disease	No	Yes	Yes
Esteban-vasallo, 2014[5]	Spain	Retrospective passive surveillance study	1 October 2009–31 December 2012	Public Health System of the Autonomous Community of Madrid	Asthma COPD DM HIV Immunodeficiency Malignancy N=1,418,095	International Classification for Primary Care (ICPC) codes	≥18	ICPC	Outpatient	IC disease Gender	No	Yes	Yes

Fernández-Ruiz, 2018[6]	Spain	Prospective other comparative study	November 2008–March 2016	Hospital Universitario "12 de Octubre", Madrid	Kidney transplantation N=444	NR	≥18	Clinical	In- and outpatient	-	No	No	Yes
Galloway, 2013[7]	United Kingdom	Prospective unmatched cohort study	January 2001–31 December 2009	Community-based	RA treated with anti-TNF therapy or receiving nonbiological DMARD (nbDMARD) N=15,554	A 28 joint count disease activity score (DAS28) >4.2	NR	NR	In-and outpatient	Treatment	No	No	Yes
Grabar, 2015[8]	France	Retrospective passive surveillance study	January 1992–December 2011	French Hospital Database on HIV; FHDH	HIV N=91,044	NR	NR	ICD codes	In- and outpatient	Years	Yes	Yes	Yes
Jansen, 2013[9]	Germany	Prospective other comparative study	1 January 1985–1 July 2010	KompNet Cohort	HIV N=14,142	NR	NR	Clinical	Outpatient	-	Yes	No	Yes
Kho, 2021[10]	The Netherlands	Retrospective other comparative study	2000–2014	Erasmus Medical Center, Rotterdam	SOT N=1,033	NR	≥18	Clinical	Outpatient	Type of transplantation	No	No	No
Muñoz-Quiles, 2017[11]	Spain	Retrospective passive surveillance study	1 January 2009–31 December 2014	Health database of the Valencia Region: Regional Health System	DM N=397,940	ICD codes	≥50	ICD codes	In- and outpatient	Gender Age	No	Yes	Yes
Muñoz-Quiles, 2018[12]	Spain	Retrospective passive surveillance study	1 January 2009–31 December 2014	Health database of the Valencia Region: Regional Health System	COPD N=161,317	ICD codes	≥50	ICD codes	In- and outpatient	Gender Age Corticosteroids use	No	Yes	No
Muñoz-Quiles, 2020[13]	Spain	Retrospective passive surveillance study	1 January 2009–31 December 2014	Valencia health system integrated database (VID)	HSCT SOT Haematological malignancy Solid organ malignancy Malignancy overall HIV RA SLE IBD Psoriasis MS	ICD codes	≥18	ICD codes	In-and outpatient	IC disease Age	No	Yes	Yes

					Immunodeficiency disorders and autoimmune diseases overall (autoimmune) N=NR								
Pavlopoulou, 2015[14]	Greece	Retrospective non-comparative study	1 January 2004–31 December 2008	The Renal Transplant Unit of "Laiko" General Hospital, Athens	Renal transplant N=450	NR	≥18	Clinical	In- and outpatient	Age	Yes	No	Yes
Redeker, 2021[15]	Germany	Prospective other comparative study	2007–October 2020	The German Rheumatoid Arthritis: Observation of biologic therapy register RABBIT	RA using biologic, targeted synthetic and conventional synthetic DMARD treatment N=13,991	NR	NR	MedDRA	Outpatient	Treatment	Yes	Yes	No
Rutherford, 2018[16]	United Kingdom	Prospective other comparative study	2001–June 2016	British Society for Rheumatology Biologics Register for Rheumatoid Arthritis	Rheumatoid arthritis patients treated with biologic therapy N=19,282	NR	≥18	Clinical	In- and outpatient	Treatment	Yes	No	No
Schröder, 2014[17]	Germany	Retrospective passive surveillance study	2006–2012	German Pharmacoepidemiological Research Database (GePaRD)	HIV Malignant neoplasms Organ transplantation Stem cell transplantation SLE CU CD Lupus erythematous RA N=NR	ICD codes	≥18	ICD codes	In- and outpatient	IC disease Year	Yes	Yes	Yes
Smitten, 2007[18]	United Kingdom	Retrospective unmatched cohort study	1990–2001	UK General Practice Research Database (GPRD)	RA N=36,821	Physician-recorded diagnosis	≥18	Read or OXMIS codes	Outpatient	-	Yes	Yes	No
Steingrímsson, 2021[19]	Sweden	Matched cohort study	1994–2013	Swedish Cancer Registry	CLL N=8,989	NR	NR	ICD codes	In- and outpatient	-	Yes	Yes	No
Strangfeld, 2009[20]	Germany	Prospective unmatched cohort study	1 May 2001–31 December 2006	German biologics register RABBIT	RA treated with anti-TNF-α agents or who changed their DMARD treatment after at least 1 DMARD failure	NR	NR	Codes, not specified	Outpatient	Treatment	Yes	No	No

					N=5,040								
Takeshita, 2018[21]	United Kingdom	Prospective matched cohort study	1994–January 2014	The Health Improvement Network (THIN)	Psoriasis N=199,700	Read code	≥18	Read codes	Outpatient	Disease severity	Yes	Yes	Yes
Thomas, 2021[22]	Greece	Prospective non-comparative study	NR	Multi-center: Participating centers included academic and non-academic rheumatology clinics, National Health System outpatient clinics and private offices	RA N=1,557	ACR/EULAR classification criteria	NR	NR	Outpatient	-	Yes	No	No
Van besouw, 2016[23]	The Netherlands	Retrospective other comparative study	April 2002–September 2014	Erasmus medical center, Rotterdam	Lung transplant recipients N=119	NR	≥19	Clinical confirmed by OCR	In- and outpatient	Gender	No	Yes	No
Yanni, 2018[24]	England	Retrospective matched cohort study	January 2000–31 March 2012	Clinical Practice Research Datalink (CPRD)	HSCT SOT Hematological malignancy HIV RA SLE IBD MS Polymyalgia rheumatica N=NR	Read codes	≥18	ICD codes or Read codes	In- and outpatient	Age	Yes	Yes	Yes

ACR/EULAR: American college of rheumatology/ European league against rheumatism; **COPD:** chronic obstructive pulmonary disease; **DMARD:** disease-modifying antirheumatic drugs; **T1/T2 DM:** type 1/type 2 diabetes mellitus; **HIV:** human immunodeficiency virus; **HSCT:** hematopoietic stem cell transplantation; **IBD:** inflammatory bowel disease; **ICD:** International Classification of Diseases; **ICPC:** International Classification for Primary Care; **MedDRA:** Medical Dictionary for Regulatory Activities; **MS:** multiple sclerosis; **N:** number; **NR:** not reported; **QAT:** Quality assessment tool; **RA:** rheumatoid arthritis; **RABBIT:** Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (German biologics register for RA); **SLE:** systemic lupus erythematosus; **SOT:** solid organ transplantation; **WHO:** World Health Organization;

Table S2. HZ summary incidence proportion (%) by IC population and subgroup

Disease	Proportion of HZ as % (number of studies)
Haematological malignancy	**0–36.4 (n=10)[25-34]**
Multiple myeloma	0–36.4 (n=5)[26,28,29,32,33]
Haematological malignancy, mixed group	8.0 (n=1)[31]
Myelofibrosis (combination of myelofibrosis and Sérazy syndrome)	1.4 (n=1)[25]
Chronic lymphocytic leukaemia	3.3 (n=1)[27]
Advanced lymphoproliferative malignancies	15.4 (n=1)[34]
Hairy cell leukaemia	6.7 (n=1)[30]
Rheumatic disorders	**0.61–4.1 (n=3)** [35-37]
RA	0.75–4.1 (n=2)[35,36]
RA, psoriatic arthritis, juvenile RA, and CD patients	1.2 (n=1)[37]
Solid organ transplantation	**0.4–12 (n=5)[38-42]**
Kidney transplant	0.4–4.6 (n=4)[38,40-42]
Liver transplant	12.0 (n=1)[39]
Inflammatory bowel diseases	**0–7.9 (n=6)[43-48]**
Inflammatory bowel disease	0.5 (n=1)[47]
Crohn's disease	0.7–2.6 (n=2)[47,48]
Ulcerative colitis	0–7.9 (n=5)[43-47]
Stem cell transplantation	**0–21.4 (n=3)[49-51]**
Hematopoietic stem cell transplant	0–21.4 (n=3)[49-51]
Lupus	**5.0–7.2 (n=2)[52,53]**
systemic lupus erythematosus	7.2 (n=1)[52]
lupus nephritis	5.0 (n=1)[53]
Psoriasis	**0–0.63 (n=1)[54]**
Solid organ malignancy	**1.9 (n=1)[55]**
Breast malignancy	1.9 (n=1)[55]
Multiple Sclerosis	**0.61–1.2 (n=2)[56,57]**

CD: Crohn's disease; **HZ:** herpes zoster; **IC:** immunocompromised; **RA:** rheumatoid arthritis;

Table S3. Meta-analysis feasibility

Author Country	Study design Study period	Setting	IC-population Sample size	IC-definition	Age groups (years) % male	Case definition	Patient type	Stratifications	HZ incidence rate			
									Cases	Denom-inator	Incid-ence	CI
Chronic respiratory disease (n=3)												
Bloechliger, 2018[3] United Kingdom	Retrospective unmatched cohort study January 2000–December 2015	Clinical Practice Research Datalink (CPRD)	Asthma N=262,847	Read codes	≥18 NR	Incident Read codes	Outpatient	**Corticosteroids** - group that have not used OCS (ICS only)	2882	614,128	4.7	4.5–4.9
								Corticosteroids - group that have ever used OCS	1293	210,560	6.1	5.8–6.5
								Corticosteroids - group currently using OCS	257	35,586	7.2	6.3–8.1
Bollaerts, 2019[4] United Kingdom	Retrospective other comparative study 2013–2016	Clinical Practice Research Datalink (CRPD-GOLD) linked with the Hospital Episode Statistics Admitted Patient Care data	Asthma N=NR	Read codes	NR	Incident Read codes or ICD codes	In- and outpatient	NA	NR	NR	11.2	9.9–12.5
Muñoz-Quiles 2018[12] Spain	Retrospective passive surveillance study 1 January 2009–31 December 2014	Health database of the Valencia Region: Regional Health System	COPD N=161,317	ICD codes	≥50 NR	ICD codes	In- and outpatient	No inhaled corticosteroids- total population (50–59/ 60–69/ 70–79/ 80+; males/females)	4629	NR	11.1	10.7–11.4
								Inhaled corticosteroids- total population 50–59/ 60–69/ 70–79/ 80+; males/females)	1164	NR	13.0	12.3–13.8
Haematological malignancy (n=2)												
Muñoz-Quiles 2020[13] Spain	Retrospective passive surveillance study 1 January 2009–31 December 2014	Valencia health system integrated database	Haematological malignancy N=NR	ICD codes	≥18 NR	ICD codes	In-and outpatient	Total population (18–29/ 30–39/ 40–49/ 50–59/ 60–69 /70–79/ 80+)	NR	NR	12.0	11.5–12.5
Yanni 2018[24] England	Retrospective matched cohort study January 2000–31 March 2012	Clinical Practice Research Datalink	Haematological malignancy N=NR	Read codes	≥18 NR	ICD codes or Read codes	In- and outpatient	Total population (18–49; 50–59; 60–64; 65–69; 70–79; 80+)	NR	NR	11.0	9.8–12.3
HIV/AIDS (n=4)												

Jansen 2013[9] Germany	Prospective other comparative study 1 January 1985–1 July 2010	KompNet Cohort	HIV N=14,142	NR	NR 84.9%	Clinical	Outpatient	Total population (0–19/ 20–29/ 30–39/ 40–49/ 50+)	1553	NR	12.2	12.6–12.8
Muñoz-Quiles 2020[13] Spain	Retrospective passive surveillance study 1 January 2009–31 December 2014	Valencia health system integrated database (VID)	HIV N=NR	ICD codes	≥18 NR	ICD codes	In-and outpatient	Total population (18–29/ 30–39/ 40–49/ 50–59/ 60–69/ 70–79/ 80+)	NR	NR	12.9	12.0–14.0
Schröder 2017[17] Germany	Retrospective passive surveillance study 2006–2012	German Pharmacoepidemiological Research Database (GePaRD)	HIV N=NR	ICD codes	≥18 NR	ICD codes	In- and outpatient	/	NR	NR	13.0	12.0–14.1
Yanni 2018[24] England	Retrospective matched cohort study January 2000–31 March 2012	Clinical Practice Research Datalink (CPRD)	HIV N=NR	Read codes	≥18 NR	ICD codes or Read codes	In- and outpatient	Total population (18–49; 50–59; 60–64; 65–69; 70–79; 80+)	NR	NR	11.8	9.5–14.4
Inflammatory bowel disease (n=3)												
Muñoz-Quiles 2020[13] Spain	Retrospective passive surveillance study 1 January 2009–31 December 2014	Valencia health system integrated database (VID)	IBD N=NR	ICD codes	≥18 NR	ICD codes	In-and outpatient	Total population (18–29/ 30–39/ 40–49/ 50–59/ 60–69/ 70–79/ 80+)	NR	NR	8.3	7.8–8.8
Schröder 2017[17] Germany	Retrospective passive surveillance study 2006–2012	German Pharmacoepidemiological Research Database (GePaRD)	CD/UC N=NR	ICD codes	≥18 NR	ICD codes	In- and outpatient	UC	NR	NR	10.8	10.2–11.4
								CD	NR	NR	10.7	9.9–11.4
Yanni 2018[24] England	Retrospective matched cohort study January 2000–31 March 2012	Clinical Practice Research Datalink (CPRD)	IBD N=NR	Read codes	≥18 NR	ICD codes or Read codes	In- and outpatient	Total population (18–49; 50–59; 60–64; 65–69; 70–79; 80+)	NR	NR	7.0	6.6–7.7
Lupus (systemic lupus erythematosus) (n=3)												
Muñoz-Quiles 2020[13] Spain	Retrospective passive surveillance study	Valencia health system integrated database (VID)	SLE N=NR	ICD codes	≥18 NR	ICD codes	In-and outpatient	Total population (18–29/ 30–39/ 40–49/ 50–59/ 60–69/ 70–79/ 80+)	NR	NR	13.4	11.8–15.1

	1 January 2009–31 December 2014											
Schröder 2017[17] Germany	Retrospective passive surveillance study 2006–2012	German Pharmacoepidemiological Research Database (GePaRD)	SLE N=NR	ICD codes	≥18 NR	ICD codes	In- and outpatient	/	NR	NR	16.5	14.4–18.9
Yanni 2018[24] England	Retrospective matched cohort study January 2000–31 March 2012	Clinical Practice Research Datalink (CPRD)	SLE N=NR	Read codes	≥18 NR	ICD codes or Read codes	In- and outpatient	Total population (18–49; 50–59; 60–64; 65–69; 70–79;80+)	NR	NR	11.0	9.8–12.3
Rheumatic disorders (rheumatoid arthritis) (n=5)												
Galloway 2013[7] United Kingdom	Prospective unmatched cohort study January 2001–31 December 2009	Community-based	RA treated with anti-TNF therapy or receiving nonbiological DMARD N=15,554	28 joint count disease activity score (DAS28) >4.2.	NR 27.7%	NR	In-and outpatient	Non-biological DMARDs	45	5417	8.0	6.0–11.0
								Anti-TNF agents	275	17048	16.0	14.0–18.0
								Etanercept	99	6122	16.0	13.0–20.0
								Infliximab	91	4529	20.0	16.0–25.0
								Adalimumab	85	6397	13.0	11.0–13.0
Muñoz-Quiles 2020[13] Spain	Retrospective passive surveillance study 1 January 2009–31 December 2014	Valencia health system integrated database	RA N=NR	ICD codes	≥18 NR	ICD codes	In-and outpatient	Total population (18–29/ 30–39/ 40–49/ 50–59/ 60–69/ 70–79/ 80+)	NR	NR	11.1	10.5–11.6
Redeker, 2021[15] Germany	Prospective other comparative study 2007–October 2020	The German Rheumatoid Arthritis: Observation of biologic therapy register RABBIT	RA using biologic, targeted synthetic and conventional synthetic DMARD treatment N=13,991	NR	NR 25.5%	MedDRA	Outpatient	Total population (monoclonal anti-TNF/soluble TNF/t-cell constimulation/B-cell targeted therapies/IL-6 inhibitors/ JAK/csDMARDs)	559	62958	8.9	8.2–9.6

Strangfeld-2009[20] Germany	Prospective unmatched cohort study 1 May 2001–31 December 2006	German biologics register RABBIT	RA treated with anti-TNF-α agents or who changed their dMARD treatment after ≥1 DMARD failure N=5,040	NR	NR NR	Codes, not specified	Outpatient	Etanercept	21	2588	8.1	5.0–12.4
								infliximab/adalimumab	39	3524	11.1	7.9–15.1
								Anti-TNF-alpha agents	60	6112	9.8	7.5–12.6
								Changed DMARD treatment after =>1 DMARD failure	22	4291	5.1	3.2–7.8
Yanni, 2018[24] England	Retrospective matched cohort study January 2000–31 March 2012	Clinical Practice Research Datalink (CPRD)	RA N=NR	Read codes	≥18 NR	ICD codes or Read codes	In- and outpatient	Total population (18–49; 50–59; 60–64; 65–69; 70–79; 80+)	NR	NR	10.6	10.1–11.1
Multiple Sclerosis (n=2)												
Muñoz-Quiles 2020[13] Spain	Retrospective passive surveillance study 1 January 2009–31 December 2014	Valencia health system integrated database (VID)	MS N=NR	ICD codes	≥18 NR	ICD codes	In-and outpatient	Total population (18–29/ 30–39/ 40–49/ 50–59/ 60–69/ 70–79/ 80+)	NR	NR	6.3	5.3–7.5
Yanni 2018[24] England	Retrospective matched cohort study January 2000–31 March 2012	Clinical Practice Research Datalink (CPRD)	MS N=NR	Read codes	≥18 NR	ICD codes or Read codes	In- and outpatient	Total population (18–49; 50–59; 60–64; 65–69; 70–79; 80+)	NR	NR	5.7	5.1–6.4
Psoriasis (n=4)												
Muñoz-Quiles 2020[13] Spain	Retrospective passive surveillance study 1 January 2009–31 December 2014	Valencia health system integrated database (VID)	Psoriasis N=NR	ICD codes	≥18 NR	ICD codes	In-and outpatient	Total population (18–29/ 30–39/ 40–49/ 50–59/ 60–69/ 70–79/ 80+)	NR	NR	6.1	5.6–6.3
Schröder 2017[17] Germany	Retrospective passive surveillance study 2006–2012	German Pharmacoepidemiological Research Database (GePaRD)	Psoriasis N=NR	ICD codes	≥18 NR	ICD codes	In- and outpatient	/	NR	NR	10.5	10.3–10.8
Takeshita 2018[21] United Kingdom	Prospective matched cohort study	The Health Improvement Network (THIN)	Psoriasis N=199,700	Read code	≥18 48.4%	Read codes	Outpatient	Total population (mild/moderate-severe psoriasis)	6537	1,209,265	5.4	5.3–5.5

	1994–January 2014											
Yanni, 2018[24] England	Retrospective matched cohort study January 2000–31 March 2012	Clinical Practice Research Datalink (CPRD)	Psoriasis N=NR	Read codes	≥18 NR	ICD codes or Read codes	In- and outpatient	Total population (18–49; 50–59; 60–64; 65–69; 70–79; 80+)	NR	NR	5.3	5.0–5.5
Solid organ malignancy (n=2)												
Muñoz-Quiles 2020[13] Spain	Retrospective passive surveillance study 1 January 2009–31 December 2014	Valencia health system integrated database (VID)	Solid organ malignancy N=NR	ICD codes	≥18 NR	ICD codes	In-and outpatient	Total population (18–29/ 30–39/ 40–49/ 50–59/ 60–69/ 70–79/ 80+)	NR	NR	11.0	10.7–11.2
Yanni, 2018[24] England	Retrospective matched cohort study January 2000–31 March 2012	Clinical Practice Research Datalink (CPRD)	Solid organ malignancy N=NR	Read codes	≥18 NR	ICD codes or Read codes	In- and outpatient	Total population (18–49; 50–59; 60–64; 65–69; 70–79 ;80+)	NR	NR	15.2	14.5–16.0
Solid organ transplant (n=4)												
Fernández-Ruiz 2018[6] Spain	Prospective other comparative study November 2008–March 2016	Hospital Universitario "12 de Octubre", Madrid	Kidney transplantation N=444	NR	≥18 62.4%	Clinical	In- and outpatient	/	35	NR	78.8	54.0–104.0
Muñoz-Quiles 2020[13] Spain	Retrospective passive surveillance study 1 January 2009–31 December 2014	Valencia health system integrated database (VID)	SOT transplantation N=NR	ICD codes	≥18 NR	ICD codes	In-and outpatient	Total population (18–29/ 30–39/ 40–49/ 50–59/ 60–69/ 70–79/ 80+)	NR	NR	12.7	11.8–13.5
Schröder 2017[17] Germany	Retrospective passive surveillance study 2006–2012	German Pharmacoepidemiological Research Database (GePaRD)	SOT transplantation N=NR	ICD codes	≥18 NR	ICD codes	In- and outpatient	/	NR	NR	14.5	12.7–16.5
Yanni, 2018[24] England	Retrospective matched cohort study January 2000–31 March 2012	Clinical Practice Research Datalink (CPRD)	SOT transplantation N=NR	Read codes	≥18 NR	ICD codes or Read codes	In- and outpatient	Total population (18–49; 50–59; 60–64; 65–69; 70–79; 80+)	NR	NR	12.1	10.5–13.7
Stem cell transplantation (n=3)												

Muñoz-Quiles 2020[13] Spain	Retrospective passive surveillance study 1 January 2009–31 December 2014	Valencia health system integrated database (VID)	HSCT N=NR	ICD codes	≥18 NR	ICD codes	In-and outpatient	Total population (18–29/ 30–39/ 40–49/ 50–59/ 60–69/ 70–79/ 80+)	NR	NR	56.1	48.9–64.0
Schröder 2017[17] Germany	Retrospective passive surveillance study 2006–2012	German Pharmacoepidemiological Research Database (GePaRD)	Stem cell transplantation: that includes HSCT and 'other organ or tissue transplantation' N=NR	ICD codes	≥18 NR	ICD codes	In-and outpatient	/	NR	NR	37.2	32.0–43.0
Yanni, 2018[24] England	Retrospective matched cohort study January 2000–31 March 2012	Clinical Practice Research Datalink (CPRD)	HSCT N=NR	Read codes	≥18 NR	ICD codes or Read codes	In- and outpatient	Total population (18–49; 50–59; 60–64; 65–69; 70–79; 80+)	NR	NR	41.7	35.7–48.4

CI: confidence interval; **COPD:** chronic obstructive pulmonary disease; **HIV:** human immunodeficiency virus; **HSCT:** hematopoietic stem cell transplantation **ICD:** International Classification of Diseases; **ICS:** inhaled corticosteroids; **MS:** multiple sclerosis; **N:** number; **NA:** not applicable; **NR:** not reported; **OCS:** oral corticosteroids; **RA:** rheumatoid arthritis; **SOT:** solid organ transplantation

Supplemental file 5. PRISMA checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	P1
ABSTRACT			
Title	2	1 Identify the report as a systematic review	P2
Objectives		2 Provide an explicit statement of the main objective(s) or question(s) the review addresses.	P2
Methods: Eligibility criteria		3 Specify the inclusion and exclusion criteria for the review.	P2
Information sources		4 Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	P2
Risk of bias		5 Specify the methods used to assess risk of bias in the included studies.	NA
Synthesis of results		6 Specify the methods used to present and synthesise results.	P2
Results: Included studies		7 Give the total number of included studies and participants and summarise relevant characteristics of studies.	P2
Synthesis of results		8 Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	P2
Discussion: Limitations		9 Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	P2
Interpretation		10 Provide a general interpretation of the results and important implications.	P2
Funding		11 Specify the primary source of funding for the review.	P2
Registration		12 Provide the register name and registration number.	NA
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	P3-4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	P4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	P6
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.	P6
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Suppl 1
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.	P6
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.	P6
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.	P6
	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.	P7
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.	P7
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.	P7
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each	P7

		synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	NA
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	NA
	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.	P7, Suppl 4 Table S3
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	NA
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	NA
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	P7 Suppl 2
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	NA
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.	P7-8 PRISMA flow
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Suppl 3
Study characteristics	17	Cite each included study and present its characteristics.	Suppl 4 Table S1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Suppl 4 Table S1
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.	P11-19
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	NA
	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.	NA
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	NA
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	NA
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	NA
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	P11-19
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	P20-21
	23b	Discuss any limitations of the evidence included in the review.	P21
	23c	Discuss any limitations of the review processes used.	P21
	23d	Discuss implications of the results for practice, policy, and future research.	P22
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.	NA
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	NA
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	P7
Competing interests	26	Declare any competing interests of review authors.	P23

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.	P23