

Rôles étiologique et pronostique de la multimorbidité dans le développement et la sévérité de l'infection par le SARS-CoV-2 : revue systématique de la littérature

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Les Rencontres de Santé publique France
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CONFLITS D'INTÉRÊTS:

Cette intervention est faite en tant que personnel de Santé publique France, organisateur de la manifestation.

Je n'ai pas de conflit d'intérêt en lien avec le sujet traité.

Réalisé dans le cadre du programme JA de l'UE

Population Health Information Research Infrastructure (PHIRI)



Belgique
République tchèque
France
Hongrie
Portugal
Espagne



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Objectifs :

1. évaluer le rôle *étiologique* de la fragilité, de la multimorbidité et du statut socio-économique sur le risque des indicateurs à court terme du SARS-CoV-2 (infection, hospitalisation, admission en USI, ventilation mécanique ou décès).
2. évaluer la valeur *pronostique* des déterminants ci-dessus en ce qui concerne l'impact à court et à long terme de COVID-19 sur la santé, comme le déclin fonctionnel, la qualité de vie, la santé mentale, l'absentéisme au travail, etc.

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Definition of multimorbidity: coexistence of ≥ 2 conditions (van den Akker, 1996)

Multimorbidité mesurée par : nombre de maladies, indice de comorbidité de Charlson (CCI), combinaisons de maladies

Approche populationnelle (population-based):

“a population-based study is defined as a study of properties of a well-defined population, such as individuals residing in a defined geographic region in a given time period” (Gail, 1998)

And

“population-based studies aim to answer research questions for defined populations; answers should be generalizable to the whole population addressed in the study hypothesis, not only to the individuals included in the study” (Lieb, 2013)

Les mots clés comprenaient les termes suivants (et leurs équivalents) :

- multimorbidité, fragilité et caractéristiques socioéconomiques
- COVID-19
- type d'étude retenues (par ex. cohorte, études transversale)

4 bases de données explorées :

PubMed, Embase, WHO covid-19 global literature on coronavirus disease and PsycINFO

Étude enregistrée dans le registre **Prospero** pour les protocoles de revue systématique : CRD42021249444

=> recherche initiale 7 avril, 2021

=> mise à jour pour la fragilité 1 février, 2022

#1	((((((((((((((((("Betacoronavirus"[MeSH Terms] OR "Coronavirus Infections"[MeSH Terms]) OR "COVID-19"[Supplementary Concept]) OR "Coronavirus"[MeSH Terms]) OR "Severe Acute Respiratory Syndrome Coronavirus 2"[Supplementary Concept]) OR "2019nCoV"[All Fields]) OR "betacoronavirus*"[All Fields]) OR "corona virus*"[All Fields]) OR "coronavirus*"[All Fields]) OR "coronavirus*"[All Fields]) OR "CoV"[All Fields]) OR "CoV2"[All Fields]) OR "COVID"[All Fields]) OR ("COVID-19"[Supplementary Concept] OR "COVID-19"[All Fields]) OR "covid19"[All Fields])) OR ((((((("COVID-19"[All Fields] OR "covid 2019"[All Fields]) OR "Severe Acute Respiratory Syndrome Coronavirus 2"[Supplementary Concept]) OR "Severe Acute Respiratory Syndrome Coronavirus 2"[All Fields]) OR "2019 nCoV"[All Fields]) OR "SARS CoV 2"[All Fields]) OR "2019nCoV"[All Fields]) OR ("wuhan"[All Fields] AND ("Coronavirus"[MeSH Terms] OR "Coronavirus"[All Fields])) AND (2019/12/1:2019/12/31[Date - Publication] OR 2020/1/1:2020/12/31[Date - Publication]))) OR "HCoV-19"[All Fields]) OR "nCoV"[All Fields]) OR "SARS CoV 2"[All Fields]) OR "SARS2"[All Fields]) OR "SARSCoV"[All Fields]) OR (((("sars virus"[MeSH Terms] OR ("sars"[All Fields] AND "virus"[All Fields])) OR "sars virus"[All Fields]) OR ("sars"[All Fields] AND "CoV"[All Fields])) OR "sars cov"[All Fields])) OR ("Severe Acute Respiratory Syndrome Coronavirus 2"[Supplementary Concept] OR "Severe Acute Respiratory Syndrome Coronavirus 2"[All Fields]) OR "SARS CoV 2"[All Fields])) OR "severe acute respiratory syndrome cov*"[All Fields]) AND (2019/11/17:3000/12/31[Date - Entry] OR 2019/11/17:3000/12/31[Date - Publication]) OR "COVID-19"[MeSH Terms] OR "SARS-Cov-2"[MeSH Terms] OR "SARS CoV-2" OR "SARS-CoV-2" OR SARSCoV2 OR "CoV-2" OR "covid 19" OR covid2019 OR "covid-2019" OR "novel CoV" OR "corona pandemic*" OR "wuhan virus*" OR "CoV 2" OR ((wuhan OR hubei OR huanan) AND ("severe acute respiratory" OR pneumonia*) AND outbreak*)
#2	frailty OR frail OR frailty[MeSH Terms]
#3	multimorbidity OR "multi-morbidity" OR "multi morbidity" OR multimorbidities OR "multi-morbidities" OR "multi morbidities" OR multimorbid OR "multi-morbid" OR "multi morbid" OR comorbidity OR "co-morbidity" OR "co morbidity" OR comorbidities OR "co-morbidities" OR "co morbidities" OR comorbid OR "co morbid" OR "multiple chronic conditions" OR "multiple chronic diseases" OR "multiple conditions" OR "multiple diseases" OR "multiple disorders" OR polymorbid* OR "poly-morbid*" OR "poly morbid*" OR polypath* OR pluripath* OR multipath* OR "multi path*" OR "multi-path*" OR "multiple pathologies" OR "disease cluster" OR "disease clusters" OR "disease pattern" OR "disease patterns" OR "concurrent chronic diseases" OR "multiple chronic disorders" OR multimorbidity[MeSH Terms] OR comorbidity[MeSH Terms]
#4	"socio economic" OR "socio-economic" OR socioeconomic OR "socio-economics" OR "socio economics" OR socioeconomic OR "social difference" OR "social differences" OR "social inequality" OR "social inequalities" OR "socioeconomic inequality" OR "socioeconomic inequalities" OR "social disparity" OR "social disparities" OR education OR literacy OR "socioprofessional" OR "socio-professional" OR "socio professional" OR "social conditions" OR "social class" OR "social classes" OR "social class"[MeSH Terms] OR "socioeconomic factors"[MeSH Terms] OR health status disparities[MeSH Terms] OR income OR poverty OR deprivation OR rural OR urban OR "housing deprivation" OR homeless OR houseless OR homelessness OR ethnic* OR race OR emigrant OR immigrant OR migrant OR "minority group" OR "minority groups" OR disadvantaged OR "marital status" OR ((characteristics OR factors OR status) AND (economic OR social OR educational)) OR ((composition OR characteristics OR size) AND (family OR household))
#5	"cross-sectional" OR "cross sectional" OR "case-control" OR "case control" OR cohort OR longitudinal OR "ecological study" OR "ecological studies" OR "ecological design" OR "ecological designs" OR observational OR "observational study" OR "observational studies" OR "observational design" OR "observational designs" OR "prospective study" OR "prospective studies" OR "prospective design" OR "prospective designs" OR "retrospective study" OR "retrospective studies" OR "retrospective design" OR "retrospective designs" OR "prospective observational study" OR "prospective observational studies" OR "retrospective observational study" OR "retrospective observational studies" OR case-control studies[MeSH Terms] OR cohort studies[MeSH Terms] OR cross-sectional studies[MeSH Terms]
#6	#2 OR #3 OR #4
#7	#1 AND #5 AND #6

Recommandations Prisma pour les revues systématiques

La revue comprenait **deux parties : biomédicale et socio-économique**

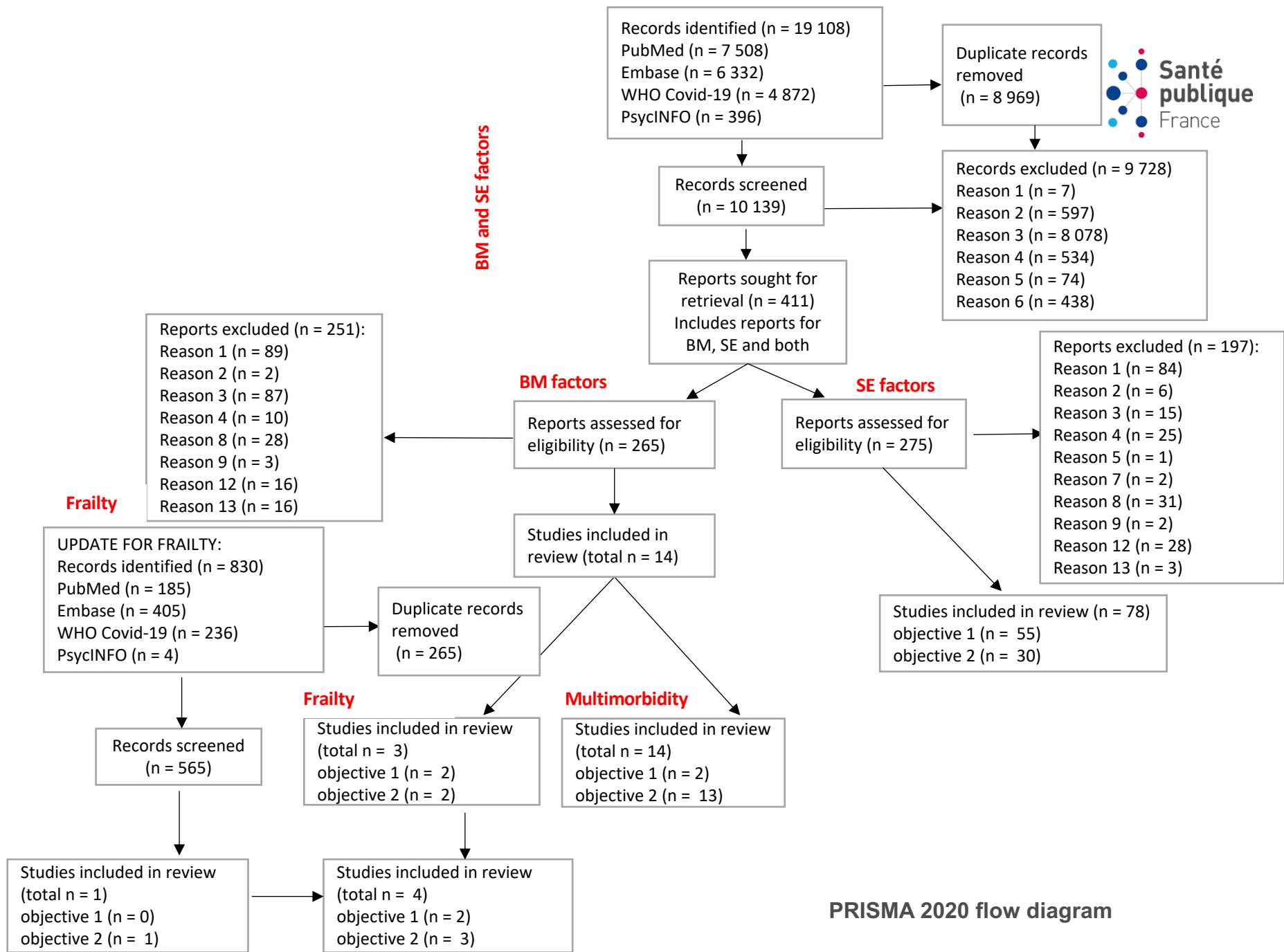
L'ensemble du processus a été **réalisé en binôme**

13 personnes ont participé au processus de revue; **2 réviseurs** sont restés stables tout au long du processus

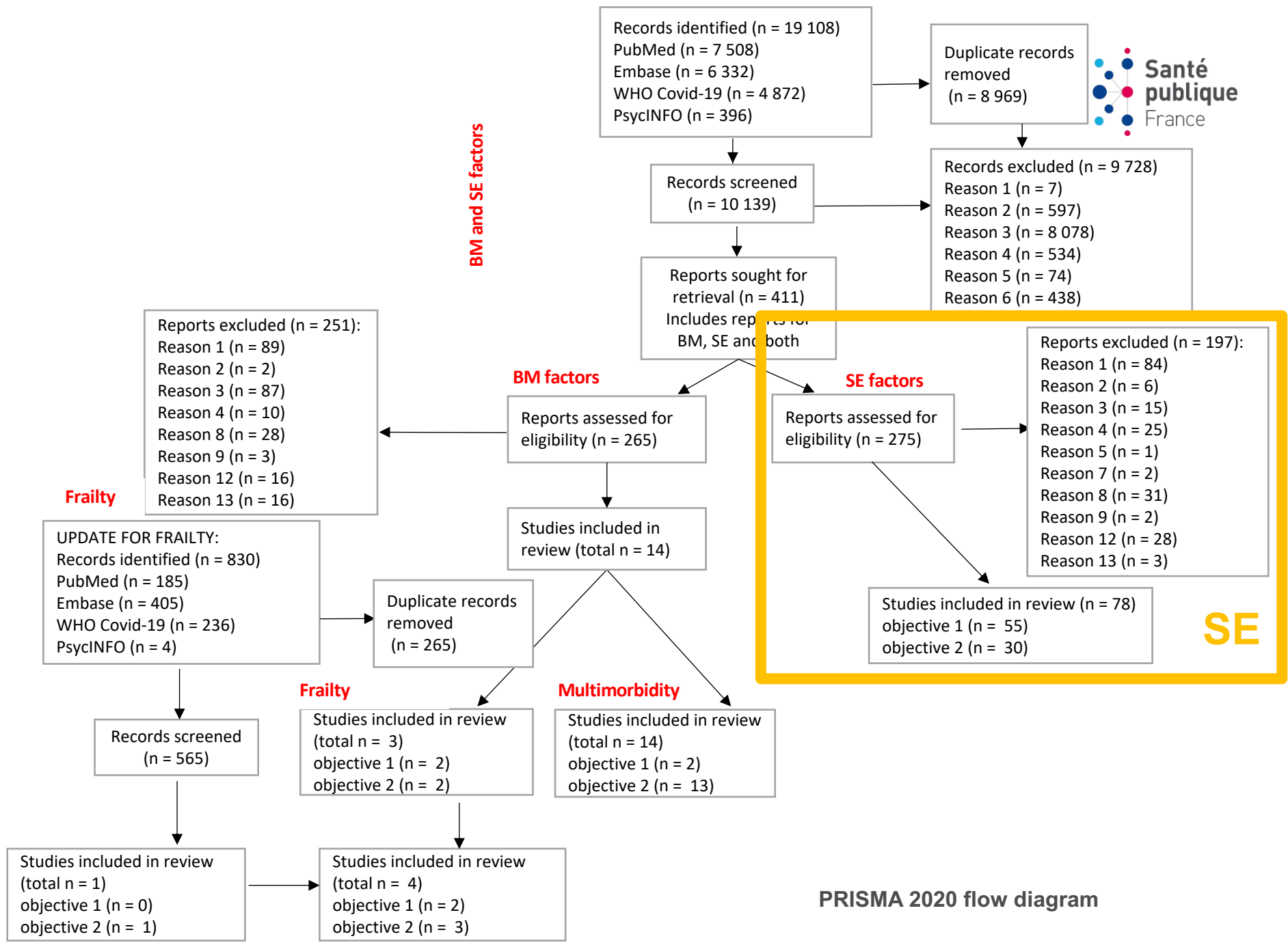
Outils: EndNote, Rayyan, Excel

Étapes:

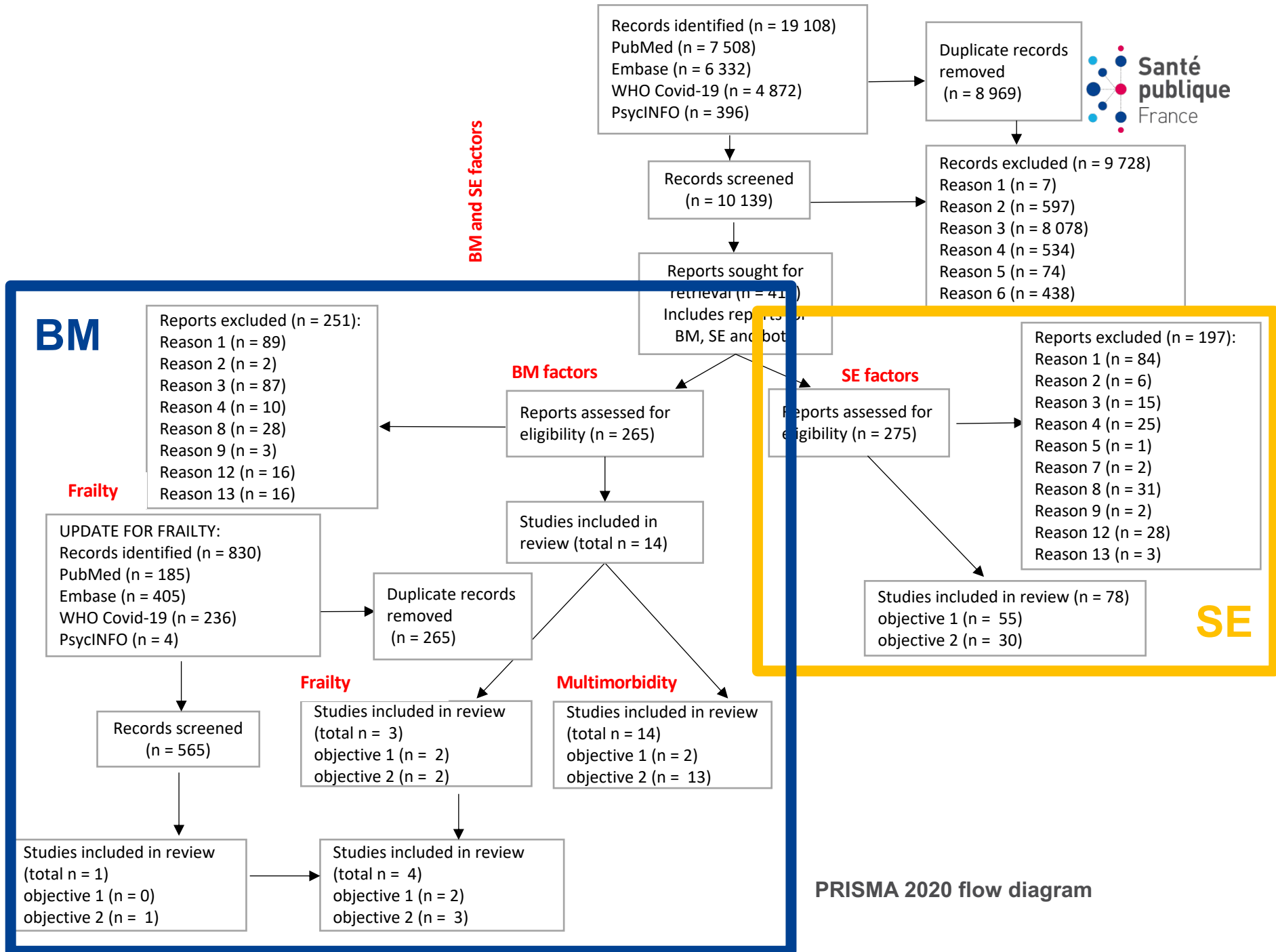
- **Combiner** des articles de 4 bases de données et **supprimer les doublons**
- **Titre/résumé** ou records => appliquer des critères **d'exclusion 1 / exclure**
- **Texte intégral** ou rapport => appliquer des critères **d'exclusion 2 / exclure**
- **Études sélectionnées** => **évaluer la qualité** (Newcastle-Ottawa scale – NOS)
=> **extraire les données**

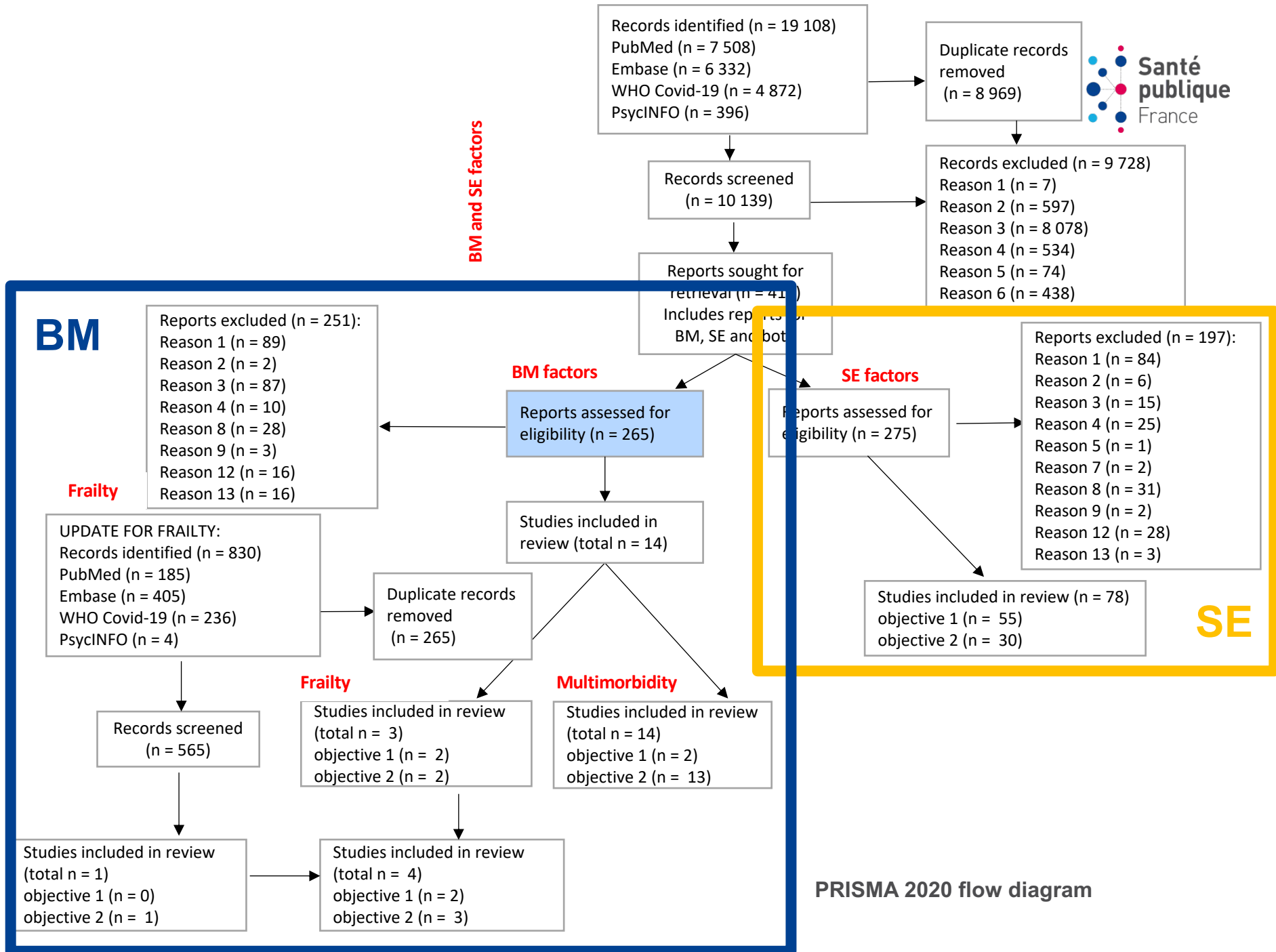


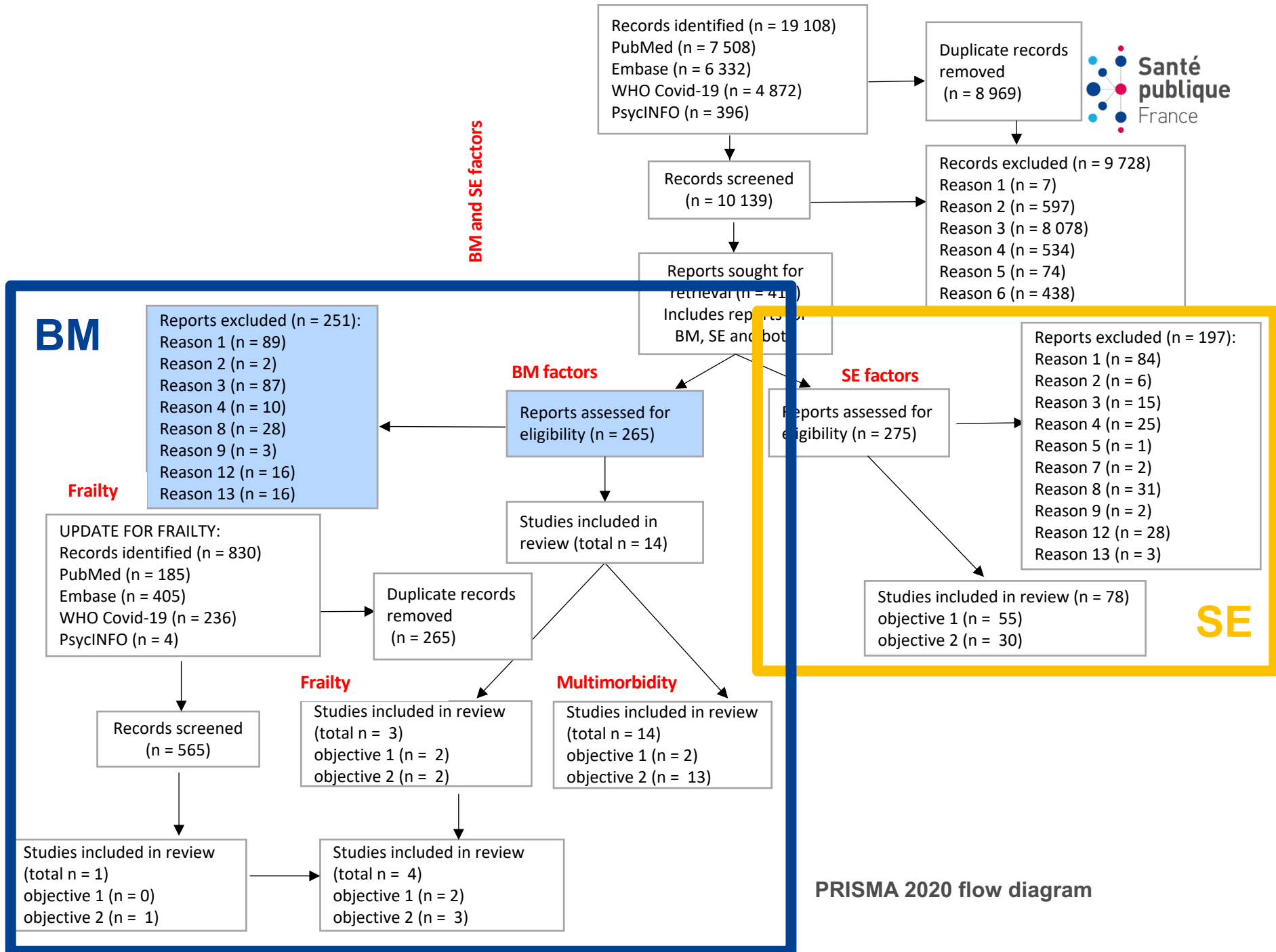
PRISMA 2020 flow diagram

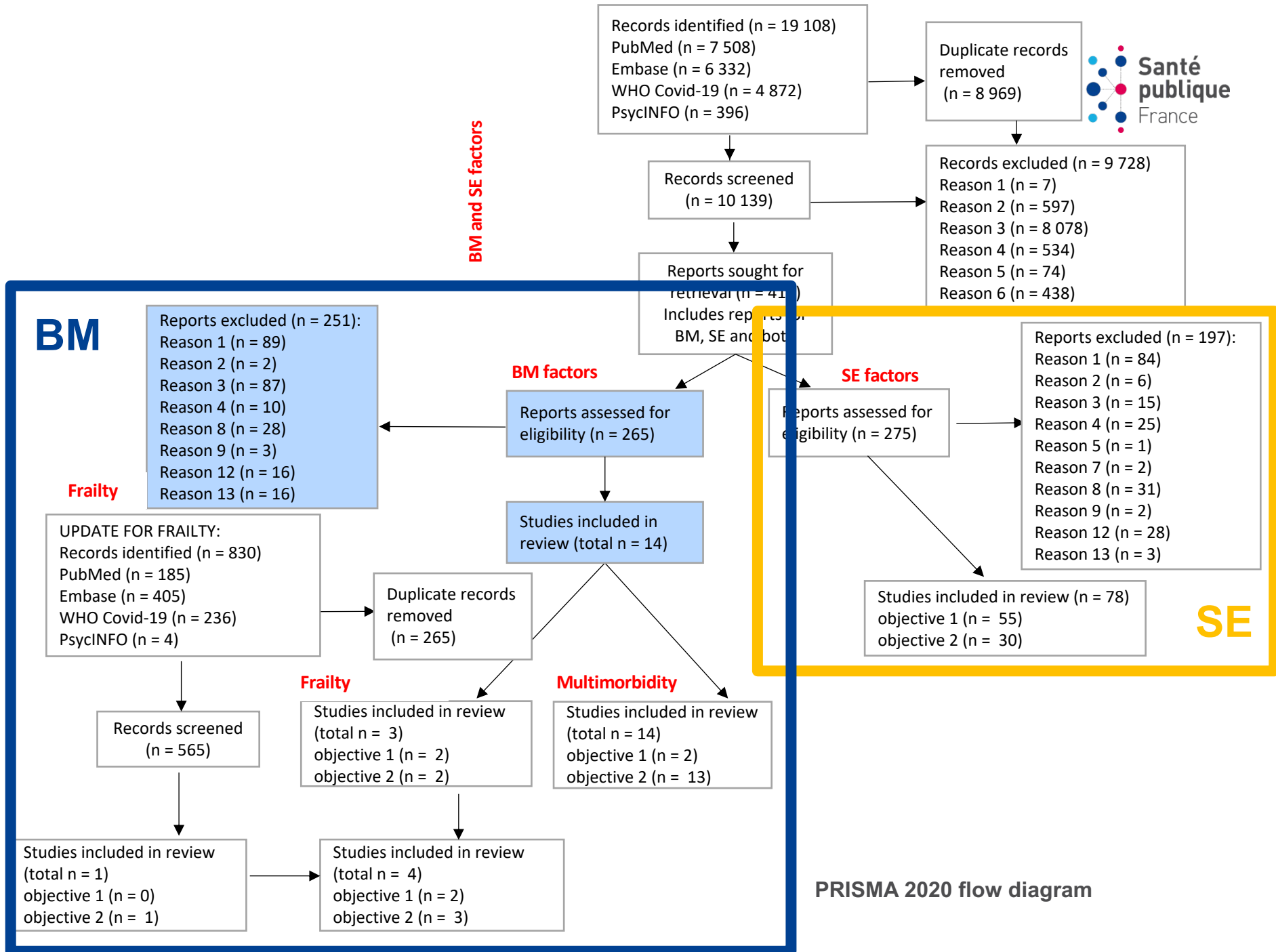


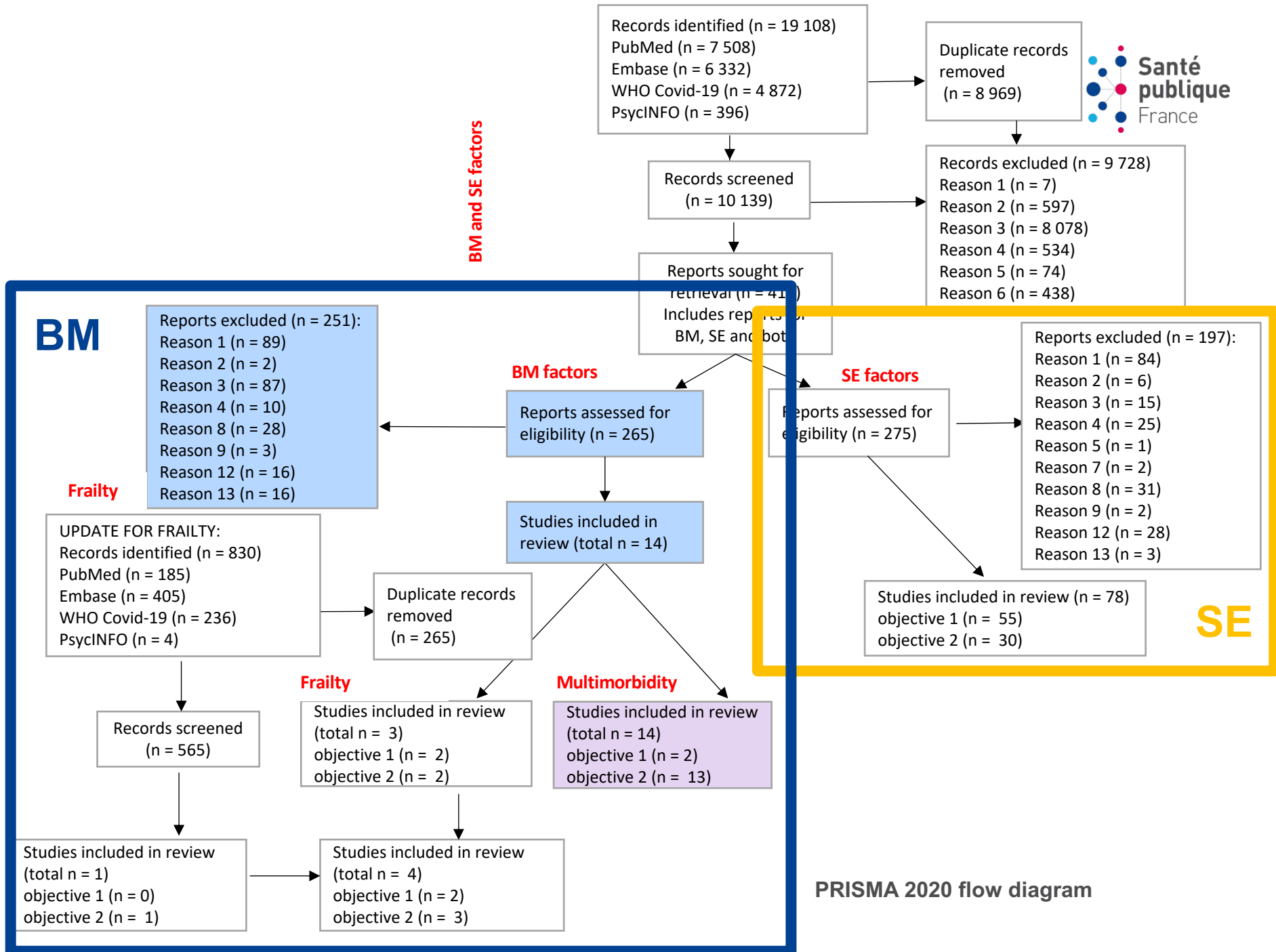
PRISMA 2020 flow diagram

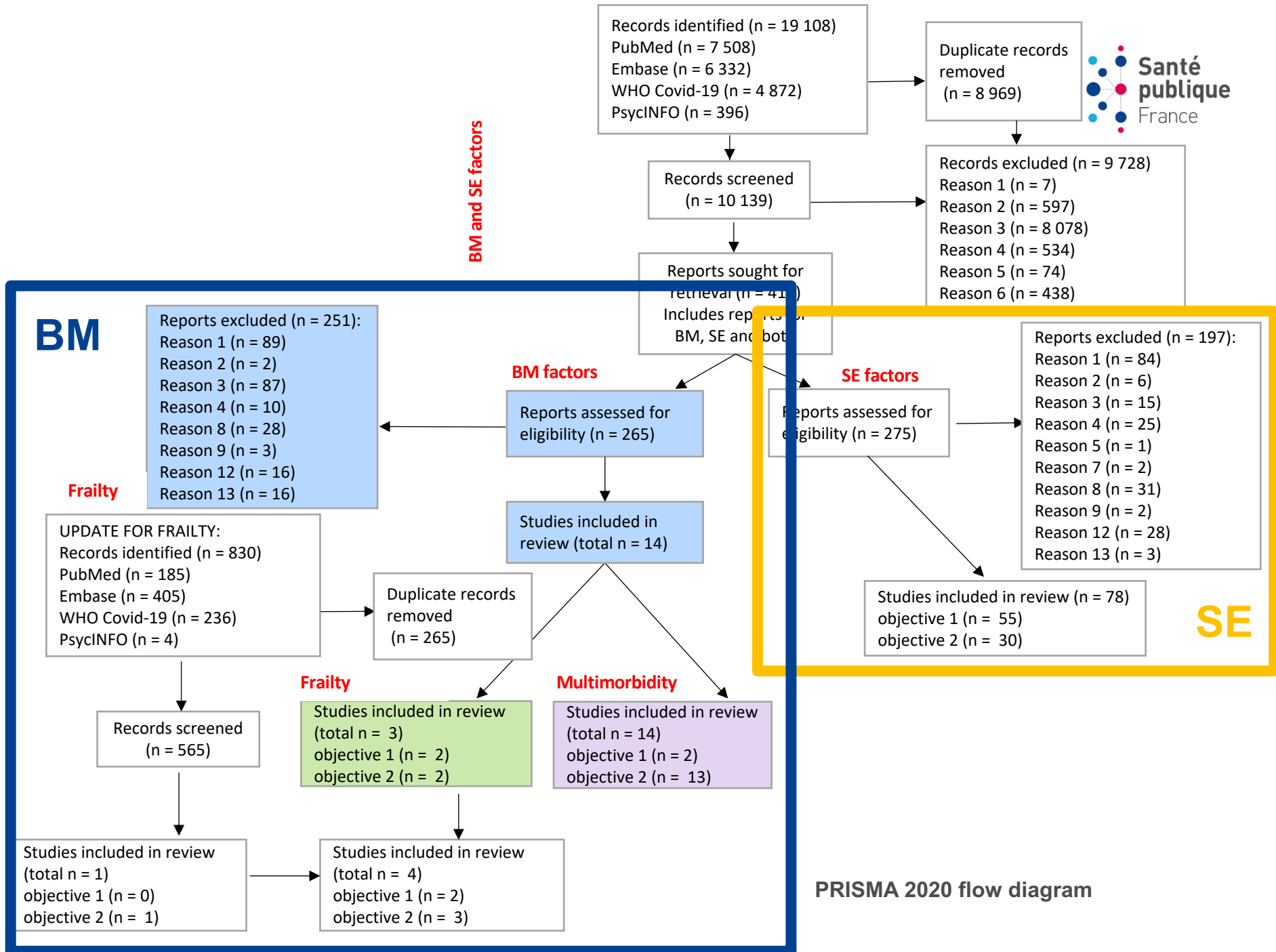


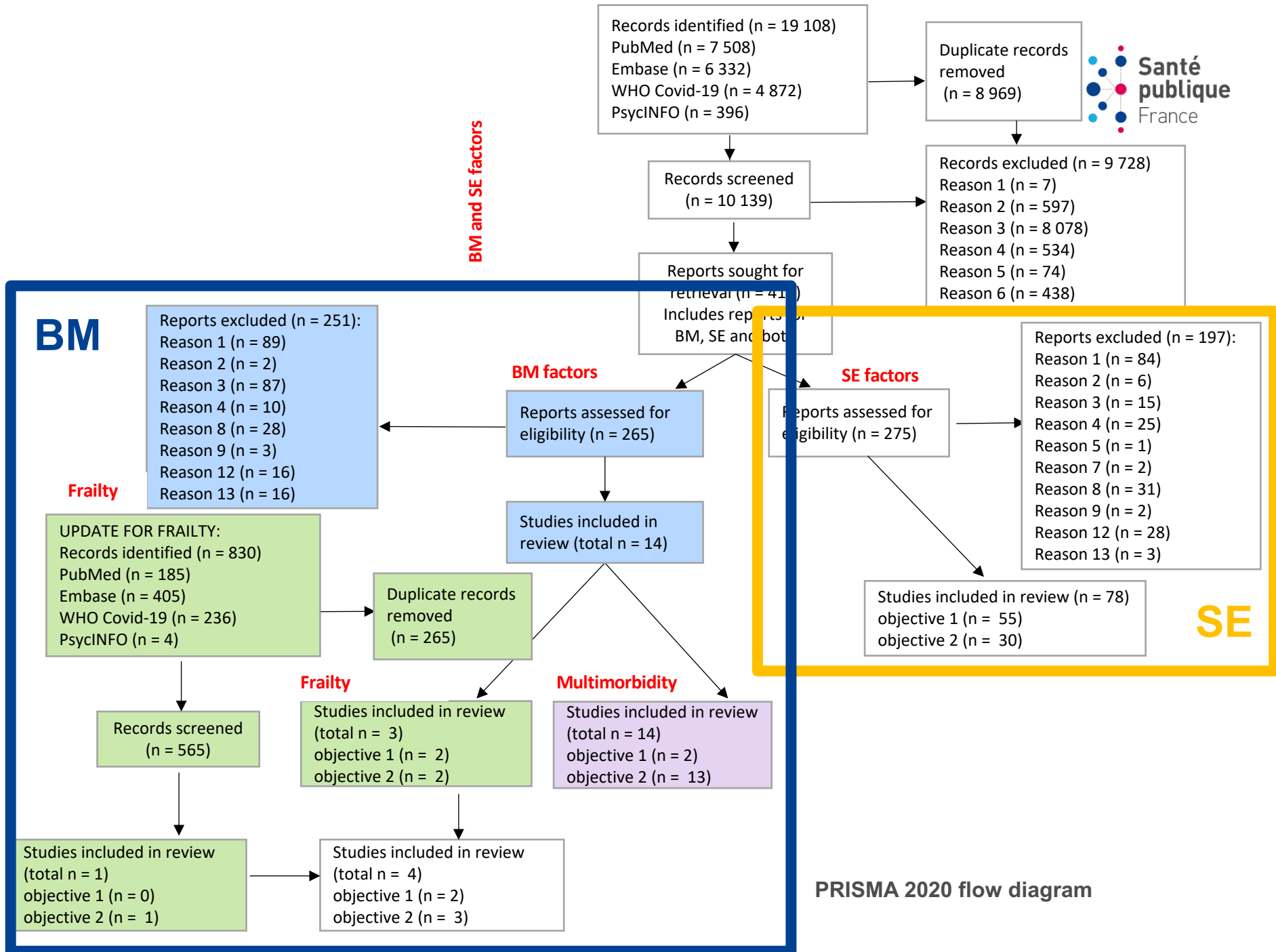


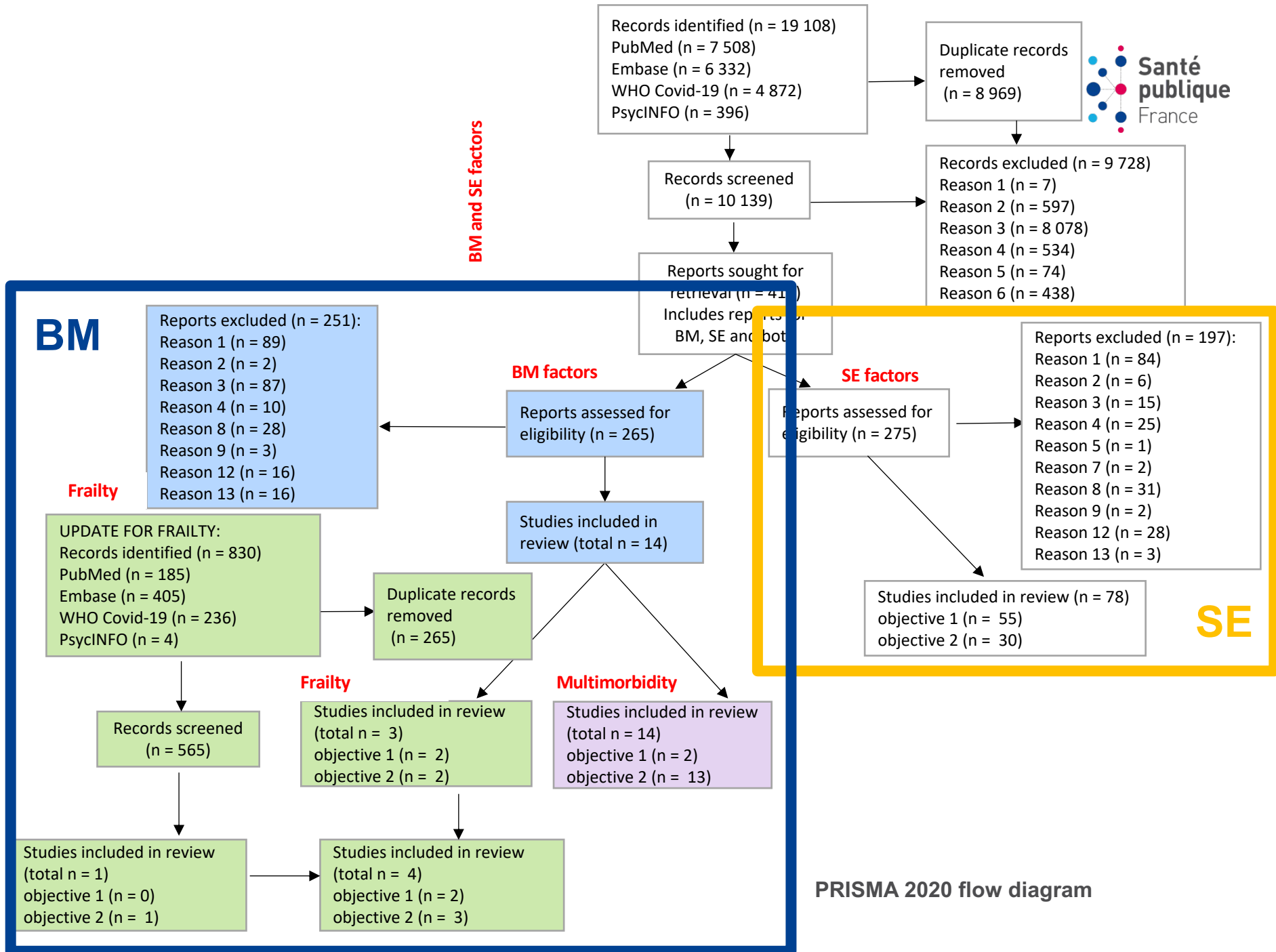












BM and SE factors

Records identified (n = 19 108)
PubMed (n = 7 508)
Embase (n = 6 332)
WHO Covid-19 (n = 4 872)
PsycINFO (n = 396)

Duplicate records removed
(n = 8 969)

Records screened
(n = 10 139)

Records excluded (n = 9 728)
Reason 1 (n = 7)
Reason 2 (n = 597)
Reason 3 (n = 8 078)
Reason 4 (n = 534)
Reason 5 (n = 74)
Reason 6 (n = 438)

Reports sought for retrieval (n = 411)
Includes reports for BM, SE and both

Reports excluded (n = 251):
Reason 1 (n = 89)
Reason 2 (n = 2)
Reason 3 (n = 87)
Reason 4 (n = 10)
Reason 8 (n = 28)
Reason 9 (n = 3)
Reason 12 (n = 16)
Reason 13 (n = 16)

BM factors

Reports assessed for eligibility (n = 265)

Critères d'exclusion 1

- 1 = Language other than English
- 2 = Not an original research (e.g. editorial, protocol, etc.) or no original results
- 3 = Unrelated topic
- 4 = Not a population-based study
- 5 = Subpopulation (medical staff, students, pregnant women, etc.)
- 6 = Duplicate

Studies included in review (total n = 14)

Critères d'exclusion 2

- 1 = Not a population-based study
- 2 = SARS-CoV-2 infection diagnosis not clear
- 3 = Study does not consider people with multimorbidity
- 4 = Outcome out of review scope
- 5 = Outcome measurement tool not clear
- 6 = Risk factor measurement tool not clear
- 7 = Subpopulation
- 8 = Not an original research
- 9 = The same or largely the same population
- 10 = Clinical trial or intervention study
- 11 = Qualitative study
- 12 = Descriptive study
- 13 = Other (explain)

Multimorbidity

Studies included in review (total n = 14)
objective 1 (n = 2)
objective 2 (n = 13)

Rôle étiologique (objectif 1) : 2 études; Rôle pronostique (objectif 2) : 13 études

Design: 9 études de cohorte, 5 études transversales

Milieu : communautaire 5 études, hospitalier 5, patients hospitalisés et ambulatoires 3 et unité de soins intensifs 1

Echantillon d'étude : min 308; max 24 367 476 participants

Évaluation de la qualité des études (NOS):

=> score excellent ou bon

Multimorbidité évaluée par le **nombre de maladies** 9 études, par **CCI** 4, **combinaisons de maladies** 1

Liste des pathologies : 7 - 60 pathologies

Seuls les résultats à court terme sont exploitables / **aucun résultat à long terme**

Facteurs **d'ajustement** principalement : **âge et sexe**

RÉSULTATS (RÔLE ÉTIOLOGIQUE)

First author (Country)	Sample	SARS-CoV-2 Infection		Hospitalisation		Mortality	
		N (%) of people for which the outcome occurred	Association with multimorbidity	N (%) of people for which the outcome occurred	Association with multimorbidity	N (%) of people for which the outcome occurred	Association with multimorbidity
Mak et al.2020 (England)	N = 410 199	N = 7 590 (1.85%)	OR (95%CI) for 1 CCI score increase = 1.30 (1.28-1.32)	N = 2 812 (0.69%)	OR (95%CI) for 1 CCI score increase = 1.47 (1.44-1.50)	N = 514 (0.1%)	OR (95%CI) for 1 CCI score increase = 1.53 (1.48-1.59)
Izurieta et al. 2021 (US)	N = 24 367 476	NA	NA	N = 27 961 (0.11%)	OR (95%CI) for CCI>0 = 1.09 (1.06-1.13)	N = 12 613 (0.05%)	OR (95%CI) for CCI>0 = 1.08 (1.03-1.14)

RÉSULTATS (RÔLE PRONOSTIQUE) – MORTALITÉ

	Mortality		
First author (Country)	Sample	N (%) of people for which the outcome occurred	Association with multimorbidity
Haase et al. 2020 (Denmark)	N = 308	N = 118 (37%)	N conditions = mortality rate (95%CI) – non adjusted 0 = 0,24 (0,16-0,35) 1 = 0,36 (0,26-0,48) 2 = 0,46 (0,35-0,58) 3 = 0,5 (0,33-0,66) 4 = 0,4 (0,12-0,74) 5 = 0,83 (0,36-1) 6 = 1
Millán-Guerrero et al. 2020 (Mexico)	N = 231 772	N = 28 510 (12.3%)	N conditions = HR (95%CI) 0 = 1 1 = 1.19 (1.16-1.23) 2 = 1.43 (1.39-1.48) 3 = 1.57 (1.50-1.65) ≥4 = 1.72 (1.60-1.84)
Reilev et al. 2020 (Denmark)	N = 11 122	N = 577 (5.2%)	N conditions = OR (95%CI) 0 = 1 1 = 2.6 (1.6-4.0) 2 = 2.6 (1.7-4.1) 3 = 3.5 (2.2-5.4) ≥4 = 5.2 (3.4-8.0)
Sousa et al. 2020 (Brasil)	N = 4 784 (2 570 Covid-19 positive patients; remaining, other SARI patients)	N = 353 (15.2%)	N conditions = OR (95%CI) 0 = 1 1 = 3.03 (2.34-3.94) ≥2 = 4.81 (3.48-6.63)

RÉSULTATS (RÔLE PRONOSTIQUE) – MORTALITÉ (SUITE)

Argoty-Pantoja et al. 2021 (Mexico)	N = 412 017	N = 45 754 (11.1%)	<p><u>Outpatients</u> Disease combinations = HR (95%CI) Obesity & hypertension = 2.84 (2.29-3.51) Diabetes & hypertension = 3.58 (3.05-4.22) Diabetes & obesity = 4.69 (3.53-6.23) Diabetes & obesity & hypertension = 5.57 (4.54-6.84)</p> <p><u>Hospitalised</u> Disease combinations = HR (95%CI) Obesity & hypertension = 1.31 (1.21-1.42) Diabetes & hypertension = 1.51 (1.43-1.59) Diabetes & obesity = 1.32 (1.18-1.46) Diabetes & obesity & hypertension = 1.66 (1.54-1.79)</p>
Hernandez-Vasquez et al. 2020 (Mexico)	N = 51 053	N = 5 233 (10.3%)	<p>N conditions = OR (95%CI) 0 = 1 1 = 1.89 (1.75-2.04) 2 = 2.51 (2.30-2.73) ≥3 = 3.49 (3.15-3.86)</p>
Cho et al. 2020 (South Korea)	N = 7 327	N = 223 (3%)	<p>HR (95%CI) for CCI score increase 1.14 (1.09-1.20)</p>
Mak et al.2020 (England)	N = 2 812	N = 417 (14.8%)	<p>OR (95%CI) for 1 CCI score increase = 1.17 (1.11-1.23)</p>
Navaratnam et al. 2020 (England)	N = 79 124	N = 28 200 (30.8%)	<p>OR (95%CI) associated with CCI :</p> <p>0 = 1.0 1 = 1.60 (1.51-1.68) 2 = 2.06 (1.94-2.18) 3 = 2.41 (2.27-2.57) ≥ 4 = 3.04 (2.88-3.22)</p>
Ticinesi et al. 2021 (Italy)	N = 1 264	N = 318 (25%)	<p>OR (95%CI) associated with multimorbidity (binary):</p> <p>0 = 1.0 ≥2 = 1.64 (1.10-2.45)</p> <p>OR (95%CI) associated with number of diseases: 1.17 (1.04-1.31)</p>

RÉSULTATS (RÔLE PRONOSTIQUE) – HOSPITALISATION ET VENTILATION MÉCANIQUE

First author (Country)	Sample	Hospitalisation		Mechanical ventilation	
		N (%) of people for which the outcome occurred	Association with multimorbidity	N (%) of people for which the outcome occurred	Association with multimorbidity
Reilev et al. 2020 (Denmark)	N = 11 122	N = 2 254 (20%)	N conditions = OR (95%CI) 0 = 1 1 = 1.7 (1.5-2.0) 2 = 2.1 (1.8-2.5) 3 = 3.1 (2.5-3.8) ≥4 = 3.9 (3.2-4.8)	NA	NA
Cho et al. 2020 (South Korea)	N = 7 327	NA	NA	N = 123 (1.7%)	OR (95%CI) per CCI score 1.10 (1.01-1.18)

RÉSULTATS (RÔLE PRONOSTIQUE) – INDICATEURS COMBINÉS

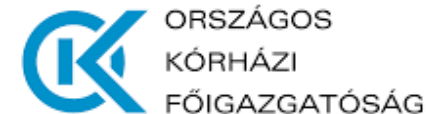
First author (Country)	Sample	Severe or critical illness ¹		ICU admission or mortality	
		N (%) of people for which the outcome occurred	Association with multimorbidity	N (%) of people for which the outcome occurred	Association with multimorbidity
Al Kuwari et al. 2020 (Qatar)	N = 5 685	Severe illness N = 82 (1.4%) Critical illness N = 35 (0.6%)	N conditions = OR (95%CI) 0 = 1 1 = 5.43 (3.41-8.63) ≥3* = 6.16 (3.35-11.32)	NA	NA
Cardoso et al. 2020 (Portugal)	N = 18 647	NA	NA	ICU admission or death N = 687 (3.7%)	N conditions = OR (95%CI) 0 = 1 1 = 2.95 (2.45-3.56) 2 = 3.57 (2.77-4.60) ≥3 = 6.00 (4.21-8.57)
Khan et al. 2020 (Saudi Arabia)	N = 648	NA	NA	ICU admission or death N = 77 (11.9%)	N conditions = OR (95%CI) ≥1 = 1.51 (0.87-2.62) ≥2 = 2.57 (1.33-4.97)

¹ World Health Organisation, Clinical management of severe acute respiratory infection when COVID-19 disease is suspected, 2020. Available: <https://www.who.int/publications/i/item/clinical-management-of-covid-19>

*as reported by authors

- Association **dose-effet négative** entre toutes les mesures de **multimorbidité** et tous les indicateurs observés
- **Rareté des études populationnelles** sur la multimorbidité, **encore moins** d'études sur le **rôle étiologique** de la multimorbidité
- **Nombre de maladies** principalement utilisé pour la mesure de la multimorbidité
- Résultats à court terme exploitables (mortalité); **aucun résultat à long terme disponible**
- **Limites** dans la comparaison des études dues aux **différents contextes**, **pathologies considérées**, **méthodes de mesure de la multimorbidité**

- **Pauvreté des connaissances** apportées sur le **rôle de la multimorbidité** à ce stade
- **Attente d'études en population**, utilisant des **mesures pertinentes et différenciées de la multimorbidité** et de ses composantes principales



Prix pour le meilleur poster, Symposium sur la multimorbidité, novembre 2021, Amsterdam, Pays-Bas

Accepté pour une présentation orale dans le cadre de l'atelier PHIRI, European Public Health Conference, novembre 2022, Berlin, Germany

Makovski et al. "Etiologic and prognostic roles of frailty, multimorbidity and socioeconomic characteristics in the development of SARS-CoV-2 infection and related severe health outcomes: protocol for systematic reviews of population-based studies"
under review BMJ Open

MERCI DE VOTRE ATTENTION