Appendix-Übersicht

PICO-Question

Duration of protective effect of a single dose of yellow fever vaccination

P(opulation) - population in endemic areas

- travellers to endemic areas

- all population groups regardless of exposure (seroconversion studies only)

} all age groups from 9 months of age

I(ntervention) Single dose of yellow fever vaccine of any substrain (regular or fractionated vaccine dose)

C(omparison) - no vaccination

- placebo, if available

- vaccination with another vaccine (not against yellow fever), if available

- booster vaccination with yellow fever vaccine

O(utcome)

Effectiveness	Importance for decision-making (GRADE)
Disease (yellow fever)	9
Death (yellow fever)	9
Surrogate marker for lack of protection (neutralizing antibody titre in PRNT <1:10)	6

Stratification

In order to investigate the duration of protection of the vaccination, all analyzes are carried out in the following strata:

< 3 months after vaccination

< 5 years after vaccination

5-10 years after vaccination

10-20 years after vaccination

> 20 years after vaccination

If the data allow it, the analyzes mentioned above are further stratified according to

a) study population:

- population in endemic areas
- travelers to endemic areas
- for seroconversion studies: independent of endemic status

b) Age of subjects:

- infants (age 9 months - 2 years)
- Children and adolescents (age 2 - 18 years)
- adults (> 18 years)
- seniors (> 60 years)

c) PRNT Threshold

- PRNT 50

- PRNT 80

- PRNT 90

d) Any immunodeficiency

Appendix 2

Search strategies

Appendix Table 1. Databases/resources searched 2020

Database/ Resource	Host	Date range	Results	Date Searched
MEDLINE; MEDLINE In-Process Citations, Medline Daily Update, and Epub Ahead of Print	Ovid	1946 to October 30, 2020	1654	2.11.20
PubMed	NLM	up to 2 November 2020	33	2.11.20
Embase	Ovid	1974 to 2020 Week 43	3562	2.11.20
Cochrane Central Register of Controlled Trials (CENTRAL)	Cochrane Library: Wiley	Issue 11 of 12, November 2020	262	2.11.20
Cochrane Database of Systematic Reviews (CDSR)	Cochrane Library: Wiley	Issue 11 of 12, November 2020	2	2.11.20
KSR Evidence	www.ksrevidence.com	Database last updated 2 Nov 2020	21	2.11.20
Database of Abstracts of Reviews of Effects (DARE)	https://www.crd.york.ac.uk/ CRDWeb/	up to 31 March 2015	2	2.11.20
Health Technology Assessment Database (HTA)	https://www.crd.york.ac.uk/ CRDWeb/	up to 31 March 2018	0	2.11.20
PROSPERO	https://www.crd.york.ac.uk/ PROSPERO/	up to 2 November 2020	49	2.11.20
WHO Global Index Medicus	https://www.globalindexmedicus.net/	up to 2 November 2020	351	2.11.20
Northern Light Life Sciences Conference Abstracts database	Ovid	2010 - 2020 Week 42	236	2.11.20
ClinicalTrials.gov	http://clinicaltrials.gov	up to 2 November 2020	63	2.11.20
WHO International Clinical Trials Register Portfolio (ICTRP)	http://www.who.int/ictrp/ search/en/	up to 2 November 2020	76	2.11.20
Total records retrieved			**6311**	
Duplicate records removed			**1823**	
Total records to screen			**4488**	

Search strategies. November 2020

MEDLINE and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily (Ovid): 1946 to October 30, 2020
Searched: 2.11.20

1 (Yellow Fever/ or Yellow fever virus/) and (exp Vaccination/ or exp Immunization/) (678)
2 (yellow fever$ adj3 (jab$ or vaccin$ or revaccin$ or immuniz$ or immunis$ or reimmuniz$ or reimmunis$ or inoculat$ or shot$ or booster$)).ti,ab. (1302)
3 yellow fever vaccine/ (784)
4 ((17D adj3 vaccin$) or (17DD adj3 vaccin$) or yf-vax or "yf vax" or stamaril or ap-yf or "ap yf" or BERNA-YF or flavimun or rki-yf or "rki yf" or "xrx 001" or xrx001).ti,ab,rn. (446)
5 or/1-4 (1854)
6 exp animals/ not humans/ (4751253)
7 5 not 6 (1654)

PubMed (NLM): up to 2 November 2020
https://pubmed.ncbi.nlm.nih.gov/
Searched: 2.11.20

5 #3 AND #4 33
4 pubstatusaheadofprint OR publisher[sb] OR pubmednotmedline[sb] 3,915,736
3 #1 AND #2 589
2 "17D vaccine" OR "17D vaccines" OR "17D vaccination" OR "17D vaccinations" OR "17DD vaccine" OR "17DD vaccines" or "17DD vaccination" or "17DD vaccinations" OR yf-vax OR "yf vax" OR stamaril OR ap-yf OR "ap yf" OR BERNA-YF OR flavimun OR rki-yf OR "rki yf" OR "xrx 001" OR xrx001 599
1 "yellow fever" AND (jab* or vaccin* or revaccin* or immuniz* or immunis* or reimmuniz* or reimmunis* or inoculat* or shot* or booster*) 2,786

Embase (Ovid): 1974 to 2020 Week 43
Searched: 2.11.20

1 (yellow fever/ or yellow fever virus/) and (exp vaccination/ or immunization/) (1631)
2 (yellow fever$ adj3 (jab$ or vaccin$ or revaccin$ or immuniz$ or immunis$ or reimmuniz$ or reimmunis$ or inoculat$ or shot$ or booster$)).ti,ab. (1456)
3 Yellow Fever Vaccine/ (2677)
4 ((17D adj3 vaccin$) or (17DD adj3 vaccin$) or yf-vax or "yf vax" or stamaril or ap-yf or "ap yf" or BERNA-YF or flavimun or rki-yf or "rki yf" or "xrx 001" or xrx001).ti,ab,rn. (505)
5 or/1-4 (3711)
6 Animal experiment/ not (human experiment/ or human/) (2288426)
7 (rat or rats or mouse or mice or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset$1).ti. and animal experiment/ (1086791)
8 5 not (6 or 7) (3562)

Cochrane Database of Systematic Reviews (CDSR) (Wiley): Issue 11 of 12, November 2020
Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley): Issue 11 of 12, November 2020
Searched: 2.11.20

#1 MeSH descriptor: [Yellow Fever] this term only 58
#2 MeSH descriptor: [Yellow fever virus] this term only 28
#3 (yellow NEAR/3 fever*):ti,ab,kw 198
#4 #1 or #2 or #3 198
#5 MeSH descriptor: [Vaccination] explode all trees 2514
#6 MeSH descriptor: [Immunization] this term only 650
#7 (jab* or vaccin* or revaccin* or immuniz* or immunis* or reimmuniz* or reimmunis* or inoculat* or shot* or booster*):ti,ab,kw 31908
#8 #5 or #6 or #7 31908
#9 #4 and #8 179
#10 MeSH descriptor: [Yellow Fever Vaccine] this term only 37
#11 (17D* or yf-vax or "yf vax" or stamaril or ap-yf or "ap yf" or BERNA-YF or flavimun or rki-yf or "rki yf" or "xrx 001" or xrx001):ti,ab,kw 148
#12 #9 or #10 or #11 264

CDSR 2 (2 reviews; 0 protocol)
CENTRAL 262

KSR Evidence (Internet): Database last updated 2 November 2020
www.ksrevidence.com
Searched: 2.11.20

1 "yellow fever*" in All text **21 results**
Database last updated Mon Nov 02 2020

Database of Abstracts of Reviews of Effects (DARE) (CRD): up to 31 March 2015
Health Technology Assessment Database (HTA) (CRD): to 31 March 2018
http://www.crd.york.ac.uk/CRDWeb/
Searched: 2.11.20

1 MeSH DESCRIPTOR Yellow Fever EXPLODE ALL TREES 1
2 MeSH DESCRIPTOR Yellow fever virus EXPLODE ALL TREES 1
3 (yellow NEAR fever*) 3
4 (17D* or yf-vax or "yf vax" or stamaril or ap-yf or "ap yf" or BERNA-YF or flavimun or rki-yf or "rki yf" or "xrx 001" or xrx001) 1
5 #1 OR #2 OR #3 OR #4 3
6 * IN DARE 4 5418
7 #5 AND #6 2
8 * IN HTA 17351
9 #5 AND #8 0

PROSPERO (International prospective register of systematic reviews): up to 2 November 2020
https://www.crd.york.ac.uk/PROSPERO/
Searched: 2.11.20

yellow fever **49**

WHO Global Index Medicus (GIM): up to 2 November 2020
https://www.globalindexmedicus.net/
Searched: 2.11.20

(mh:(("Yellow Fever" OR "Yellow fever virus") AND ("Vaccination" OR "Immunization"))) OR (tw:("yellow fever" AND (jab* or vaccin* or revaccin* or immuniz* or immunis* or reimmuniz* or reimmunis* or inoculat* or shot* or booster*))) OR (mh:("Yellow Fever Vaccine")) OR (tw:("17D vaccine" OR "17D vaccines" OR "17D vaccination" OR "17D vaccinations" OR "17DD vaccine" OR "17DD vaccines" or "17DD vaccination" or "17DD vaccinations" OR yf-vax OR "yf vax" OR stamaril OR ap-yf OR "ap yf" OR BERNA-YF OR flavimun OR rki-yf OR "rki yf" OR "xrx 001" OR xrx001))
Results 351

Northern Light Life Sciences Conference Abstracts (Ovid): 2010 – 2020 Week 42
Searched: 2.11.20

1 Yellow Fever/ and Vaccines/ (156)
2 (yellow fever$ adj3 (jab$ or vaccin$ or revaccin$ or immuniz$ or immunis$ or reimmuniz$ or reimmunis$ or inoculat$ or shot$ or booster$)).ti,ab. (125)
3 Yellow Fever Vaccine/ (5)
4 ((17D adj3 vaccin$) or (17DD adj3 vaccin$) or yf-vax or "yf vax" or stamaril or ap-yf or "ap yf" or BERNA-YF or flavimun or rki-yf or "rki yf" or "xrx 001" or xrx001).ti,ab. (34)
5 or/1-4 (236)

ClinicalTrials.gov (Internet): up to 2 November 2020
http://clinicaltrials.gov/ct2/search/advanced
Searched: 2.11.20

Expert search option

(("yellow fever" AND (vaccine OR vaccines OR vaccinate OR vaccination OR vaccinations OR revaccinate OR revaccination OR revaccinations OR immunization OR immunisation OR immunizations OR immunisations OR immunize OR immunise OR reimmunization OR reimmunisation OR reimmunizations OR reimmunisations OR reimmunize OR reimmunise OR shot OR shots OR booster OR boosters)) OR ("17D vaccine" OR "17D vaccines" OR "17D vaccination" OR "17D vaccinations" OR "17DD vaccine" OR "17DD vaccines" or "17DD vaccination" or "17DD vaccinations" OR yf-vax OR "yf vax" OR stamaril OR ap-yf OR "ap yf" OR BERNA-YF OR flavimun OR rki-yf OR "rki yf" OR "xrx 001" OR xrx001))
63 Studies found

WHO International Clinical Trials Register Platform (ICTRP) (Internet): up to 2 Nov. 2020
https://apps.who.int/trialsearch/
Searched: 2.11.20

yellow fever

(83 records for) 76 trials found

Appendix Table 2. Databases/resources searched. Update 2021

Database/ Resource	Host	Date range	Results	Date Searched
MEDLINE; MEDLINE In-Process Citations, Medline Daily Update, and Epub Ahead of Print	Ovid	1946 to November 11, 2021	107	12.11.21
PubMed	NLM	up to 12 November 2021	11	12.11.21
Embase	Ovid	1974 to 2021 Week 44	233	12.11.21
Cochrane Central Register of Controlled Trials (CENTRAL)	Cochrane Library: Wiley	Issue 11 of 12, November 2021	28	12.11.21
Cochrane Database of Systematic Reviews (CDSR)	Cochrane Library: Wiley	Issue 11 of 12, November 2021	0	12.11.21
KSR Evidence	www.ksrevidence.com	Database last updated 12 Nov 2021	6	12.11.21
Database of Abstracts of Reviews of Effects (DARE)*	https://www.crd.york.ac.uk/ CRDWeb/	up to 31 March 2015*	-	-
Health Technology Assessment Database (HTA)*	https://www.crd.york.ac.uk/ CRDWeb/	up to 31 March 2018*	-	-
PROSPERO	https://www.crd.york.ac.uk/ PROSPERO/	up to 12 November 2021	17	12.11.21
WHO Global Index Medicus	https://www.globalindexmedicus.net/	up to 12 November 2021	15	12.11.21
Northern Light Life Sciences Conference Abstracts database	Ovid	2010 - 2021 Week 44	17	12.11.21
ClinicalTrials.gov	http://clinicaltrials.gov	up to 12 November 2021	8	12.11.21
WHO International Clinical Trials Register Portfolio (ICTRP)	http://www.who.int/ictrp/ search/en/	up to 12 November 2021	5	12.11.21
Total records retrieved			**447**	
Duplicate records removed			**139**	
Total records to screen			**308**	

*New records have not been added to DARE since March 2015 and HTA since March 2018.

Search strategies. November 2021 update

MEDLINE and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily (Ovid): 1946 to November 11, 2021
Searched: 12.11.21

1 (Yellow Fever/ or Yellow fever virus/) and (exp Vaccination/ or exp Immunization/) (721)
2 (yellow fever$ adj3 (jab$ or vaccin$ or revaccin$ or immuniz$ or immunis$ or reimmuniz$ or reimmunis$ or inoculat$ or shot$ or booster$)).ti,ab. (1388)
3 yellow fever vaccine/ (862)
4 ((17D adj3 vaccin$) or (17DD adj3 vaccin$) or yf-vax or "yf vax" or stamaril or ap-yf or "ap yf" or BERNA-YF or flavimun or rki-yf or "rki yf" or "xrx 001" or xrx001).ti,ab,rn. (470)
5 or/1-4 (1963)
6 exp animals/ not humans/ (4913651)
7 5 not 6 (1759)

PubMed (NLM): up to 12 November 2021

https://pubmed.ncbi.nlm.nih.gov/

Searched: 12.11.21

5 #3 AND #4 41
4 pubstatusaheadofprint OR publisher[sb] OR pubmednotmedline[sb] 4,418,762
3 #1 AND #2 620
2 "17D vaccine" OR "17D vaccines" OR "17D vaccination" OR "17D vaccinations" OR "17DD vaccine" OR "17DD vaccines" or "17DD vaccination" or "17DD vaccinations" OR yf-vax OR "yf vax" OR stamaril OR ap-yf OR "ap yf" OR BERNA-YF OR flavimun OR rki-yf OR "rki yf" OR "xrx 001" OR xrx001 631
1 "yellow fever" AND (jab* or vaccin* or revaccin* or immuniz* or immunis* or reimmuniz* or reimmunis* or inoculat* or shot* or booster*) 2,963

Embase (Ovid): 1974 to 2021 Week 44
Searched: 12.11.21

1 (yellow fever/ or yellow fever virus/) and (exp vaccination/ or immunization/) (1754)
2 (yellow fever$ adj3 (jab$ or vaccin$ or revaccin$ or immuniz$ or immunis$ or reimmuniz$ or reimmunis$ or inoculat$ or shot$ or booster$)).ti,ab. (1545)
3 Yellow Fever Vaccine/ (2812)
4 ((17D adj3 vaccin$) or (17DD adj3 vaccin$) or yf-vax or "yf vax" or stamaril or ap-yf or "ap yf" or BERNA-YF or flavimun or rki-yf or "rki yf" or "xrx 001" or xrx001).ti,ab,rn. (525)
5 or/1-4 (3928)
6 Animal experiment/ not (human experiment/ or human/) (2365551)
7 (rat or rats or mouse or mice or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset$1).ti. and animal experiment/ (1126979)
8 5 not (6 or 7) (3775)

Cochrane Database of Systematic Reviews (CDSR) (Wiley): Issue 11 of 12, November 2021
Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley): Issue 11 of 12, November 2021

Searched: 12.11.21

#1 MeSH descriptor: [Yellow Fever] this term only 64
#2 MeSH descriptor: [Yellow fever virus] this term only 29
#3 (yellow NEAR/3 fever*):ti,ab,kw 223
#4 #1 or #2 or #3 223
#5 MeSH descriptor: [Vaccination] explode all trees 2696
#6 MeSH descriptor: [Immunization] this term only 671
#7 (jab* or vaccin* or revaccin* or immuniz* or immunis* or reimmuniz* or reimmunis* or inoculat* or shot* or booster*):ti,ab,kw 34772
#8 #5 or #6 or #7 34772
#9 #4 and #8 201
#10 MeSH descriptor: [Yellow Fever Vaccine] this term only 43
#11 (17D* or yf-vax or "yf vax" or stamaril or ap-yf or "ap yf" or BERNA-YF or flavimun or rki-yf or "rki yf" or "xrx 001" or xrx001):ti,ab,kw 162
#12 #9 or #10 or #11 293

CDSR 2 (2 reviews; 0 protocol)
CENTRAL 291

KSR Evidence (Internet): Database last updated 12 November 2021
www.ksrevidence.com
Searched: 12.11.21

1 "yellow fever*" in All text **27 results**
Database last updated Fri Nov 12 2021

Database of Abstracts of Reviews of Effects (DARE) (CRD): up to 31 March 2015
Health Technology Assessment Database (HTA) (CRD): to 31 March 2018
http://www.crd.york.ac.uk/CRDWeb/
Searched: 2.11.20

1 MeSH DESCRIPTOR Yellow Fever EXPLODE ALL TREES 1
2 MeSH DESCRIPTOR Yellow fever virus EXPLODE ALL TREES 1
3 (yellow NEAR fever*) 3
4 (17D* or yf-vax or "yf vax" or stamaril or ap-yf or "ap yf" or BERNA-YF or flavimun or rki-yf or "rki yf" or "xrx 001" or xrx001) 1
5 #1 OR #2 OR #3 OR #4 3
6 * IN DARE 4 5418
7 #5 AND #6 2
8 * IN HTA 17351
9 #5 AND #8 0

PROSPERO (International prospective register of systematic reviews): up to 12 November 2021
https://www.crd.york.ac.uk/PROSPERO/
Searched: 12.11.21

yellow fever 65

WHO Global Index Medicus (GIM): up to 12 November 2021
https://www.globalindexmedicus.net/
Searched: 12.11.21

(mh:(("Yellow Fever" OR "Yellow fever virus") AND ("Vaccination" OR "Immunization"))) OR (tw:("yellow fever" AND (jab* or vaccin* or revaccin* or immuniz* or immunis* or reimmuniz* or reimmunis* or inoculat* or shot* or booster*))) OR (mh:("Yellow Fever Vaccine")) OR (tw:("17D vaccine" OR "17D vaccines" OR "17D vaccination" OR "17D vaccinations" OR "17DD vaccine" OR "17DD vaccines" or "17DD vaccination" or "17DD vaccinations" OR yf-vax OR "yf vax" OR stamaril OR ap-yf OR "ap yf" OR BERNA-YF OR flavimun OR rki-yf OR "rki yf" OR "xrx 001" OR xrx001))
Results 377

Northern Light Life Sciences Conference Abstracts (Ovid): 2010 – 2021 Week 44
Searched: 12.11.21

1 Yellow Fever/ and Vaccines/ (0)
2 (yellow fever$ adj3 (jab$ or vaccin$ or revaccin$ or immuniz$ or immunis$ or reimmuniz$ or reimmunis$ or inoculat$ or shot$ or booster$)).ti,ab. (153)
3 Yellow Fever Vaccine/ (8)
4 ((17D adj3 vaccin$) or (17DD adj3 vaccin$) or yf-vax or "yf vax" or stamaril or ap-yf or "ap yf" or BERNA-YF or flavimun or rki-yf or "rki yf" or "xrx 001" or xrx001).ti,ab. (37)
5 or/1-4 (163)

ClinicalTrials.gov (Internet): up to 12 November 2021
http://clinicaltrials.gov/ct2/search/advanced
Searched: 12.11.21

Expert search option
(("yellow fever" AND (vaccine OR vaccines OR vaccinate OR vaccination OR vaccinations OR revaccinate OR revaccination OR revaccinations OR immunization OR immunisation OR immunizations OR immunisations OR immunize OR immunise OR reimmunization OR reimmunisation OR reimmunizations OR reimmunisations OR reimmunize OR reimmunise OR shot OR shots OR booster OR boosters)) OR ("17D vaccine" OR "17D vaccines" OR "17D vaccination" OR "17D vaccinations" OR "17DD vaccine" OR "17DD vaccines" or "17DD vaccination" or "17DD vaccinations" OR yf-vax OR "yf vax" OR stamaril OR ap-yf OR "ap yf" OR BERNA-YF OR flavimun OR rki-yf OR "rki yf" OR "xrx 001" OR xrx001))
68 Studies found

WHO International Clinical Trials Register Platform (ICTRP) (Internet): up to 12 Nov. 2021
https://apps.who.int/trialsearch/
Searched: 12.11.21

yellow fever

(91 records for) **85 trials found**

Appendix 3 - Table 3: Excluded studies with reasons for exclusion

Citation	Comment
Aarhus University Hospital. Immune response following vaccination against yellow fever. EUCTR2019-001731-31-DK. In: WHO International Clinical Trials Registry Platform (ICTRP) [Internet]. Geneva: World Health Organization (WHO). 2019 [accessed 02.11.20]. Available from: https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2019-001731-31	No relevant outcome
Abreu A, Braga JU, Wigg L, Caetano R. Safety of yellow fever vaccine in elderly: systematic review. PROSPERO 2020 CRD42020160430. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020160430	No relevant study design
Academic Medical Center, Amsterdam, the Netherlands. Protection after yellow fever vaccination in patients using medication suppressing the immune system. NTR3581. In: WHO International Clinical Trials Registry Platform (ICTRP) [Internet]. Geneva: World Health Organization (WHO). 2012 [accessed 02.11.20]. Available from: https://trialregister.nl/trial/3430	No relevant outcome
Adetokunboh O, Ndwandwe D, Awotiwon A, Uthman O. Evaluating the efficacy and effectiveness of vaccines among HIV–infected and HIV-exposed uninfected children: a systematic review and meta-analysis. PROSPERO 2018 CRD42018095334. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42018095334	No relevant study design
Adler M, Lapierre V, Castilla-Llorente C, Bourhis J-H, Gachot B, Wyplosz B. Persistence of Yellow Fever Vaccine-Induced Antibodies After Allogeneic Haematopoietic Stem-Cell Transplantation. In: European Congress of Clinical Microbiology and Infectious Diseases 2017; 22-Apr-2017, 2017. Available from: European Society of Clinical Microbiology and Infectious Diseases (ESCMID)	No relevant study design
Adler M, Lapierre V, Sakr R, Bourhis JH, Gachot B, Castilla-Llorente C, et al. Persistence of yellow fever immunization-induced antibodies in allogeneic hematopoietic stem cell transplant recipients. J Infect Dis 2018;217(11):1844-5.	No relevant study design
Alberer M, Burchard G, Jelinek T, Reisinger E, Beran J, Hlavata LC, et al. Safety and immunogenicity of typhoid fever and yellow fever vaccines when administered concomitantly with quadrivalent meningococcal ACWY glycoconjugate vaccine in healthy adults. J Travel Med 2015;22(1):48-56.	No relevant information
Anderson CR, Gast-Galvis A. Immunity to yellow fever five years after vaccination. Am J Epidemiol 1947;45(3):302-4.	Un-obtainable
Avelino-Silva VI, Freire Mda S, Rocha V, Rodrigues CA, Novis YS, Sabino EC, et al. Persistence of yellow fever vaccine-induced antibodies after cord blood stem cell transplant. Hum Vaccin Immunother 2016;12(4):937-8.	No relevant study design
Avelino-Silva VI, Miyaji KT, Simoes M, Freire M, Sartori A, Hunt PW, et al. Immune activation impairs yellow fever vaccine efficacy in HIV-infected patients. Paper presented at 2015 Conference on Retroviruses and Opportunistic Infections, CROI 2015; 23-26 Feb 2015; Seattle: United States. Top Antivir Med 2015;23(E-1):133.	No relevant study design

Citation	Comment
Azamor T, da Silva AMV, Melgaco JG, Dos Santos AP, Xavier-Carvalho C, Alvarado-Arnez LE, et al. Activation of an effective immune response after yellow fever vaccination is associated with the genetic background and early response of IFN-γ and CLEC5A. Viruses 2021;13(1):96.	No relevant outcome
Baudon D, Robert V, Roux J. [The yellow fever epidemic in Burkina Faso in 1983]. Bull World Health Organ 1986;64(6):873-82.	No relevant study design
Bio-Manguinhos/Fiocruz (Brazil). Yellow fever vaccine dose-response study on children. ISRCTN36905484. In: WHO International Clinical Trials Registry Platform (ICTRP) [Internet]. Geneva: World Health Organization (WHO). 2011 [accessed 02.11.20]. Available from: http://isrctn.com/ISRCTN36905484	No relevant outcome
Bouree P, Bisaro F. Yellow fever immunization for the solid organ recipients travellers. Paper presented at 12th conference of the International Society of Travel Medicine; 8-12 May 2011; Boston: United States. 2011.	No relevant outcome
Bovay A, Nassiri S, Maby-El Hajjami H, Marcos Mondejar P, Akondy RS, Ahmed R, et al. Minimal immune response to booster vaccination against yellow fever associated with pre-existing antibodies. Vaccine 2020;38(9):2172-82.	No relevant study design
Boyd AT, Dombaxe D, Moreira R, Oliveira MS, Manuel E, Colorado CN, et al. Notes from the field: investigation of patients testing positive for yellow fever viral RNA after vaccination during a mass yellow fever vaccination campaign - Angola, 2016. MMWR Morb Mortal Wkly Rep 2017;66(10):282-3.	No relevant study design
Brick IB. Residuals of yellow fever vaccine after ten years; a medical and legal problem. AMA Arch Intern Med 1953;92(2):221-7.	Un-obtainable
Buhler S, Jaeger VK, Eperon G, Furrer H, Fux CA, Jansen S, et al. Safety and immunogenicity of a primary yellow fever vaccination under low-dose methotrexate therapy - a prospective multi-centre pilot study. J Travel Med 2020;27(6):taaa126.	No relevant study design
Camacho LAB. Further Data On the Need For Booster Doses of Yellow Fever Vaccine (YFV). In: World Congress of Epidemiology 2014; 17-Aug-2014, 2014. Available from: World Congress of Epidemiology (WCE) https://discovery.northernlight.com/document.php?datasource=PHE&docid=PE20140811110001070&context=WK%40northernlight.com	No relevant study design
Campi-Azevedo A, Luiza-Silva M, Pacheco LP, Martins MA, Camacho LB, Homma A, et al. The 17D-213/77 seed-lot and the 17DD sub-strain of yellow fever vaccine trigger comparable overall cytokine signatures in vaccinated children. Paper presented at 15th Annual Conference on Vaccine Research; 7-9 May 2012; Baltimore: United States. 2012.	Un-obtainable
Caparroz ALMA, Trevisani VFM, Pileggi GCS. A systematic review of the safety and effectiveness of immunization on children and adolescents with chronic immune-mediated inflammatory diseases undergoing treatment with biologic and targeted synthetic disease-modifying antirheumatic drugs. PROSPERO 2019 CRD42019140927 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019140927	No relevant study design

Citation	Comment
Casey RM, Harris JB, Ahuka-Mundeke S, Dixon MG, Kizito GM, Nsele PM, et al. Immunogenicity of fractional-dose vaccine during a yellow fever outbreak - final report. N Engl J Med 2019;381(5):444-454.	No relevant study design
Centers for Disease Control and Prevention, Infectious Disease Institute, Kampala, Uganda, MRC/UVRI Uganda Research Unit on Aids, Ministry of Health, Uganda. Immunogenicity of fractional one-fifth and one-half doses of yellow fever vaccine compared to full dose in children 9-23 months old. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2018-2019 [cited 2020 Nov 2]. Available from: http://clinicaltrials.gov/show/NCT03725618. NLM Identifier: NCT03725618	Ongoing
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Stoffella-Dutra AG, Silva de Oliveira J, Barbosa Costa G, Geessien Kroon E, Santos Abrahao J, Desiree LaBeaud A, et al. Absence of YF-neutralizing antibodies in vulnerable populations of Brazil: a warning for epidemiological surveillance and the potential risks for future outbreaks. Vaccine 2020;38(42):6592-9.	No relevant study design
Stuhec M. Yellow fever vaccine used in a psoriatic arthritis patient treated with methotrexate: a case report. Acta dermatovenerolog 2014;23(3):63-4.	No relevant outcome
Suzano CE, Amaral E, Sato HK, Papaiordanou PM, Campinas Group on Yellow Fever Immunization during Pregnancy. The effects of yellow fever immunization (17DD) inadvertently used in early pregnancy during a mass campaign in Brazil. Vaccine 2006;24(9):1421-6.	No relevant study design
Takeda. Immunogenicity and safety of tetravalent dengue vaccine (TDV) administered with a yellow fever vaccine in adults. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2018-2019 [cited 2020 Nov 2]. Available from: http://clinicaltrials.gov/show/NCT03342898. NLM Identifier: NCT03342898	Ongoing
Takey PRG, Brasil P, Guaraldo L, Pedro RS. Effectiveness and safety of the yellow fever vaccine (attenuated): systematic review and meta-analysis. PROSPERO 2020 CRD42020157929. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020157929	No relevant study design
Tattevin P, Depatureaux AG, Chapplain JM, Dupont M, Souala F, Arvieux C, et al. Yellow fever vaccine is safe and effective in HIV-infected patients. AIDS 2004;18(5):825-7.	No relevant study design
Tokyo Medical University Hospital. Long-term immunity after Yellow fever vaccination. JPRN-UMIN000040526. In: WHO International Clinical Trials Registry Platform (ICTRP) [Internet]. Geneva: World Health Organization (WHO). 2020 [accessed 02.11.20]. Available from: https://upload.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000046155	Ongoing
University of Oxford, KEMRI-Wellcome Trust Collaborative Research Program, Institut Pasteur, MRC/UVRI Uganda Research Unit on Aids, Epicentre, Paris, France. Non-inferiority fractional-doses trial for yellow fever vaccine. In: ClinicalTrials.gov [Internet]. Bethesda (MD):	Ongoing

Citation	Comment
National Library of Medicine (US). 2019- [cited 2020 Nov 2]. Available from: http://clinicaltrials.gov/show/NCT04059471. NLM Identifier: NCT04059471	
University of Sao Paulo General Hospital. Yellow fever vaccine in patients with rheumatic diseases. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2018-2019 [cited 2020 Nov 2]. Available from: http://clinicaltrials.gov/show/NCT03430388. NLM Identifier: NCT03430388	No relevant outcome
University of Zurich, Swiss Tropical & Public Health Institute, Kantonsspital Aarau, University Hospital Inselspital, Berne, University Hospital, Geneva, Centre Hospitalier Universitaire Vaudois. Yellow fever vaccination under low dose methotrexate therapy. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2014-2016 [cited 2020 Nov 2]. Available from: http://clinicaltrials.gov/show/NCT02383680. NLM Identifier: NCT02383680	No relevant study design
Valim V, Gouvea SA, Lima SMB, Azevedo ACC, Carvalho AT, Pascoal VPM, et al. Effectiveness and safety of yellow fever vaccine in patients with primary Sjogren's syndrome. Paper presented at 14th International Symposium on Sjogren's Syndrome; 17-20 Apr 2018; Washington DC: United States. Clin Exp Rheumatol 2018;36(3 Suppl 112):S326.	No relevant outcome
Vasconcelos PFC, Barrett ADT. Are booster doses of yellow fever vaccine needed? Lancet Infect Dis 2019;19(12):1275-6.	No relevant study design
Wieten RW, Goorhuis A, Jonker EFF, de Bree GJ, de Visser AW, van Genderen PJJ, et al. 17D yellow fever vaccine elicits comparable long-term immune responses in healthy individuals and immune-compromised patients. J Infect 2016;72(6):713-22.	No relevant study design
Wieten RW, Jonker E, De Bree G, Goorhuis A, Visser LG, Van Leeuwen E, et al. Yellow fever vaccination immune responses are measurable up to 38 years after vaccination. Paper presented at 16th International Congress on Infectious Diseases, ICID 2014; 2-5 Apr 2014; Cape Town: South Africa. Int J Infect Dis 2014;21(Suppl 1):437.	No relevant outcome
Wieten RW, Jonker EF, Pieren DK, Hodiamont CJ, van Thiel PP, van Gorp EC, et al. Comparison of the PRNT and an immune fluorescence assay in yellow fever vaccinees receiving immunosuppressive medication. Vaccine 2016;34(10):1247-51.	No relevant study design
Wieten RW, Jonker EF, van Leeuwen EM, Remmerswaal EB, Ten Berge IJ, de Visser AW, et al. A single 17D yellow fever vaccination provides lifelong immunity; characterization of yellow-fever-specific neutralizing antibody and T-cell responses after vaccination. PLoS One 2016;11(3):e0149871.	No relevant study design
Willcox AC, Collins MH, Jadi R, Keeler C, Parr JB, Mumba D, et al. Seroepidemiology of dengue, Zika, and yellow fever viruses among children in the Democratic Republic of the Congo. Am J Trop Med Hyg 2018;99(3):756-63.	No relevant study design

Citation	Comment
Wilder-Smith A, Barrett A, Vannice K, Hombach J. Long-term protection after fractional-dose yellow fever vaccination. Ann Intern Med 2019;171(2):145-6.	No relevant study design
Wisseman CL, Jr., Sweet BH. Immunological studies with group B arthropod-borne viruses. III. Response of human subjects to revaccination with 17D strain yellow fever vaccine. Am J Trop Med Hyg 1962;11(4):570-5.	Un-obtainable
Wyplosz B, Burdet C, Francois H, Durrbach A, Duclos-Vallee JC, Mamzer-Bruneel MF, et al. Persistence of yellow fever vaccine-induced antibodies after solid organ transplantation. Am J Transplant 2013;13(9):2458-61.	No relevant study design
Wyplosz B, Burdet C, Francois H, Durrbach A, Duclos-Vallee JC, Mamzer-Bruneel MF, et al. Persistence of yellow fever vaccine induced antibodies after solid organ transplantation. Paper presented at European Congress of Clinical Microbiology and Infectious Diseases 2014; 10-13 May 2014; Barcelona: Spain. 2014.	No relevant study design
Yamoah P, Bangalee V, Oosthuizen F. A review of the safety of vaccines used in routine immunization in Africa. Afr Health Sci 2020;20(1):227-37.	No relevant study design
Zhao, L., Miao, F., Chen, T., Du, H. & Zhao, J. Stablity of yellow fever virus neutralising antibody titres. Lancet Infect Dis 20, 166-167, doi:http://dx.doi.org/10.1016/S1473-3099%2819%2930703-0 (2020).	No relevant study design

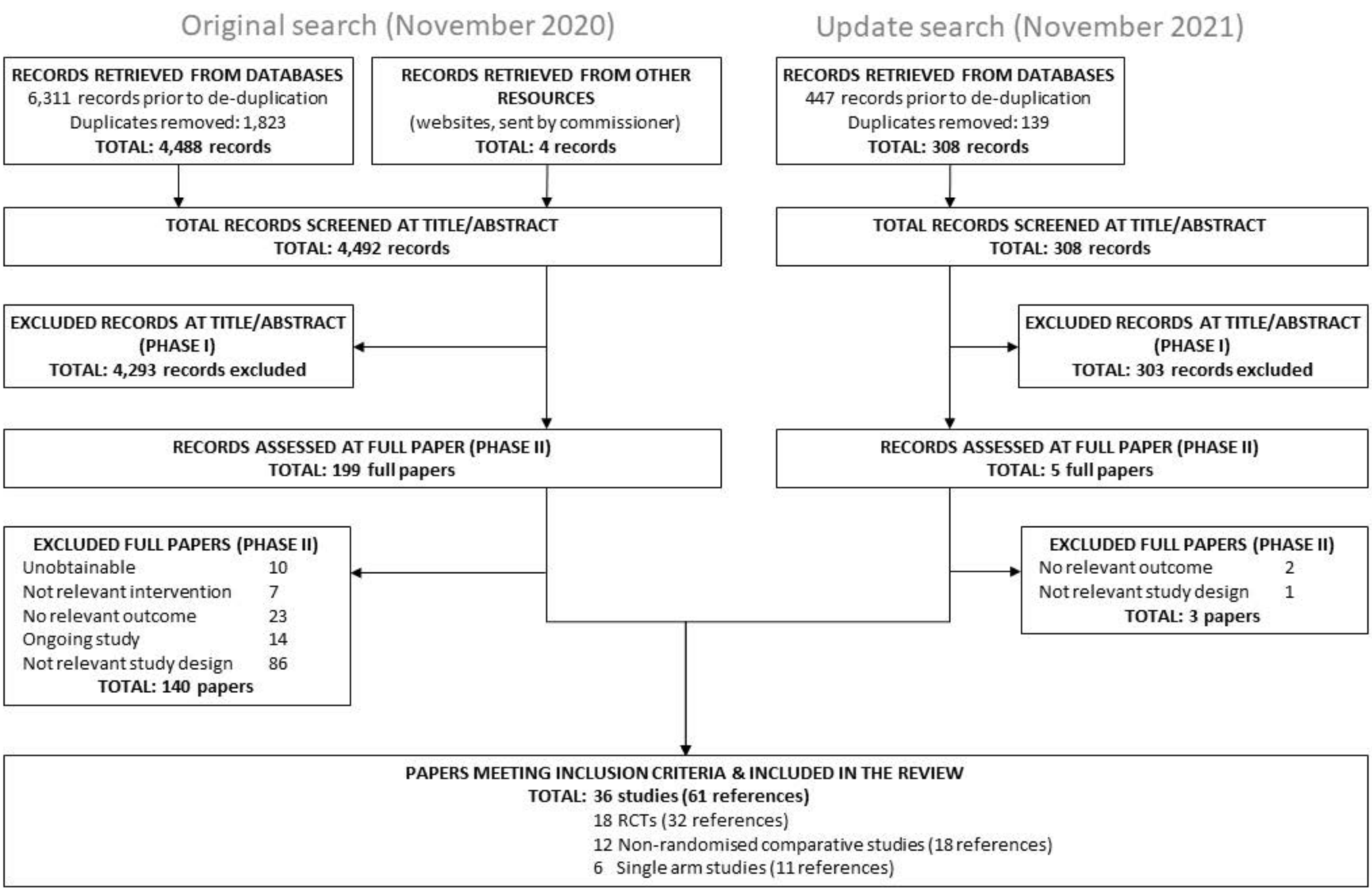
Appendix 4 - Table 4: Included studies

Study	Reference
Randomised controlled trials (18 studies, 32 references)	
Asante 2020 (NCT02699099)	Asante KP, Ansong D, Kaali S, Adjei S, Lievens M, Nana Badu L, et al. Immunogenicity and safety of the RTS,S/AS01 malaria vaccine co-administered with measles, rubella and yellow fever vaccines in Ghanaian children: a phase IIIb, multi-center, non-inferiority, randomized, open, controlled trial. Vaccine 2020;38(18):3411-21.
	GlaxoSmithKline. Immunogenicity and safety study of GSK biologicals' candidate malaria vaccine given at 6, 7.5 and 9 months of age in co-administration with measles, rubella and yellow fever (YF) vaccines followed by a booster of the malaria vaccine. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2017-2020 [cited 2020 Nov 2]. Available from: https://ClinicalTrials.gov/show/NCT02699099. NLM Identifier: NCT02699099
Belmusto-Worn 2005	Belmusto-Worn VE, Sanchez JL, McCarthy K, Nichols R, Bautista CT, Magill AJ, et al. Randomized, double-blind, phase III, pivotal field trial of the comparative immunogenicity, safety, and tolerability of two yellow fever 17D vaccines (Arilvax and YF-VAX) in healthy infants and children in Peru. Am J Trop Med Hyg 2005;72(2):189-97.
Camacho 2004	Camacho LA, de Aguiar SG, Freire Mda S, Leal Mda L, do Nascimento JP, Iguchi T, et al. Reactogenicity of yellow fever vaccines in a randomized, placebo-controlled trial. Rev Saude Publica 2005;39(3):413-20.
	Camacho LAB, Freire Mda S, Leal Mda L, de Aguiar SG, do Nascimento JP, Iguchi T, et al. Immunogenicity of WHO-17D and Brazilian 17DD yellow fever vaccines: a randomized trial. Rev Saude Publica 2004;38(5):671-8.
Campi-Azevedo 2014 (NCT0338231; ISRCTN38082350)	de Menezes Martins R, Maia MLS, de Lima SMB, de Noronha TG, Xavier JR, Camacho LAB, et al. Duration of post-vaccination immunity to yellow fever in volunteers eight years after a dose-response study. Vaccine 2018;36(28):4112-7.
	da Costa-Rocha IA, Campi-Azevedo AC, Peruhype-Magalhaes V, Coelho-Dos-Reis JG, Fradico JRB, Souza-Lopes T, et al. Duration of humoral and cellular immunity 8 years after administration of reduced doses of the 17DD-yellow fever vaccine. Front Immunol 2019;10:1211.
	Campi-Azevedo AC, de Almeida Estevam P, Coelho-Dos-Reis JG, Peruhype-Magalhaes V, Villela-Rezende G, Quaresma PF, et al. Subdoses of 17DD yellow fever vaccine elicit equivalent virological/immunological kinetics timeline. BMC Infect Dis 2014;14:391.
	Martins RM, Maia Mde L, Farias RH, Camacho LA, Freire MS, Galler R, et al. 17DD yellow fever vaccine: a double blind, randomized clinical trial of immunogenicity and safety on a dose-response study. Hum Vaccin Immunother 2013;9(4):879-88.
	The Immunobiological Technology Institute (Bio-Manguinhos) / Oswaldo Cruz Foundation (Fiocruz). Clinical study of immunity duration of yellow fever vaccine in military. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2017-2017 [cited 2020 Nov 2]. Available from: http://clinicaltrials.gov/show/NCT03338231. NLM Identifier: NCT03338231
	Bio-Manguinhos/Fiocruz (Brazil). Yellow fever vaccine dose-response study. ISRCTN38082350. In: WHO International Clinical Trials Registry Platform (ICTRP) [Internet]. Geneva: World Health Organization (WHO). 2008 [accessed 02.11.20]. Available from: http://isrctn.com/ISRCTN38082350
Chan 2016 (NCT01943305)	Chan KR, Wang X, Saron WAA, Gan ES, Tan HC, Mok DZL, et al. Cross-reactive antibodies enhance live attenuated virus infection for increased immunogenicity. Nat Microbiol 2016;1:16164.
	Low JG, Wijaya L, Li GK, Lim EY, Shum AK, Cheung YB, et al. The role of pre-existing cross-reactive antibodies in determining the efficacy of vaccination in humans: study protocol for a randomized controlled trial. Trials 2015;16:147.
Collaborative Group for Studies of Yellow Fever Vaccine 2015 (ISRCTN72367932)	Collaborative Group for Studies of Yellow Fever Vaccine. A randomised double-blind clinical trial of two yellow fever vaccines prepared with substrains 17DD and 17D-213/77 in children nine-23 months old. Mem Inst Oswaldo Cruz 2015;110(6):771-80.
	Campi-Azevedo AC, de Araujo-Porto LP, Luiza-Silva M, Batista MA, Martins MA, Sathler-Avelar R, et al. 17DD and 17D-213/77 yellow fever substrains trigger a balanced cytokine profile in primary vaccinated children. PLoS One 2012;7(12):e49828.
	Collaborative Group for Studies with Yellow Fever Vaccine. Randomized, double-blind, multicenter study of the immunogenicity and reactogenicity of 17DD and WHO 17D-213/77 yellow fever vaccines in children: implications for the Brazilian National Immunization Program. Vaccine 2007;25(16):3118-23.
	Bio-Manguinhos (Brazil). Multicentre, randomised, double-blind trial comparing yellow fever vaccines from 17D and WHO 17DD-213/77 substrains in children. ISRCTN72367932. In: WHO International Clinical Trials Registry Platform (ICTRP) [Internet]. Geneva: World Health Organization (WHO). 2006 [accessed 02.11.20]. Available from: http://isrctn.com/ISRCTN72367932
Coursaget 1995	Coursaget P, Fritzell B, Blondeau C, Saliou P, Diop-Mar I. Simultaneous injection of plasma-derived or recombinant hepatitis B vaccines with yellow fever and killed polio vaccines. Vaccine 1995;13(1):109-11.

Study	Reference
Edupuganti 2013	Edupuganti S, Eidex RB, Keyserling H, Akondy RS, Lanciotti R, Orenstein W, et al. A randomized, double-blind, controlled trial of the 17D yellow fever virus vaccine given in combination with immune globulin or placebo: comparative viremia and immunogenicity. Am J Trop Med Hyg 2013;88(1):172-7.
Guirakhoo 2006	Guirakhoo F, Kitchener S, Morrison D, Forrat R, McCarthy K, Nichols R, et al. Live attenuated chimeric yellow fever dengue type 2 (ChimeriVax-DEN2) vaccine: phase I clinical trial for safety and immunogenicity: effect of yellow fever pre-immunity in induction of cross neutralizing antibody responses to all 4 dengue serotypes. Hum Vaccin 2006;2(2):60-7.
Juan-Giner 2021	Juan-Giner A, Kimathi D, Grantz KH, Hamaluba M, Kazooba P, Njuguna P, et al. Immunogenicity and safety of fractional doses of yellow fever vaccines: a randomised, double-blind, non-inferiority trial. Lancet 2021;397(10269):119-27.
Lang 1999	Lang J, Zuckerman J, Clarke P, Barrett P, Kirkpatrick C, Blondeau C. Comparison of the immunogenicity and safety of two 17D yellow fever vaccines. Am J Trop Med Hyg 1999;60(6):1045-50.
Lopez 2016 (NCT01436396; EudraCT 2014-001714-26)	Lopez P, Lanata CF, Zambrano B, Cortes M, Andrade T, Amemiya I, et al. Immunogenicity and safety of yellow fever vaccine (Stamaril) when administered concomitantly with a tetravalent dengue vaccine candidate in healthy toddlers at 12-13 months of age in Colombia and Peru: a randomized trial. Pediatr Infect Dis J 2016;35(10):1140-7.
	Sanofi Pasteur, a Sanofi Company. Study of yellow fever vaccine administered with tetravalent dengue vaccine in healthy toddlers. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2011-2013 [cited 2020 Nov 2]. Available from: http://clinicaltrials.gov/show/NCT01436396. NLM Identifier: NCT01436396
Monath 2002	Monath TP, Nichols R, Archambault WT, Moore L, Marchesani R, Tian J, et al. Comparative safety and immunogenicity of two yellow fever 17D vaccines (ARILVAX and YF-VAX) in a phase III multicenter, double-blind clinical trial. Am J Trop Med Hyg 2002;66(5):533-41
Nasveld 2010 (NCT00982137)	Nasveld PE, Marjason J, Bennett S, Aaskov J, Elliott S, McCarthy K, et al. Concomitant or sequential administration of live attenuated Japanese encephalitis chimeric virus vaccine and yellow fever 17D vaccine: randomized double-blind phase II evaluation of safety and immunogenicity. Hum Vaccin 2010;6(11):906-14.
	Sanofi. Study of live attenuated Japanese encephalitis vaccine (ChimeriVax™-JE) and yellow fever vaccine (STAMARIL®). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2004-2007 [cited 2020 Nov 2]. Available from: http://clinicaltrials.gov/show/NCT00982137. NLM Identifier: NCT00982137
Novartis 2011 (EUCTR2011-000475-14-DE; NCT01466387)	Novartis Vaccines and Diagnostics S.r.l. Study to evaluate the safety and immunogenicity of travel vaccines when administered concomitantly with meningococcal ACWY conjugate vaccine in healthy adults. EUCTR2011-000475-14-DE. In: WHO International Clinical Trials Registry Platform (ICTRP) [Internet]. Geneva: World Health Organization (WHO). 2011 [accessed 02.11.20]. Available from: https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2011-000475-14
Osei-Kwasi 2001	Osei-Kwasi M, Dunyo SK, Koram KA, Afari EA, Odoom JK, Nkrumah FK. Antibody response to 17D yellow fever vaccine in Ghanaian infants. Bull World Health Organ 2001;79(11):1056-9.
Roukens 2008 (ISRCTN46326316)	Roukens AHE, van Halem K, de Visser AW, Visser LG. Long-term protection after fractional-dose yellow fever vaccination: follow-up study of a randomized, controlled, noninferiority trial. Ann Intern Med 2018;169(11):761-5.
	Roukens AH, Vossen AC, Bredenbeek PJ, van Dissel JT, Visser LG. Intradermally administered yellow fever vaccine at reduced dose induces a protective immune response: a randomized controlled non-inferiority trial. PLoS One 2008;3(4):e1993.
Stefano 1999	Stefano I, Sato HK, Pannuti CS, Omoto TM, Mann G, Freire MS, et al. Recent immunization against measles does not interfere with the sero-response to yellow fever vaccine. Vaccine 1999;17(9-10):1042-6.
Non-randomised comparative studies (12 studies, 18 references)	
Avelino-Silva 2016a	Avelino-Silva VI, Miyaji KT, Hunt PW, Huang Y, Simoes M, Lima SB, et al. CD4/CD8 ratio and KT ratio predict yellow fever vaccine immunogenicity in HIV-infected patients. PLoS Negl Trop Dis 2016;10(12):e0005219.
Avelino-Silva 2016b	Avelino-Silva VI, Miyaji KT, Mathias A, Costa DA, de Carvalho Dias JZ, Lima SB, et al. CD4/CD8 ratio predicts yellow fever vaccine-induced antibody titers in virologically suppressed HIV-infected patients. J Acquir Immune Defic Syndr 2016;71(2):189-95.
Burkhard 2020	Burkhard J, Ciurea A, Gabay C, Hasler P, Muller R, Niedrig M, et al. Long-term immunogenicity after yellow fever vaccination in immunosuppressed and healthy individuals. Vaccine 2020;38(19):3610-7.
Campi-Azevedo 2016	Campi-Azevedo AC, Costa-Pereira C, Antonelli LR, Fonseca CT, Teixeira-Carvalho A, Villela-Rezende G, et al. Booster dose after 10 years is recommended following 17DD-YF primary vaccination. Hum Vaccin Immunother 2016;12(2):491-502.
Collaborative Group for Studies of Yellow Fever Vaccine 2019a	Collaborative Group for Studies on Yellow Fever Vaccines. Duration of immunity in recipients of two doses of 17DD yellow fever vaccine. Vaccine 2019;37(35):5135.

Study	Reference
Collaborative Group for Studies of Yellow Fever Vaccine 2019b	Campi-Azevedo AC, Peruhype-Magalhaes V, Coelho-Dos-Reis JG, Antonelli LR, Costa-Pereira C, Speziali E, et al. 17DD yellow fever revaccination and heightened long-term immunity in populations of disease-endemic areas, Brazil. Emerg Infect Dis 2019;25(8):1511-21.
de Verdiere 2018 (NCT01426243)	Colin de Verdiere N, Durier C, Samri A, Meiffredy V, Launay O, Matheron S, et al. Immunogenicity and safety of yellow fever vaccine in HIV-1-infected patients. AIDS 2018;32(16):2291-9.
	Durier C, Mercier-Delarue S, De Verdiere NC, Meiffredy V, Matheron S, Samri A, et al. Long-term immune response to yellow fever vaccination in HIV-infected and non-infected adults: ANRS EP46 study. Paper presented at European Congress of Clinical Microbiology and Infectious Diseases; 18-21 Apr 2020; Paris: France. 2020.
	Colin de Verdiere N. Safety and immunogenicity of yellow fever vaccine in HIV+ patients: ANRS EP46 NOVAA. Paper presented at International AIDS Conference, IAS 2015; 19-22 Jul 2015; Vancouver: Canada. 2015.
Kernéis 2013	Kernéis S, Launay O, Ancelle T, Iordache L, Naneix-Laroche V, Mechai F, et al. Safety and immunogenicity of yellow fever 17D vaccine in adults receiving systemic corticosteroid therapy: an observational cohort study. Arthritis Care Res 2013;65(9):1522-8.
Michel 2015	Michel R, Berger F, Ravelonarivo J, Dussart P, Dia M, Nacher M, et al. Observational study on immune response to yellow fever and measles vaccines in 9 to 15-month old children. Is it necessary to wait 4 weeks between two live attenuated vaccines? Vaccine 2015;33(20):2301-6.
Project RETRO-CI	Sibailly TS, Wiktor SZ, Tsai TF, Cropp BC, Ekpini ER, Adjorlolo-Johnson G, et al. Poor antibody response to yellow fever vaccination in children infected with human immunodeficiency virus type 1. Pediatr Infect Dis J 1997;16(12):1177-9.
Roukens 2011	Roukens AH, Soonawala D, Joosten SA, de Visser AW, Jiang X, Dirksen K, et al. Elderly subjects have a delayed antibody response and prolonged viraemia following yellow fever vaccination: a prospective controlled cohort study. PLoS One 2011;6(12):e27753.
	Roukens AH, Soonawala D, Joosten SA, Visser AWD, Jiang X, Bredenbeek PJ, et al. Delayed antibody response to yellow fever vaccination in elderly coincides with prolonged viraemia. Paper presented at 12th conference of the International Society of Travel Medicine; 8-12 May 2011; Boston: United States. 2011.
	AHE Roukens and LG Visser. Immunity induced by yellow fever vaccination in the elderly (60 yrs or older) traveller. NTR1040. In: WHO International Clinical Trials Registry Platform (ICTRP) [Internet]. Geneva: World Health Organization (WHO). 2007 [accessed 02.11.20]. Available from: https://trialregister.nl/trial/1011
	Rosenstein MD, de Visser AW, Visser LG, Roukens AHE. Long-term immunity after a single yellow fever vaccination in travelers vaccinated at 60 years or older: a 10-year follow-up study. J Travel Med 2021;Online ahead of print.
Valim 2020	Valim V, Machado KLLL, Miyamoto ST, Pinto AD, Rocha PCM, Serrano EV, et al. Planned yellow fever primary vaccination is safe and immunogenic in patients with autoimmune diseases: a prospective non-interventional study. Front Immunol 2020;11:1382.
	Valim V, Pinto AD, Rocha PCM, Miyamoto ST, Serrano EV, Duque RH, et al. Safety and efficacy of primary yellow fever vaccination in autoimmune disease: a prospective controlled study. Ann Rheum Dis 2019;78(Suppl 2):2110.
Single arm studies (6 studies, 11 references)	
Campi-Azevedo 2019 (NCT02990182)	Campi-Azevedo AC, Reis LR, Peruhype-Magalhaes V, Coelho-Dos-Reis JG, Antonelli LR, Fonseca CT, et al. Short-lived immunity after 17DD yellow fever single dose indicates that booster vaccination may be required to guarantee protective immunity in children. Front Immunol 2019;10:2192.
	Oswaldo Cruz Foundation. Complementary study of the duration of post-vaccination against yellow fever immunity in children. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2015-2017 [cited 2020 Nov 2]. Available from: http://clinicaltrials.gov/show/NCT02990182. NLM Identifier: NCT02990182
Domingo 2019 (ISRCTN82484612)	Domingo C, Fraissinet J, Ansah PO, Kelly C, Bhat N, Sow SO, et al. Long-term immunity against yellow fever in children vaccinated during infancy: a longitudinal cohort study. Lancet Infect Dis 2019;19(12):1363-70.
	Roy Chowdhury P, Meier C, Laraway H, Tang Y, Hodgson A, Sow SO, et al. Immunogenicity of yellow fever vaccine coadministered with MenAfriVac in healthy infants in Ghana and Mali. Clin Infect Dis 2015;61 Suppl 5:S586-93.
	Serum Institute of India Limited. A phase II, double-blind, randomised, controlled, dose ranging study to evaluate the safety, immunogenicity, dose response and schedule response of a meningococcal A conjugate vaccine administered concomitantly with local expanded program on immunisation (EPI) vaccines in healthy infants. ISRCTN82484612. In: WHO International Clinical Trials Registry Platform (ICTRP) [Internet]. Geneva: World Health Organization (WHO). 2008 [dated accessed 02.11.20]. Available from: http://isrctn.com/ISRCTN82484612
Idoko 2020	Idoko OT, Domingo C, Tapia MD, Sow SO, Geldmacher C, Saathoff E, et al. Serological protection 5-6 years post vaccination against yellow fever in African infants vaccinated in routine programmes. Front Immunol 2020;11:577751.
Jia 2019 (ChCTR1800017024)	Jia Q, Jia C, Liu Y, Yang Y, Qi J, Tong L, et al. Clinical evidence for the immunogenicity and immune persistence of vaccination with yellow fever virus strain 17D in Chinese peacekeepers deployed to Africa. Antiviral Res 2019;162:1-4.

Study	Reference
	Jinan Military Region Center for Disease Control and Prevention. Study of immunogenicity and persistence of yellow fever attenuated live vaccine. ChiCTR1800017024. In: WHO International Clinical Trials Registry Platform (ICTRP) [Internet]. Geneva: World Health Organization (WHO). 2018 [accessed 02.11.20]. Available from: http://www.chictr.org.cn/showproj.aspx?proj=28675
Kareko 2020	Kareko BW, Booty BL, Nix CD, Lyski ZL, Slifka MK, Amanna IJ, et al. Persistence of neutralizing antibody responses among yellow fever virus 17D vaccinees living in a nonendemic setting. J Infect Dis 2020;221(12):2018-25.
Veit 2018	Veit O, Domingo C, Niedrig M, Staehelin C, Sonderegger B, Hequet D, et al. Long-term immune response to yellow fever vaccination in human immunodeficiency virus (HIV)-infected individuals depends on HIV RNA suppression status: implications for vaccination schedule. Clin Infect Dis 2018;66(7):1099-108.
	Veit O, Niedrig M, Chapuis-Taillard C, Cavassini M, Mossdorf E, Schmid P, et al. Immunogenicity and safety of yellow fever vaccination for 102 HIV-infected patients. Clin Infect Dis 2009;48(5):659-66.


Original search (November 2020)
Update search (November 2021)
RECORDS RETRIEVED FROM DATABASES
6,311 records prior to de-duplication
Duplicates removed: 1,823
TOTAL: 4,488 records
RECORDS RETRIEVED FROM OTHER RESOURCES
(websites, sent by commissioner)
TOTAL: 4 records
RECORDS RETRIEVED FROM DATABASES
447 records prior to de-duplication
Duplicates removed: 139
TOTAL: 308 records
TOTAL RECORDS SCREENED AT TITLE/ABSTRACT
TOTAL: 4,492 records
TOTAL RECORDS SCREENED AT TITLE/ABSTRACT
TOTAL: 308 records
EXCLUDED RECORDS AT TITLE/ABSTRACT (PHASE I)
TOTAL: 4,293 records excluded
EXCLUDED RECORDS AT TITLE/ABSTRACT (PHASE I)
TOTAL: 303 records excluded
RECORDS ASSESSED AT FULL PAPER (PHASE II)
TOTAL: 199 full papers
RECORDS ASSESSED AT FULL PAPER (PHASE II)
TOTAL: 5 full papers
EXCLUDED FULL PAPERS (PHASE II)
Unobtainable 10
Not relevant intervention 7
No relevant outcome 23
Ongoing study 14
Not relevant study design 86
TOTAL: 140 papers
EXCLUDED FULL PAPERS (PHASE II)
No relevant outcome 2
Not relevant study design 1
TOTAL: 3 papers
PAPERS MEETING INCLUSION CRITERIA & INCLUDED IN THE REVIEW
TOTAL: 36 studies (61 references)
18 RCTs (32 references)
12 Non-randomised comparative studies (18 references)
6 Single arm studies (11 references)

Appendix 6 - Table 5: **Risk of bias of randomised controlled trials (RCT)**

Study	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Domain 6	Domain 7	Domain 8	Overall ROB
Asante 2020[1]	low	low	high	high	high	high	low	low	**High**
Belmusto-Worn 2005[2]	unclear	low	low	low	low	high	unclear	low	**Unclear**
Camacho 2004[3]	low	low	low	low	high	low	low	low	**Low**
Campi-Azevedo 2014[4]	unclear	unclear	unclear	unclear	unclear	low	low	low	**Unclear**
Chan 2016[5]	unclear	unclear	high	high	high	low	low	low	**High**
Collaborative Group for Studies of Yellow Fever Vaccine 2015[6]	low	low	low	low	low	low	low	low	**Low**
Coursaget 1995[7]	unclear	unclear	unclear	unclear	unclear	high	unclear	unclear	**High**
Edupuganti 2013[8]	unclear	high	unclear	unclear	high	low	low	unclear	**High**
Guirakhoo 2006[9]	unclear	high	low	unclear	high	low	low	low	**High**
Juan-Giner 2021[10]	low	low	low	high	low	low	low	low	**Low**
Lang 1999[11]	unclear	unclear	low	low	low	high	low	low	**Unclear**
Lopez 2016[12]	low	low	low	low	low	high	low	low	**High**
Monath 2002[13]	unclear	unclear	unclear	unclear	unclear	high	unclear	low	**Unclear**
Nasveld 2010[14]	low	high	high	high	high	high	unclear	low	**High**
Novartis 2011[15]	unclear	unclear	high	high	low	low	low	low	**High**
Osei-Kwasi 2001[16]	unclear	low	low	unclear	high	high	low	low	**High**
Roukens 2008[17]	low	low	unclear	high	unclear	low	unclear	low	**Low**
Stefano 1999[18]	unclear	high	high	high	high	low	low	low	**High**

See Supplementary XX for details of ROB tool. Briefly, domain 1 (randomisation), domain 2 (allocation concealment), domain 3 (participant blinding), domain 4 (personnel blinding), domain 5 (assessor blinding), domain 6 (data completeness), domain 7 (selective reporting), domain 8 (other biases).
RCT = randomised controlled trial; ROB = risk of bias

Appendix 6 - Table 6: Risk of bias of non-randomised studies (Non-RCT and single arm studies)

Study	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Domain 6	Domain 7	Domain 8	Domain 9	Overall ROB
Non-randomised comparative studies										
Avelino-Silva 2016a[19]	yes	unclear	unclear	yes	yes	yes	yes	yes	yes	**Unclear**
Avelino-Silva 2016b[20]	yes	no	unclear	yes	no	unclear	yes	yes	NA	**High**
Burkhard 2010[21]	yes	unclear	unclear	yes	no	yes	yes	yes	yes	**High**
Campi-Azevado 2016[22]	yes	unclear	yes	no	yes	yes	yes	yes	yes	**High**
Collaborative Group for Studies of Yellow Fever Vaccine 2019a[23]	yes	yes	yes	unclear	unclear	yes	yes	yes	unclear	**Unclear**
Collaborative Group for Studies of Yellow Fever Vaccine 2019b[24]	yes	yes	yes	no	yes	yes	yes	yes	yes	**High**
De Verdiere 2018[25]	yes	no	yes	yes	yes	yes	yes	yes	yes	**High**
Kernéis 2013[26]	yes	yes	yes	yes	yes	yes	yes	yes	yes	**Low**
Michel 2015[27]	yes	yes	yes	yes	no	yes	yes	yes	yes	**High**
Project RETRO-CI[28]	yes	NA	NA	no	yes	no	yes	no	NA	**High**
Roukens 2011[29]	yes	unclear	yes	yes	yes	yes	yes	yes	yes	**Unclear**
Valim 2020[30]	yes	yes	yes	yes	yes	yes	yes	yes	yes	**Low**
Single arm studies										
Campi-Azevado 2019[31]	yes	NA	NA	no	yes	unclear	yes	yes	yes	**High**
Domingo 2019[32]	yes	yes	unclear	no	no	no	yes	yes	yes	**High**
Idoko 2020[33]	yes	yes	NA	no	no	unclear	yes	yes	NA	**High**
Jia 2019[34]	yes	NA	NA	no	yes	yes	yes	yes	yes	**High**
Kareko 2018[35]	yes	NA	NA	no	no	unclear	yes	yes	NA	**High**
Veit 2018[36]	yes	yes	yes	NA	NA	yes	yes	yes	no	**High**

See Supplementary XX for details of ROB tool for non-randomised studies. Briefly, domain 1 (clarity of 'cause' and 'effect'), domain 2 (comparison similarities), domain 3 (comparisons of similar treatments), domain 4 (control group), domain 5 (multiple measurements pre and post), domain 6 (follow up), domain 7 (similarity of outcome measures), domain 8 (measurement reliability), domain 9 appropriate statistical analysis).
NA = not applicable; ROB = risk of bias

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Appendix 7 - Table 7: Protection after single dose of YF vaccine - results of the meta-analysis

Forest Plot	Population	N studies	N data-points	N subjects	Effect estimate	95% CI	I^2
≤3 months							
001	**Adults**	**16**	**27**	**3115**	**0.98**	**0.97 to 0.98**	**64%**
002	Endemic	4	7	587	0.97	0.95 to 0.99	0%
003	Non-endemic	12	20	2528	0.98	0.97 to 0.99	68%
004	**Children**	**10**	**21**	**5654**	**0.94**	**0.90 to 0.96**	**92%**
005	Endemic	10	21	5654	0.94	0.90 to 0.96	92%
006	Non-endemic	0	0	0	N/A	N/A	N/A
007	**Immunodeficient**	**3**	**3**	**208**	**0.92**	**0.65 to 0.98**	**66%**
008	Endemic	1	1	160	0.78	0.71 to 0.84	N/A
009	Non-endemic	2	2	48	0.98	0.84 to 1.00	0%
>3 months to ≤5 years							
010	**Adults**	**8**	**13**	**790**	**0.97**	**0.95 to 0.98**	**0%**
011	Endemic	3	6	514	0.98	0.95 to 0.99	0%
012	Non-endemic	5	7	276	0.96	0.93 to 0.98	0%
013	**Children**	**3**	**4**	**1208**	**0.52**	**0.33 to 0.71**	**96%**
014	Endemic	3	4	1208	0.52	0.33 to 0.71	96%
015	Non-endemic	0	0	0	N/A	N/A	N/A
016	**Immunodeficient**	**4**	**4**	**198**	**0.86**	**0.31 to 0.99**	**91%**
017	Endemic	1	1	18	0.17	0.04 to 0.41	N/A
018	Non-endemic	3	3	180	0.94	0.77 to 0.99	56%
>5 years to ≤10 years							
019	**Adults**	**6**	**7**	**267**	**0.88**	**0.78 to 0.93**	**53%**
020	Endemic	2	2	45	0.88	0.75 to 0.95	0%
021	Non-endemic	4	5	222	0.89	0.74 to 0.96	63%
022	**Children**	**3**	**3**	**1044**	**0.54**	**0.37 to 0.70**	**97%**
023	Endemic	3	3	1044	0.54	0.37 to 0.70	97%
024	Non-endemic	0	0	0	N/A	N/A	N/A
025	**Immunodeficient**	**2**	**2**	**67**	**0.75**	**0.64 to 0.84**	**0%**
026	Endemic	0	0	0	N/A	N/A	N/A
027	Non-endemic	2	2	67	0.75	0.64 to 0.84	0%

Forest Plot	Population	N studies	N data-points	N subjects	Effect estimate	95% CI	I^2
>10 years to ≤20 years							
028	**Adults**	**4**	**4**	**231**	**0.71**	**0.62 to 0.79**	**36%**
029	Endemic	3	3	193	0.74	0.63 to 0.82	43%
030	Non-endemic	1	1	38	0.63	0.46 to 0.78	N/A
031	**Children***	**0**	**0**	**0**	**N/A**	**N/A**	**N/A**
034	**Immunodeficient**	**1**	**1**	**8**	**0.62**	**0.24 to 0.91**	**N/A**
035	Endemic	0	0	0	N/A	N/A	N/A
036	Non-endemic	1	1	8	0.62	0.24 to 0.91	N/A
>20 years							
037	**Adults**	**1**	**1**	**1**	**0.00**	**0.00 to 0.98**	**N/A**
038	Endemic	0	0	0	N/A	N/A	N/A
039	Non-endemic	1	1	1	0.00	0.00 to 0.98	N/A
040	**Children***	**0**	**0**	**0**	**N/A**	**N/A**	**N/A**
043	**Immunodeficient**	**1**	**1**	**17**	**0.94**	**0.71 to 1.00**	**N/A**
044	Endemic	0	0	0	N/A	N/A	N/A
045	Non-endemic	1	1	17	0.94	0.71 to 1.00	N/A

*No data

Appendix 8 - Table 8: Protection after one booster dose of YF vaccine - results of the meta-analysis

Forest Plot	Population	N studies	N data-points	N sub-jects	Effect estimate	95% CI	I2
≤3 months							
046	Adults	2	2	64	0.98	0.89 to 1.00	0%
047	Endemic	1	1	45	1.00	0.92 to 1.00	N/A
048	Non-endemic	1	1	19	1.00	0.82 to 1.00	N/A
049	Children*	0	0	0	N/A	N/A	N/A
052	Immunodeficient	1	1	11	1.00	0.72 to 1.00	N/A
053	Endemic	0	0	0	N/A	N/A	N/A
054	Non-endemic	1	1	11	1.00	0.72 to 1.00	N/A
>3 months to ≤5 years							
055	Adults	2	2	62	0.92	0.82 to 0.97	0%
056	Endemic	1	1	47	0.91	0.80 to 0.98	N/A
057	Non-endemic	1	1	15	1.00	0.78 to 1.00	N/A
058	Children*	0	0	0	N/A	N/A	N/A
061	Immunodeficient*	0	0	0	N/A	N/A	N/A
>5 years to ≤10 years							
064	Adults	3	3	258	0.88	0.84 to 0.92	0%
065	Endemic	2	2	249	0.88	0.83 to 0.91	0%
066	Non-endemic	1	1	9	1.00	0.66 to 1.00	N/A
067	Children*	0	0	0	N/A	N/A	N/A
070	Immunodeficient*	0	0	0	N/A	N/A	N/A
>10 years to ≤20 years							
073	Adults	2	2	17	0.86	0.61 to 0.96	0%
074	Endemic	1	1	12	0.83	0.52 to 0.98	N/A
075	Non-endemic	1	1	5	1.00	0.48 to 1.00	N/A
076	Children*	0	0	0	N/A	N/A	N/A
079	Immunodeficient*	0	0	0	N/A	N/A	N/A
>20 years							
082	Adults*	0	0	0	N/A	N/A	N/A
085	Children*	0	0	0	N/A	N/A	N/A

Forest Plot	Population	N studies	N data-points	N sub-jects	Effect estimate	95% CI	I2
088	Immunodeficient	1	1	40	0.88	0.73 to 0.96	N/A
089	Endemic	0	0	0	N/A	N/A	N/A
090	Non-endemic	1	1	40	0.88	0.73 to 0.96	N/A

*No data

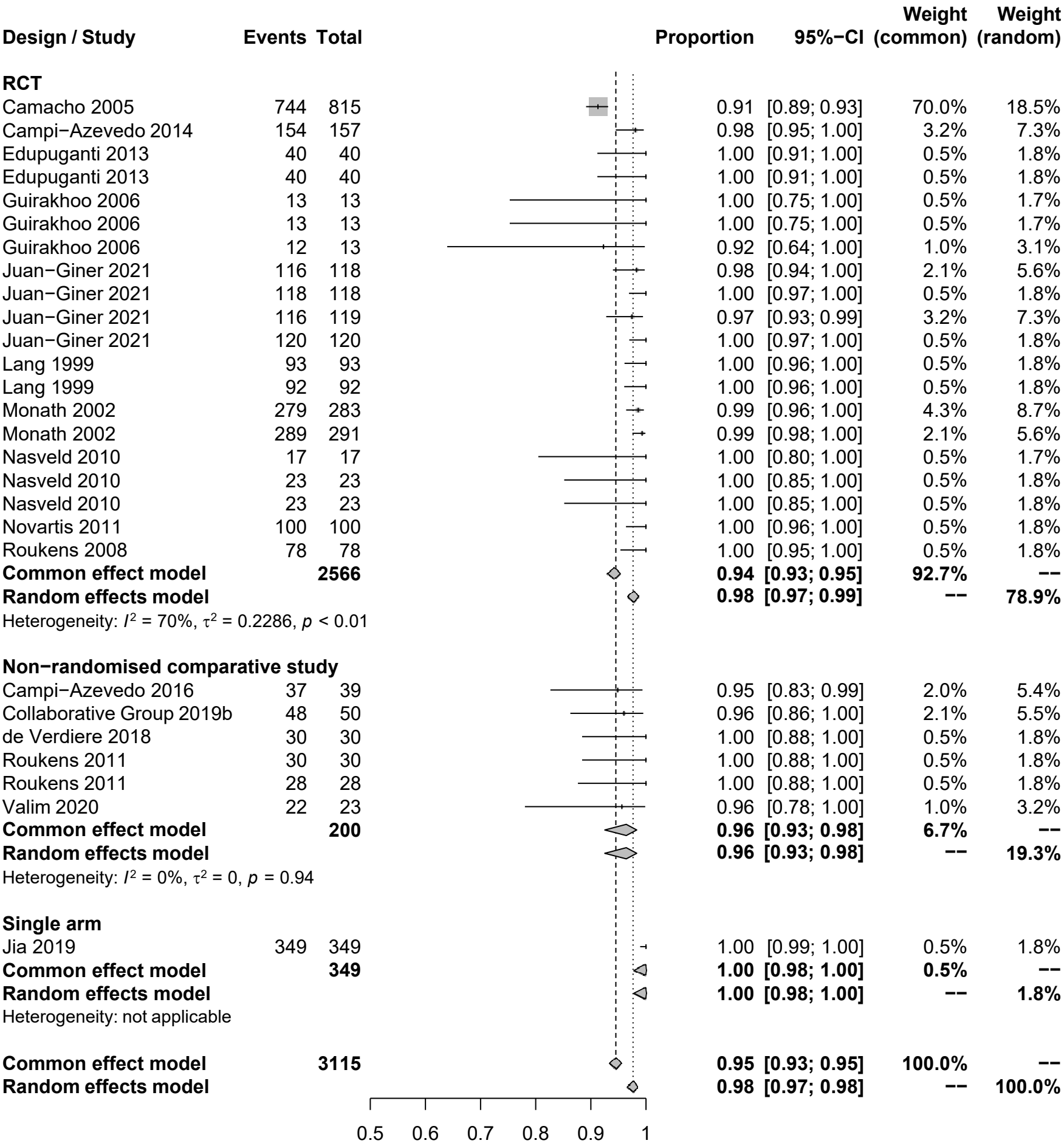
Appendix 9 - Table 9: Protection after two or more booster doses of YF vaccine - results of the meta-analysis

Forest Plot	Population	N studies	N data-points	N subjects	Effect estimate	95% CI	I^2
≤3 months							
092	**Adults***	**0**	**0**	**0**	**N/A**	**N/A**	**N/A**
095	**Children***	**0**	**0**	**0**	**N/A**	**N/A**	**N/A**
097	**Immunodeficient***	**0**	**0**	**0**	**N/A**	**N/A**	**N/A**
>3 months to ≤5 years							
100	**Adults**	**2**	**2**	**14**	**0.90**	**0.62 to 0.98**	**0%**
101	Endemic	2	2	14	0.90	0.62 to 0.98	0%
102	Non-endemic	0	0	0	N/A	N/A	N/A
103	**Children***	**0**	**0**	**0**	**N/A**	**N/A**	**N/A**
106	**Immunodeficient***	**0**	**0**	**0**	**N/A**	**N/A**	**N/A**
>5 years to ≤10 years							
109	**Adults***	**0**	**0**	**0**	**N/A**	**N/A**	**N/A**
112	**Children***	**0**	**0**	**0**	**N/A**	**N/A**	**N/A**
115	**Immunodeficient***	**0**	**0**	**0**	**N/A**	**N/A**	**N/A**
>10 years to ≤20 years							
118	**Adults***	**0**	**0**	**0**	**N/A**	**N/A**	**N/A**
121	**Children***	**0**	**0**	**0**	**N/A**	**N/A**	**N/A**
124	**Immunodeficient***	**1**	**1**	**2**	**1.00**	**0.16 to 1.00**	**N/A**
125	Endemic	0	0	0	N/A	N/A	N/A
126	Non-endemic	1	1	2	1.00	0.16 to 1.00	N/A
>20 years							
127	**Adults***	**0**	**0**	**0**	**N/A**	**N/A**	**N/A**
130	**Children***	**0**	**0**	**0**	**N/A**	**N/A**	**N/A**
133	**Immunodeficient**	**1**	**1**	**3**	**1.00**	**0.29 to 1.00**	**N/A**
134	Endemic	0	0	0	N/A	N/A	N/A
135	Non-endemic	1	1	3	1.00	0.29 to 1.00	N/A

*No data

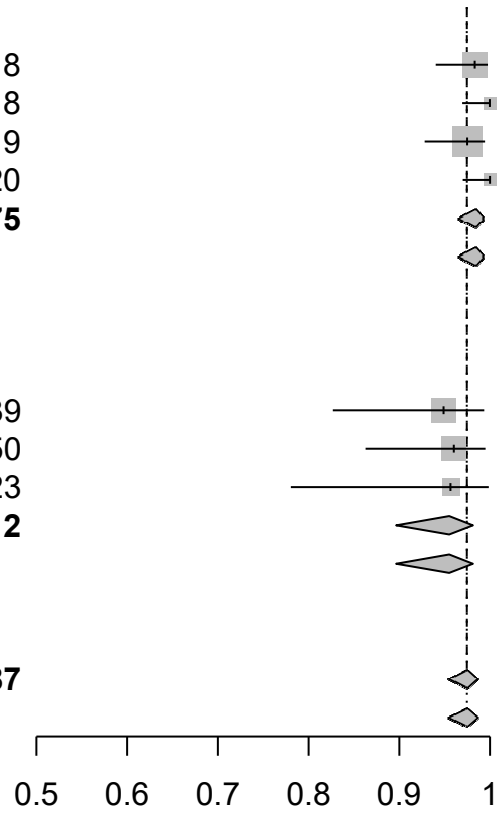
Appendix 10 - Forest plots figures 001-135

001



002

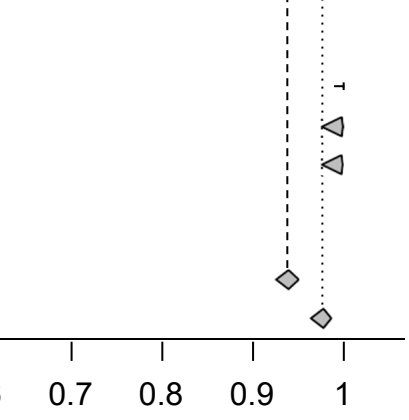
Design / Study	Events	Total	Proportion	95%−CI	Weight (common)	Weight (random)
RCT						
Juan−Giner 2021	116	118	0.98	[0.94; 1.00]	18.4%	18.4%
Juan−Giner 2021	118	118	1.00	[0.97; 1.00]	4.7%	4.7%
Juan−Giner 2021	116	119	0.97	[0.93; 0.99]	27.4%	27.4%
Juan−Giner 2021	120	120	1.00	[0.97; 1.00]	4.7%	4.7%
Common effect model		**475**	**0.98**	**[0.96; 0.99]**	**55.2%**	**--**
Random effects model			**0.98**	**[0.96; 0.99]**	**--**	**55.2%**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.48						
Non−randomised comparative study						
Campi−Azevedo 2016	37	39	0.95	[0.83; 0.99]	17.8%	17.8%
Collaborative Group 2019b	48	50	0.96	[0.86; 1.00]	18.0%	18.0%
Valim 2020	22	23	0.96	[0.78; 1.00]	9.0%	9.0%
Common effect model		**112**	**0.96**	**[0.90; 0.98]**	**44.8%**	**--**
Random effects model			**0.96**	**[0.90; 0.98]**	**--**	**44.8%**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.97						
Common effect model		**587**	**0.97**	**[0.95; 0.99]**	**100.0%**	**--**
Random effects model			**0.97**	**[0.95; 0.99]**	**--**	**100.0%**



Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.49
Test for subgroup differences (fixed effect): χ^2_1 = 2.86, df = 1 (p = 0.09)
Test for subgroup differences (random effects): χ^2_1 = 2.86, df = 1 (p = 0.09)

003

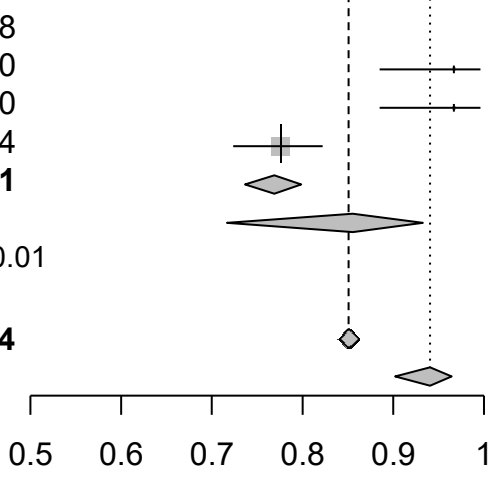
Design / Study	Events	Total	Proportion	95%−CI	Weight (common)	Weight (random)
RCT						
Camacho 2005	744	815	0.91	[0.89; 0.93]	79.1%	23.4%
Campi−Azevedo 2014	154	157	0.98	[0.95; 1.00]	3.6%	10.5%
Edupuganti 2013	40	40	1.00	[0.91; 1.00]	0.6%	2.7%
Edupuganti 2013	40	40	1.00	[0.91; 1.00]	0.6%	2.7%
Guirakhoo 2006	13	13	1.00	[0.75; 1.00]	0.6%	2.7%
Guirakhoo 2006	13	13	1.00	[0.75; 1.00]	0.6%	2.7%
Guirakhoo 2006	12	13	0.92	[0.64; 1.00]	1.1%	4.7%
Lang 1999	93	93	1.00	[0.96; 1.00]	0.6%	2.7%
Monath 2002	279	283	0.99	[0.96; 1.00]	4.8%	12.3%
Monath 2002	289	291	0.99	[0.98; 1.00]	2.4%	8.2%
Nasveld 2010	17	17	1.00	[0.80; 1.00]	0.6%	2.7%
Nasveld 2010	23	23	1.00	[0.85; 1.00]	0.6%	2.7%
Nasveld 2010	23	23	1.00	[0.85; 1.00]	0.6%	2.7%
Novartis 2011	100	100	1.00	[0.96; 1.00]	0.6%	2.7%
Roukens 2008	78	78	1.00	[0.95; 1.00]	0.6%	2.7%
Common effect model		**2091**	**0.94**	**[0.92; 0.95]**	**97.6%**	**--**
Random effects model			**0.98**	**[0.96; 0.99]**	**--**	**89.1%**
Heterogeneity: I^2 = 70%, τ^2 = 0.2631, p < 0.01						
Non−randomised comparative study						
de Verdiere 2018	30	30	1.00	[0.88; 1.00]	0.6%	2.7%
Roukens 2011	30	30	1.00	[0.88; 1.00]	0.6%	2.7%
Roukens 2011	28	28	1.00	[0.88; 1.00]	0.6%	2.7%
Common effect model		**88**	**0.98**	**[0.92; 1.00]**	**1.8%**	**--**
Random effects model			**0.98**	**[0.92; 1.00]**	**--**	**8.2%**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 1.00						
Single arm						
Jia 2019	349	349	1.00	[0.99; 1.00]	0.6%	2.8%
Common effect model		**349**	**1.00**	**[0.98; 1.00]**	**0.6%**	**--**
Random effects model			**1.00**	**[0.98; 1.00]**	**--**	**2.8%**
Heterogeneity: not applicable						
Common effect model		**2528**	**0.94**	**[0.93; 0.95]**	**100.0%**	**--**
Random effects model			**0.98**	**[0.97; 0.99]**	**--**	**100.0%**



Heterogeneity: I^2 = 68%, τ^2 = 0.2498, p < 0.01
Test for subgroup differences (fixed effect): χ^2_2 = 10.04, df = 2 (p < 0.01)
Test for subgroup differences (random effects): χ^2_2 = 3.95, df = 2 (p = 0.14)

004

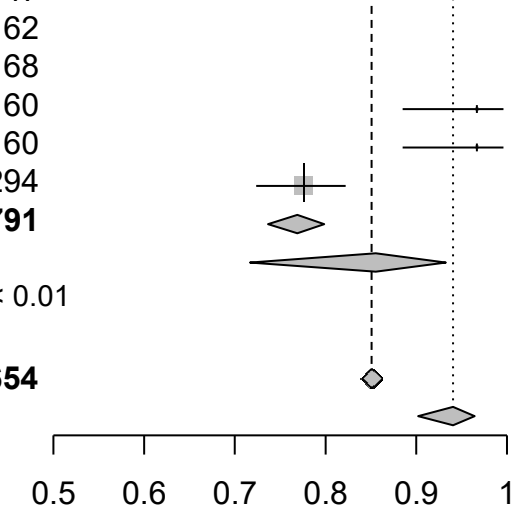
Design / Study	Events	Total	Proportion	95%−CI	Weight (common)	Weight (random)
RCT						
Asante 2020	202	206	0.98	[0.95; 0.99]	0.8%	4.7%
Asante 2020	213	216	0.99	[0.96; 1.00]	0.6%	4.5%
Belmusto−Worn 2005	619	652	0.95	[0.93; 0.96]	6.1%	5.5%
Belmusto−Worn 2005	298	329	0.91	[0.87; 0.94]	5.5%	5.4%
Collaborative Group 2015	803	981	0.82	[0.79; 0.84]	28.4%	5.6%
Collaborative Group 2015	820	985	0.83	[0.81; 0.86]	26.8%	5.6%
Coursaget 1995	53	55	0.96	[0.87; 1.00]	0.4%	4.0%
Coursaget 1995	53	55	0.96	[0.87; 1.00]	0.4%	4.0%
Coursaget 1995	59	62	0.95	[0.87; 0.99]	0.6%	4.4%
Lopez 2016	373	378	0.99	[0.97; 1.00]	1.0%	4.9%
Lopez 2016	375	376	1.00	[0.99; 1.00]	0.2%	3.2%
Osei−Kwasi 2001	137	139	0.99	[0.95; 1.00]	0.4%	4.1%
Osei−Kwasi 2001	147	150	0.98	[0.94; 1.00]	0.6%	4.5%
Common effect model		**4584**	**0.87**	**[0.86; 0.88]**	**71.6%**	**−−**
Random effects model			**0.96**	**[0.93; 0.98]**	**−−**	**60.4%**
Heterogeneity: I^2 = 93%, τ^2 = 1.1445, p < 0.01						
Non−randomised comparative study						
Michel 2015	49	54	0.91	[0.80; 0.97]	0.9%	4.8%
Michel 2015	209	225	0.93	[0.89; 0.96]	2.9%	5.3%
Common effect model		**279**	**0.92**	**[0.89; 0.95]**	**3.8%**	**−−**
Random effects model			**0.92**	**[0.89; 0.95]**	**−−**	**10.1%**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.59						
Single arm						
Campi−Azevedo 2019	40	47	0.85	[0.72; 0.94]	1.2%	5.0%
Domingo 2019	121	162	0.75	[0.67; 0.81]	6.0%	5.5%
Domingo 2019	120	168	0.71	[0.64; 0.78]	6.7%	5.5%
Domingo 2019	58	60	0.97	[0.88; 1.00]	0.4%	4.0%
Domingo 2019	58	60	0.97	[0.88; 1.00]	0.4%	4.0%
Stefano 1999	228	294	0.78	[0.72; 0.82]	10.0%	5.5%
Common effect model		**791**	**0.77**	**[0.74; 0.80]**	**24.6%**	**−−**
Random effects model			**0.86**	**[0.72; 0.93]**	**−−**	**29.5%**
Heterogeneity: I^2 = 78%, τ^2 = 0.9485, p < 0.01						
Common effect model		**5654**	**0.85**	**[0.84; 0.86]**	**100.0%**	**−−**
Random effects model			**0.94**	**[0.90; 0.96]**	**−−**	**100.0%**



Heterogeneity: I^2 = 92%, τ^2 = 1.3502, p < 0.01
Test for subgroup differences (fixed effect): χ^2_2 = 55.26, df = 2 (p < 0.01)
Test for subgroup differences (random effects): χ^2_2 = 7.71, df = 2 (p = 0.02)

005

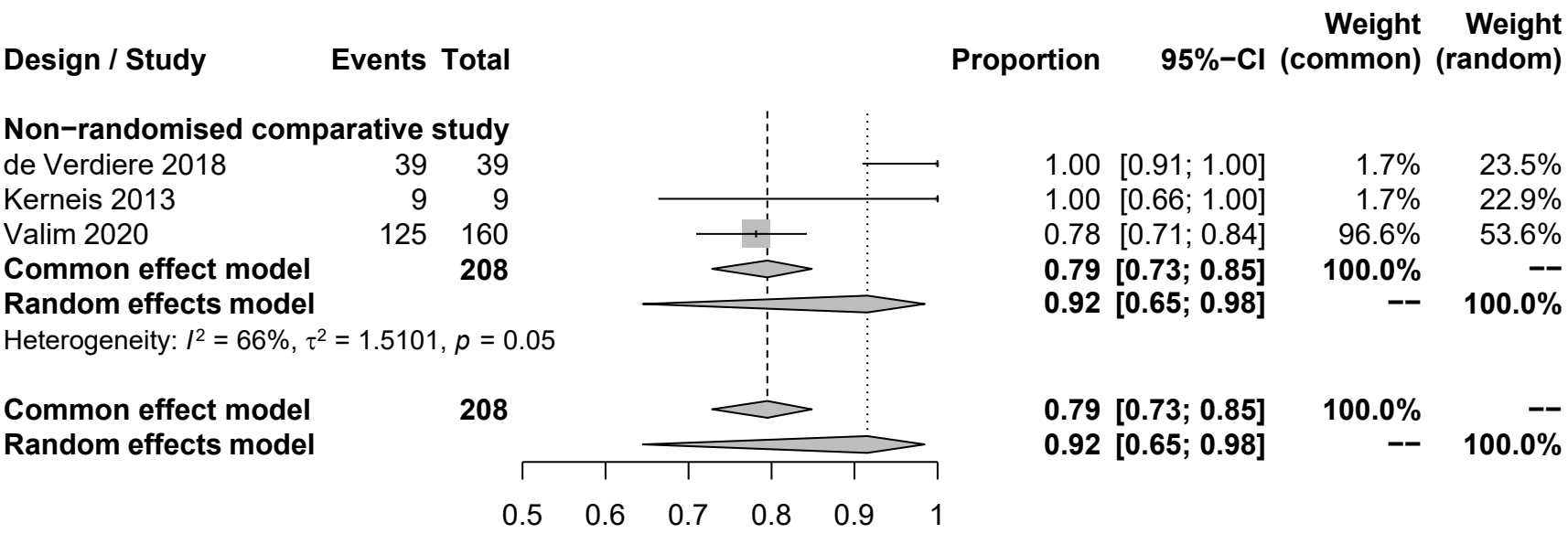
Design / Study	Events	Total	Proportion	95%−CI	Weight (common)	Weight (random)
RCT						
Asante 2020	202	206	0.98	[0.95; 0.99]	0.8%	4.7%
Asante 2020	213	216	0.99	[0.96; 1.00]	0.6%	4.5%
Belmusto−Worn 2005	619	652	0.95	[0.93; 0.96]	6.1%	5.5%
Belmusto−Worn 2005	298	329	0.91	[0.87; 0.94]	5.5%	5.4%
Collaborative Group 2015	803	981	0.82	[0.79; 0.84]	28.4%	5.6%
Collaborative Group 2015	820	985	0.83	[0.81; 0.86]	26.8%	5.6%
Coursaget 1995	53	55	0.96	[0.87; 1.00]	0.4%	4.0%
Coursaget 1995	59	62	0.95	[0.87; 0.99]	0.6%	4.4%
Lopez 2016	373	378	0.99	[0.97; 1.00]	1.0%	4.9%
Lopez 2016	375	376	1.00	[0.99; 1.00]	0.2%	3.2%
Osei−Kwasi 2001	137	139	0.99	[0.95; 1.00]	0.4%	4.1%
Osei−Kwasi 2001	147	150	0.98	[0.94; 1.00]	0.6%	4.5%
Common effect model		**4584**	**0.87**	**[0.86; 0.88]**	**71.6%**	**−−**
Random effects model			**0.96**	**[0.93; 0.98]**	**−−**	**60.4%**
Heterogeneity: I^2 = 93%, τ^2 = 1.1445, p < 0.01						
Non−randomised comparative study						
Michel 2015	49	54	0.91	[0.80; 0.97]	0.9%	4.8%
Michel 2015	209	225	0.93	[0.89; 0.96]	2.9%	5.3%
Common effect model		**279**	**0.92**	**[0.89; 0.95]**	**3.8%**	**−−**
Random effects model			**0.92**	**[0.89; 0.95]**	**−−**	**10.1%**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.59						
Single arm						
Campi−Azevedo 2019	40	47	0.85	[0.72; 0.94]	1.2%	5.0%
Domingo 2019	121	162	0.75	[0.67; 0.81]	6.0%	5.5%
Domingo 2019	120	168	0.71	[0.64; 0.78]	6.7%	5.5%
Domingo 2019	58	60	0.97	[0.88; 1.00]	0.4%	4.0%
Domingo 2019	58	60	0.97	[0.88; 1.00]	0.4%	4.0%
Stefano 1999	228	294	0.78	[0.72; 0.82]	10.0%	5.5%
Common effect model		**791**	**0.77**	**[0.74; 0.80]**	**24.6%**	**−−**
Random effects model			**0.86**	**[0.72; 0.93]**	**−−**	**29.5%**
Heterogeneity: I^2 = 78%, τ^2 = 0.9485, p < 0.01						
Common effect model		**5654**	**0.85**	**[0.84; 0.86]**	**100.0%**	**−−**
Random effects model			**0.94**	**[0.90; 0.96]**	**−−**	**100.0%**



Heterogeneity: I^2 = 92%, τ^2 = 1.3502, p < 0.01
Test for subgroup differences (fixed effect): χ^2_2 = 55.26, df = 2 (p < 0.01)

Test for subgroup differences (random effects): χ^2_2 = 7.71, df = 2 (p = 0.02)

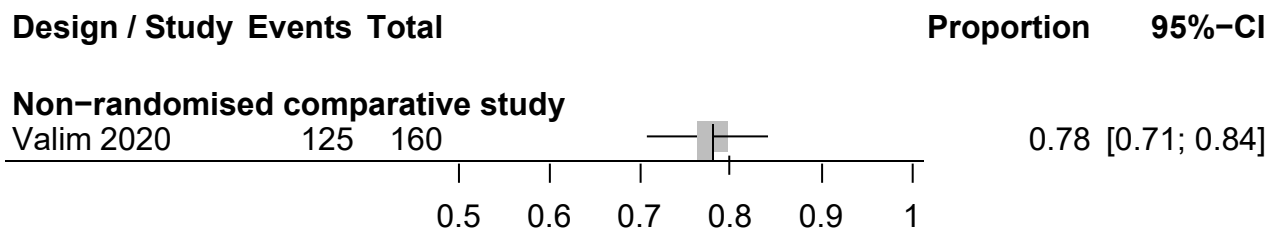
007



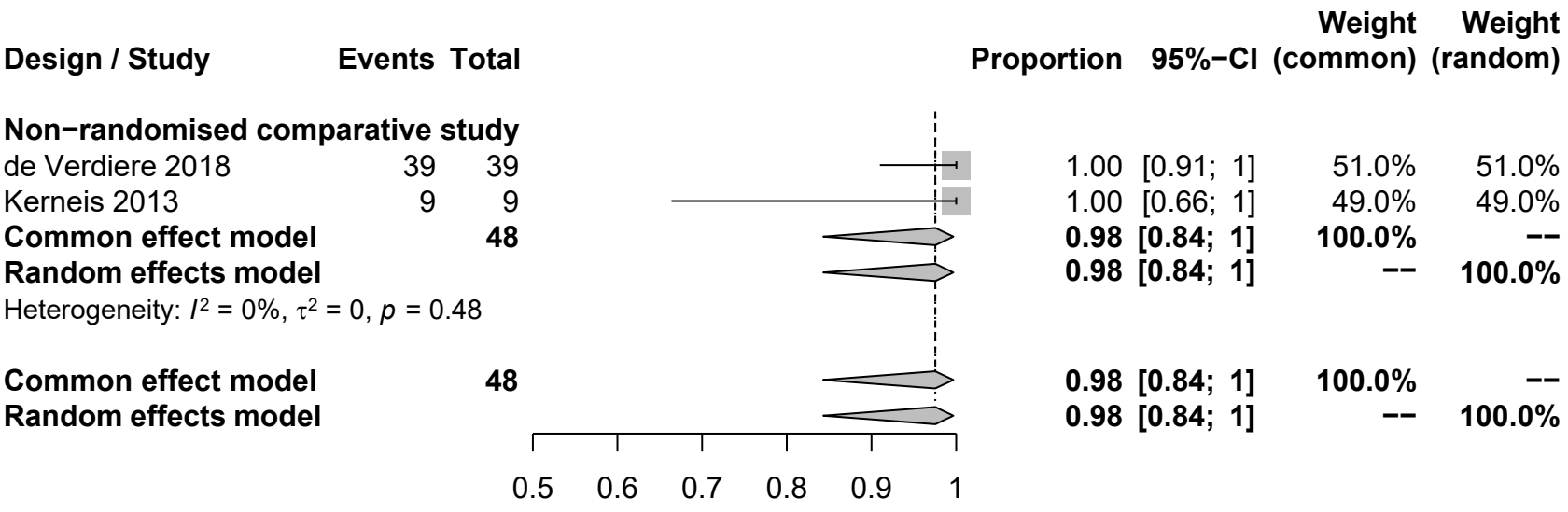
Heterogeneity: I^2 = 66%, τ^2 = 1.5101, p = 0.05
Test for subgroup differences (fixed effect): χ^2_0 = 0.00, df = 0 (p = NA)

Test for subgroup differences (random effects): χ^2_0 = 0.00, df = 0 (p = NA)

008


Design / Study Events Total
Proportion 95%−CI
Non−randomised comparative study
Valim 2020 125 160 0.78 [0.71; 0.84]
0.5 0.6 0.7 0.8 0.9 1

009

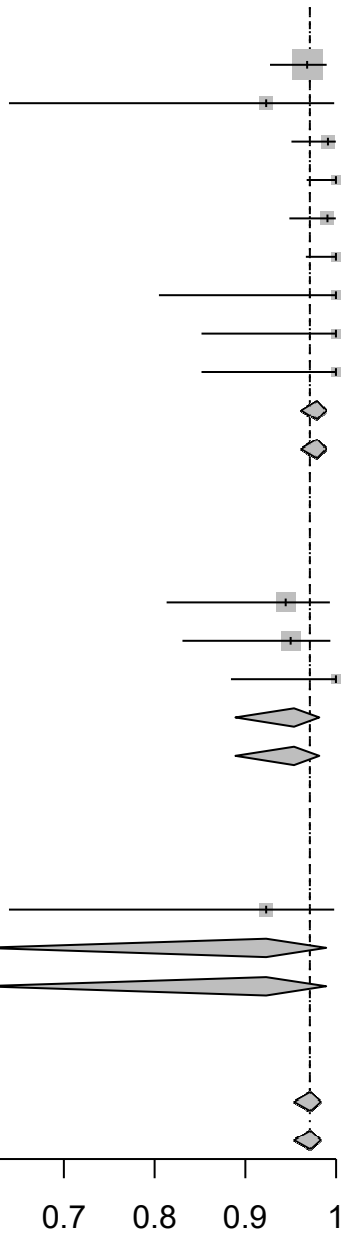


Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.48
Test for subgroup differences (fixed effect): χ^2_0 = 0.00, df = 0 (p = NA)

Test for subgroup differences (random effects): χ^2_0 = 0.00, df = 0 (p = NA)

010

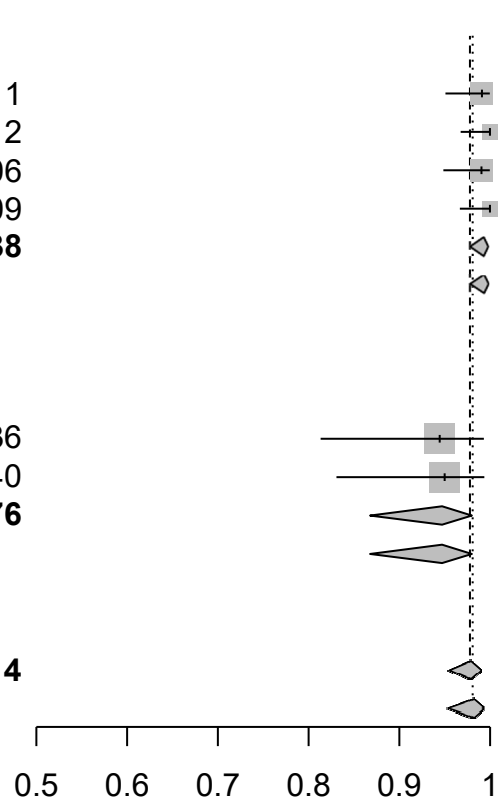
Design / Study	Events	Total	Proportion	95%−CI	Weight (common)	Weight (random)
RCT						
Campi−Azevedo 2014	152	157	0.97	[0.93; 0.99]	31.4%	31.4%
Guirakhoo 2006	12	13	0.92	[0.64; 1.00]	6.0%	6.0%
Juan−Giner 2021	110	111	0.99	[0.95; 1.00]	6.4%	6.4%
Juan−Giner 2021	112	112	1.00	[0.97; 1.00]	3.2%	3.2%
Juan−Giner 2021	105	106	0.99	[0.95; 1.00]	6.4%	6.4%
Juan−Giner 2021	109	109	1.00	[0.97; 1.00]	3.2%	3.2%
Nasveld 2010	17	17	1.00	[0.80; 1.00]	3.2%	3.2%
Nasveld 2010	23	23	1.00	[0.85; 1.00]	3.2%	3.2%
Nasveld 2010	23	23	1.00	[0.85; 1.00]	3.2%	3.2%
Common effect model		**671**	**0.98**	**[0.96; 0.99]**	**66.2%**	**--**
Random effects model			**0.98**	**[0.96; 0.99]**	**--**	**66.2%**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.60						
Non−randomised comparative study						
Campi−Azevedo 2016	34	36	0.94	[0.81; 0.99]	12.3%	12.3%
Collaborative Group 2019b	38	40	0.95	[0.83; 0.99]	12.3%	12.3%
de Verdiere 2018	30	30	1.00	[0.88; 1.00]	3.2%	3.2%
Common effect model		**106**	**0.95**	**[0.89; 0.98]**	**27.8%**	**--**
Random effects model			**0.95**	**[0.89; 0.98]**	**--**	**27.8%**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.72						
Single arm						
Kareko 2020	12	13	0.92	[0.64; 1.00]	6.0%	6.0%
Common effect model		**13**	**0.92**	**[0.61; 0.99]**	**6.0%**	**--**
Random effects model			**0.92**	**[0.61; 0.99]**	**--**	**6.0%**
Heterogeneity: not applicable						
Common effect model		**790**	**0.97**	**[0.95; 0.98]**	**100.0%**	**--**
Random effects model			**0.97**	**[0.95; 0.98]**	**--**	**100.0%**



Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.61
Test for subgroup differences (fixed effect): χ^2_2 = 2.93, df = 2 (p = 0.23)
Test for subgroup differences (random effects): χ^2_2 = 2.93, df = 2 (p = 0.23)

011

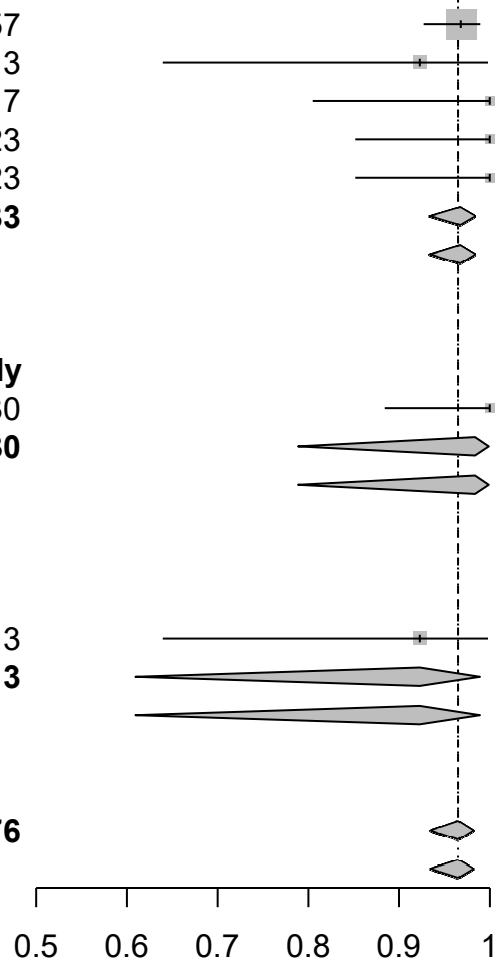
Design / Study	Events	Total	Proportion	95%−CI	Weight (common)	Weight (random)
RCT						
Juan−Giner 2021	110	111	0.99	[0.95; 1.00]	14.6%	16.1%
Juan−Giner 2021	112	112	1.00	[0.97; 1.00]	7.4%	9.4%
Juan−Giner 2021	105	106	0.99	[0.95; 1.00]	14.6%	16.1%
Juan−Giner 2021	109	109	1.00	[0.97; 1.00]	7.4%	9.4%
Common effect model		**438**	**0.99**	**[0.98; 1.00]**	**44.0%**	**--**
Random effects model			**0.99**	**[0.98; 1.00]**	**--**	**50.9%**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.95						
Non−randomised comparative study						
Campi−Azevedo 2016	34	36	0.94	[0.81; 0.99]	27.9%	24.5%
Collaborative Group 2019b	38	40	0.95	[0.83; 0.99]	28.1%	24.6%
Common effect model		**76**	**0.95**	**[0.87; 0.98]**	**56.0%**	**--**
Random effects model			**0.95**	**[0.87; 0.98]**	**--**	**49.1%**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.91						
Common effect model		**514**	**0.98**	**[0.95; 0.99]**	**100.0%**	**--**
Random effects model			**0.98**	**[0.95; 0.99]**	**--**	**100.0%**



Heterogeneity: I^2 = 31%, τ^2 = 0.3837, p = 0.20
Test for subgroup differences (fixed effect): χ^2_1 = 6.88, df = 1 (p < 0.01)
Test for subgroup differences (random effects): χ^2_1 = 6.88, df = 1 (p < 0.01)

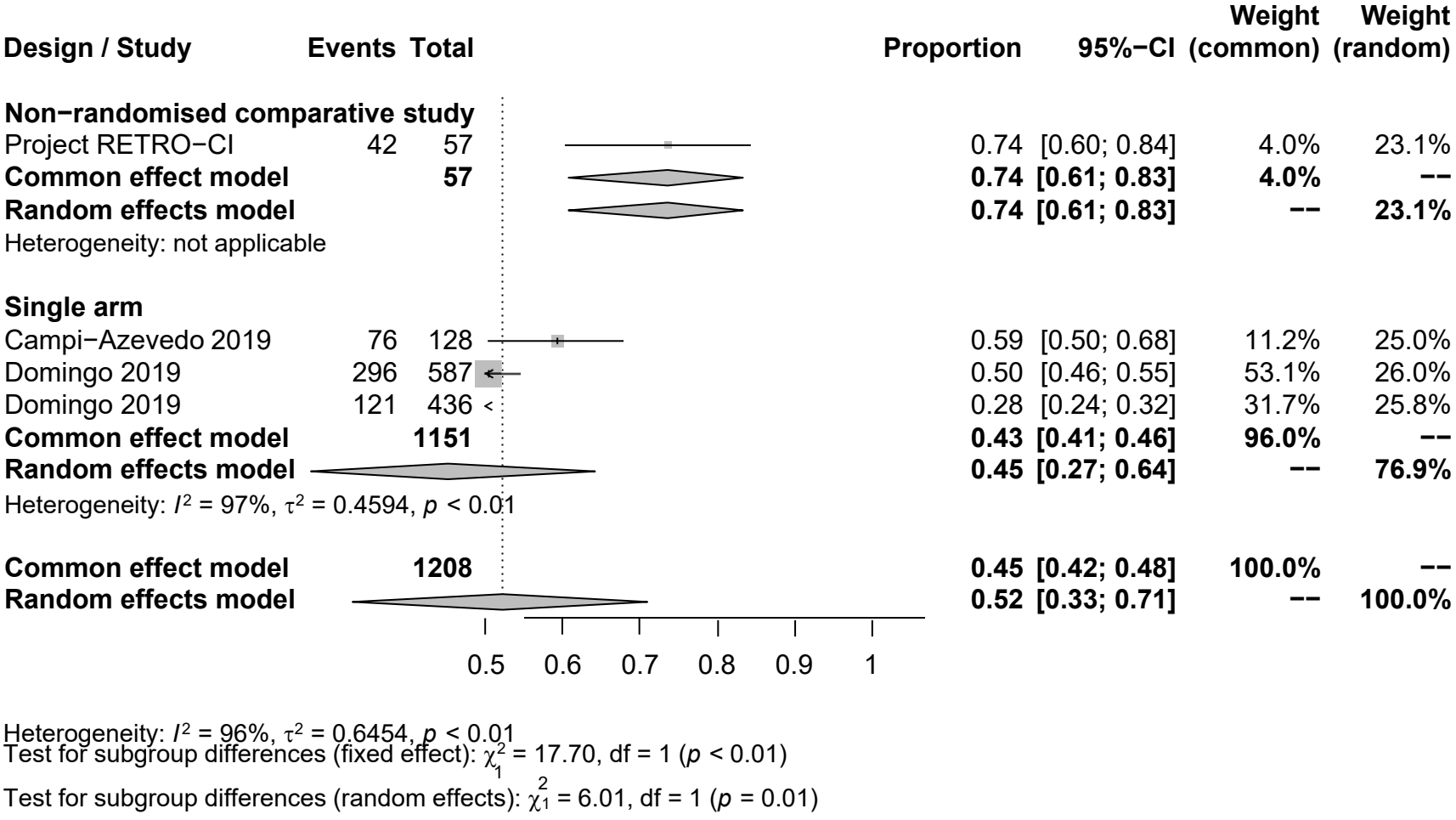
012

Design / Study	Events	Total	Proportion	95%−CI	Weight (common)	Weight (random)
RCT						
Campi−Azevedo 2014	152	157	0.97	[0.93; 0.99]	56.0%	56.0%
Guirakhoo 2006	12	13	0.92	[0.64; 1.00]	10.7%	10.7%
Nasveld 2010	17	17	1.00	[0.80; 1.00]	5.6%	5.6%
Nasveld 2010	23	23	1.00	[0.85; 1.00]	5.7%	5.7%
Nasveld 2010	23	23	1.00	[0.85; 1.00]	5.7%	5.7%
Common effect model		**233**	**0.97**	**[0.93; 0.98]**	**83.6%**	**−−**
Random effects model			**0.97**	**[0.93; 0.98]**	**−−**	**83.6%**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.91						
Non−randomised comparative study						
de Verdiere 2018	30	30	1.00	[0.88; 1.00]	5.7%	5.7%
Common effect model		**30**	**0.98**	**[0.79; 1.00]**	**5.7%**	**−−**
Random effects model			**0.98**	**[0.79; 1.00]**	**−−**	**5.7%**
Heterogeneity: not applicable						
Single arm						
Kareko 2020	12	13	0.92	[0.64; 1.00]	10.7%	10.7%
Common effect model		**13**	**0.92**	**[0.61; 0.99]**	**10.7%**	**−−**
Random effects model			**0.92**	**[0.61; 0.99]**	**−−**	**10.7%**
Heterogeneity: not applicable						
Common effect model		**276**	**0.96**	**[0.93; 0.98]**	**100.0%**	**−−**
Random effects model			**0.96**	**[0.93; 0.98]**	**−−**	**100.0%**



Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.93
Test for subgroup differences (fixed effect): χ^2_2 = 0.97, df = 2 (p = 0.62)
Test for subgroup differences (random effects): χ^2_2 = 0.97, df = 2 (p = 0.62)

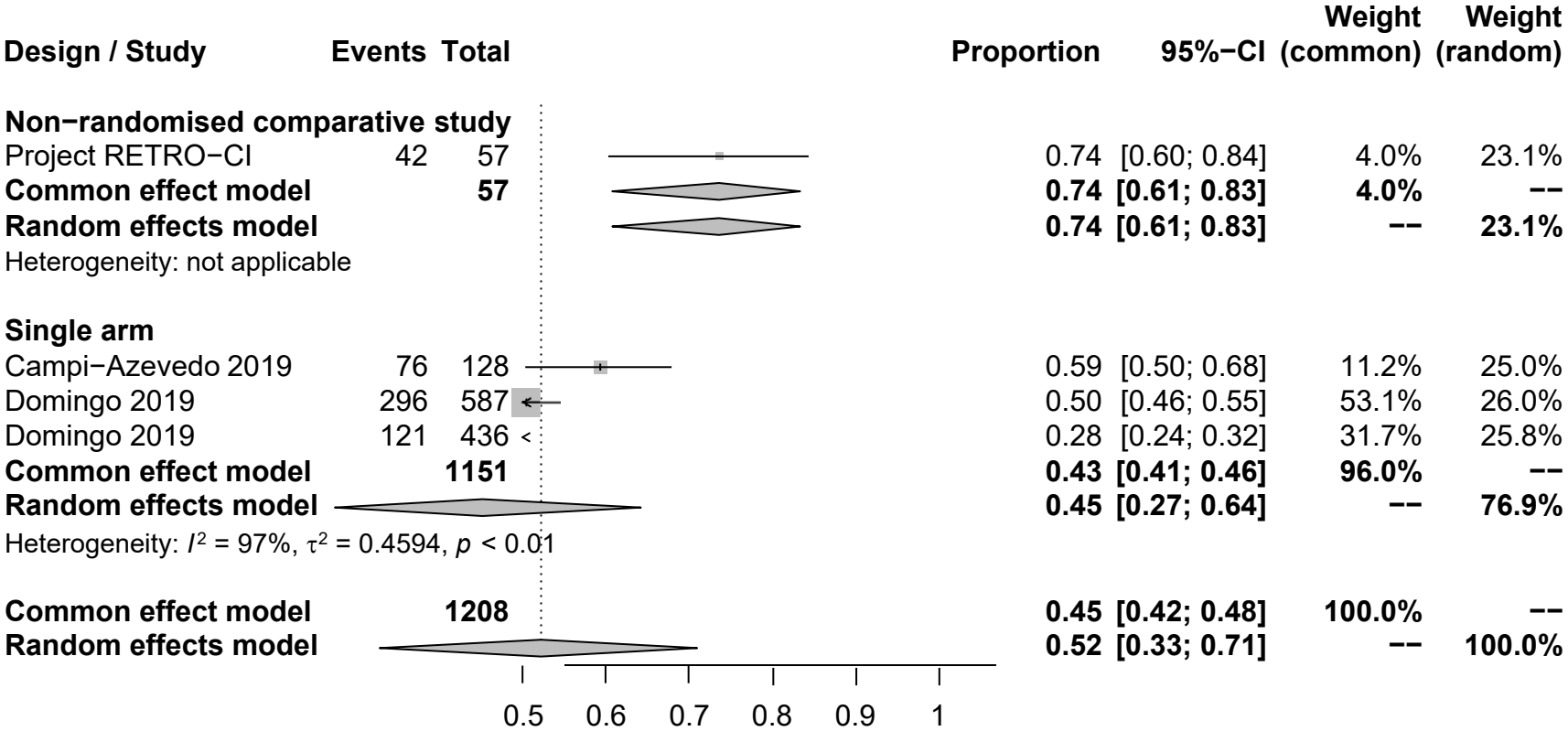
013



Heterogeneity: I^2 = 96%, τ^2 = 0.6454, p < 0.01
Test for subgroup differences (fixed effect): χ^2_1 = 17.70, df = 1 (p < 0.01)

Test for subgroup differences (random effects): χ^2_1 = 6.01, df = 1 (p = 0.01)

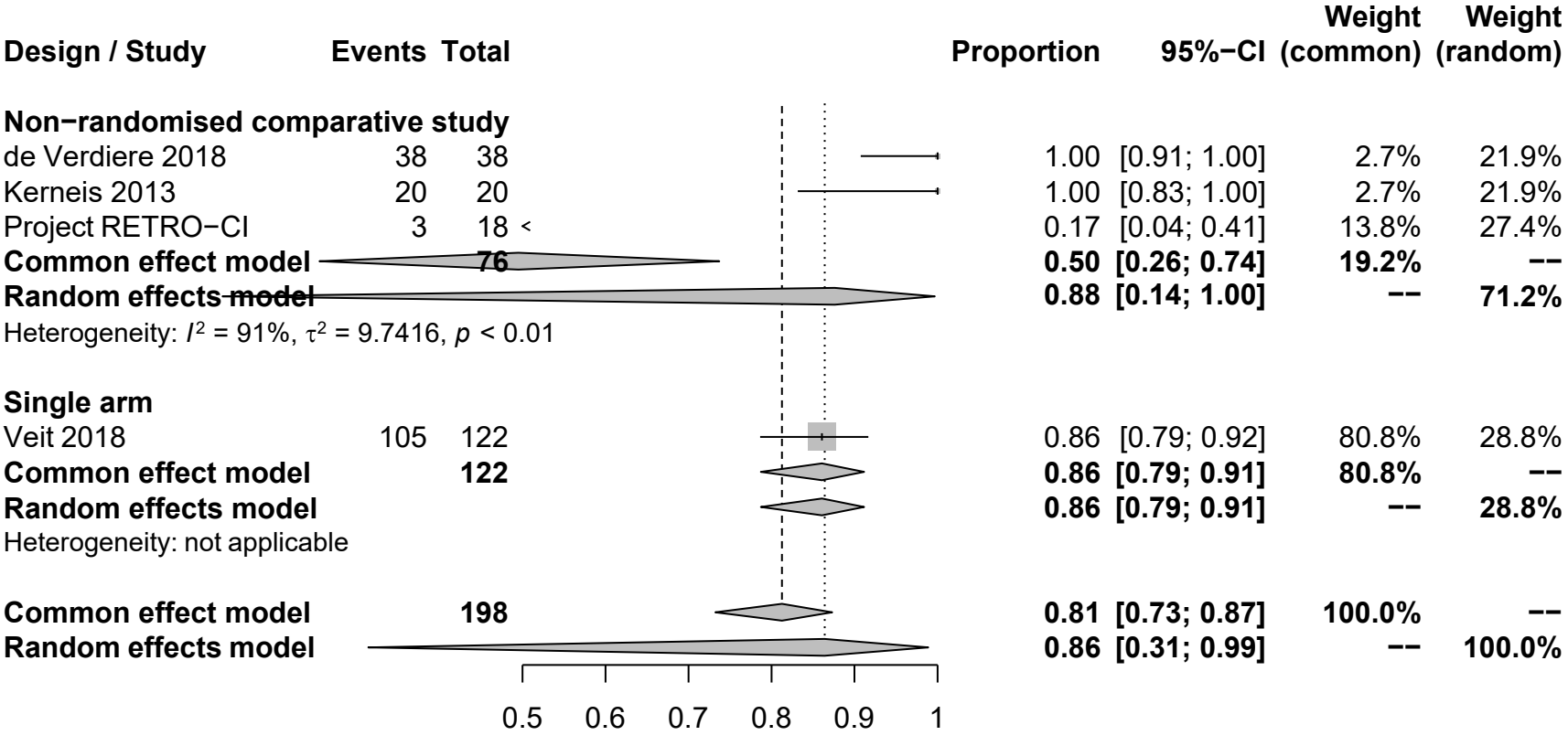
014



Heterogeneity: I^2 = 96%, τ^2 = 0.6454, p < 0.01
Test for subgroup differences (fixed effect): χ^2_1 = 17.70, df = 1 (p < 0.01)

Test for subgroup differences (random effects): χ^2_1 = 6.01, df = 1 (p = 0.01)

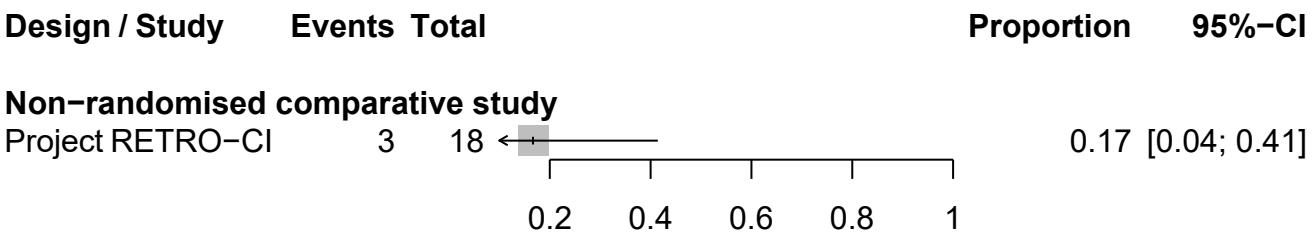
016



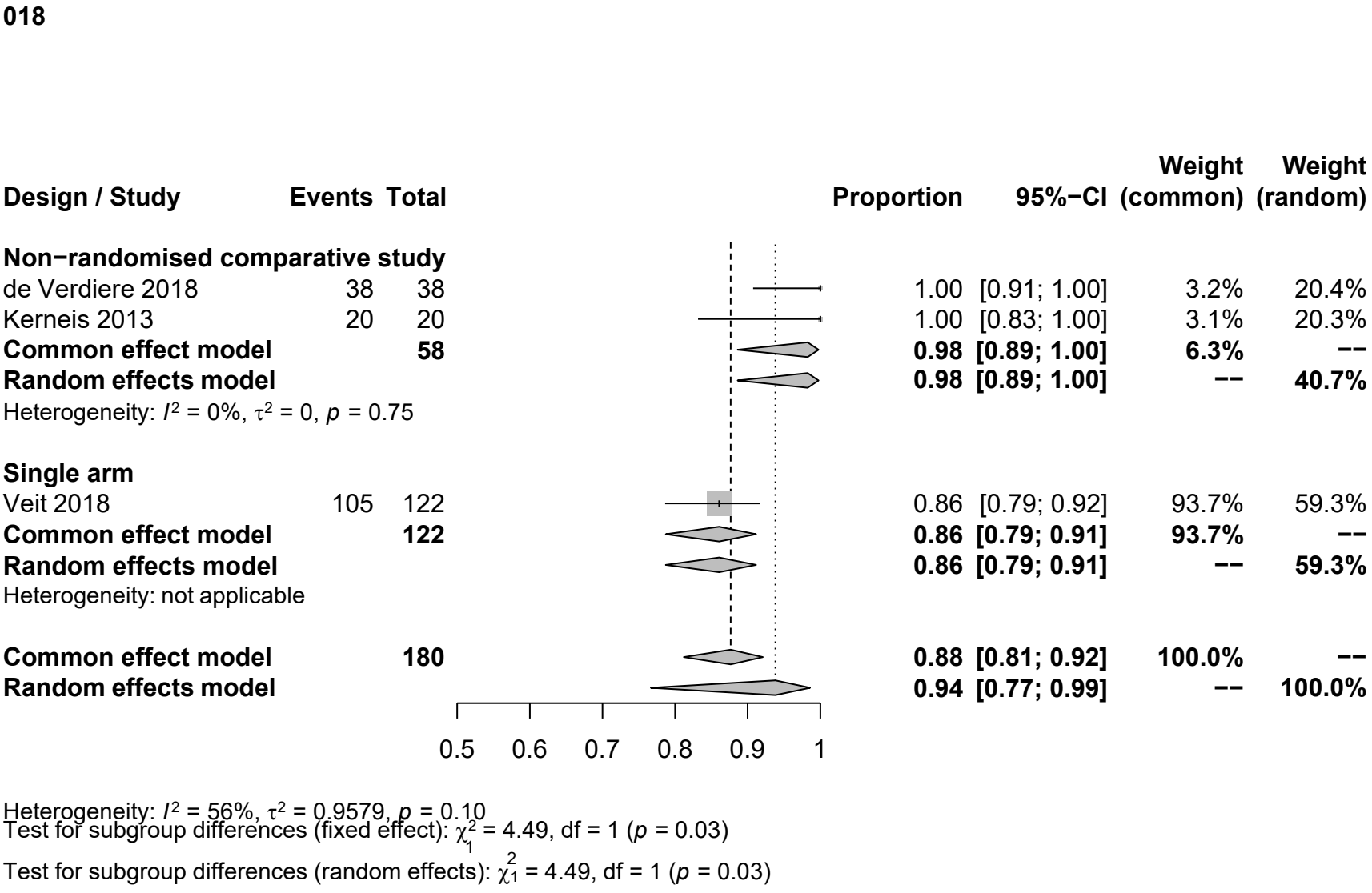
Heterogeneity: I^2 = 91%, τ^2 = 6.1773, p < 0.01
Test for subgroup differences (fixed effect): χ^2_1 = 9.52, df = 1 (p < 0.01)

Test for subgroup differences (random effects): χ^2_1 = 0.00, df = 1 (p = 0.94)

017


Design / Study
Events
Total
Proportion
95%−CI
Non−randomised comparative study
Project RETRO−CI
3
18
0.17 [0.04; 0.41]
0.2
0.4
0.6
0.8
1

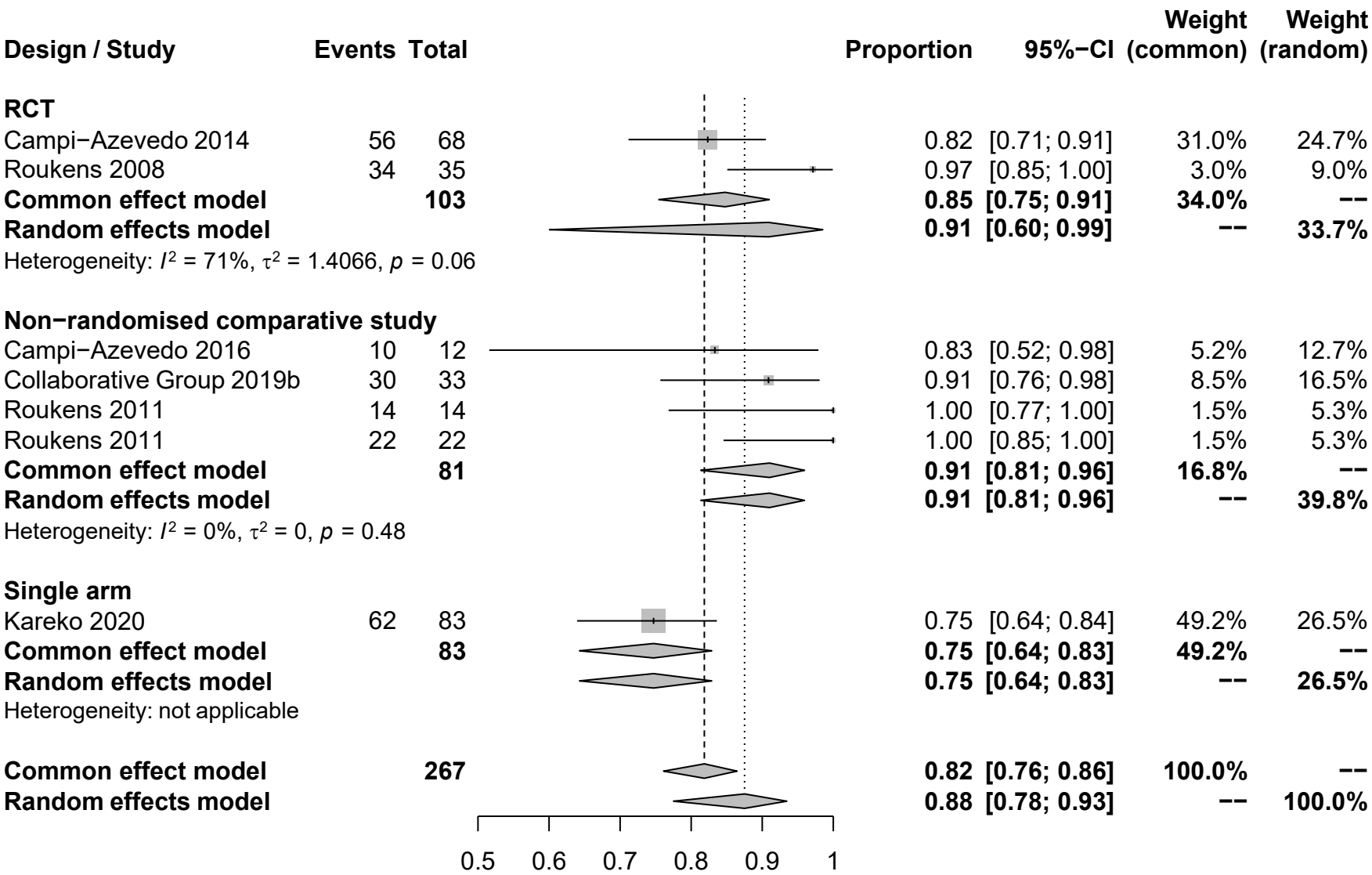
018



Heterogeneity: I^2 = 56%, τ^2 = 0.9579, p = 0.10
Test for subgroup differences (fixed effect): χ^2_1 = 4.49, df = 1 (p = 0.03)

Test for subgroup differences (random effects): χ^2_1 = 4.49, df = 1 (p = 0.03)

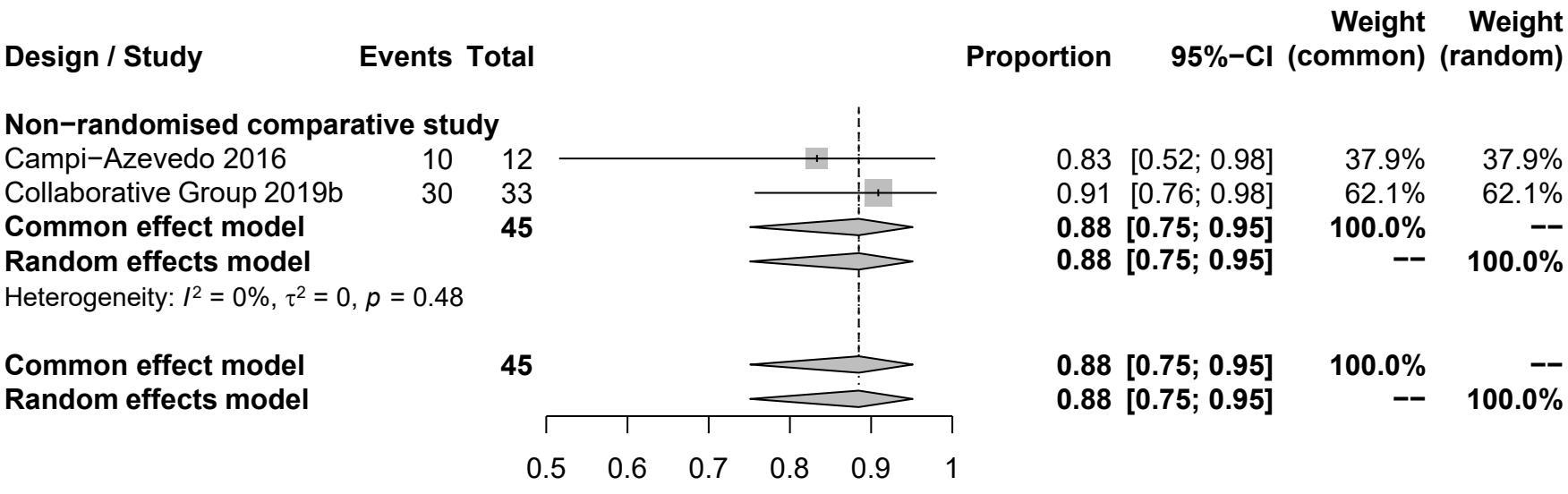
019



Heterogeneity: I^2 = 53%, τ^2 = 0.4313, p = 0.05
Test for subgroup differences (fixed effect): χ^2_2 = 6.86, df = 2 (p = 0.03)

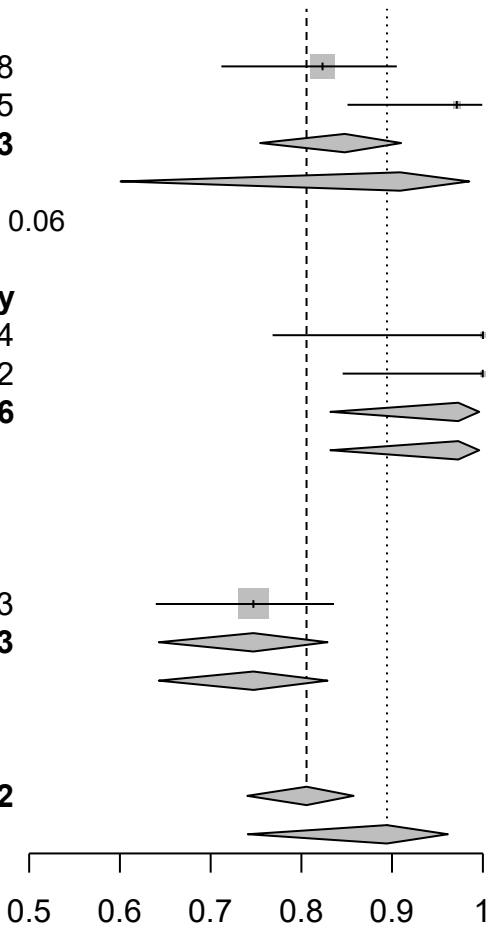
Test for subgroup differences (random effects): χ^2_2 = 6.96, df = 2 (p = 0.03)

020


Design / Study
Events
Total
Proportion
95%−CI
Weight (common)
Weight (random)
Non−randomised comparative study
Campi−Azevedo 2016 10 12 0.83 [0.52; 0.98] 37.9% 37.9%
Collaborative Group 2019b 30 33 0.91 [0.76; 0.98] 62.1% 62.1%
Common effect model 45 0.88 [0.75; 0.95] 100.0% --
Random effects model 0.88 [0.75; 0.95] -- 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.48
Common effect model 45 0.88 [0.75; 0.95] 100.0% --
Random effects model 0.88 [0.75; 0.95] -- 100.0%
0.5
0.6
0.7
0.8
0.9
1
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.48
Test for subgroup differences (fixed effect): χ^2_0 = 0.00, df = 0 (p = NA)
Test for subgroup differences (random effects): χ^2_0 = 0.00, df = 0 (p = NA)

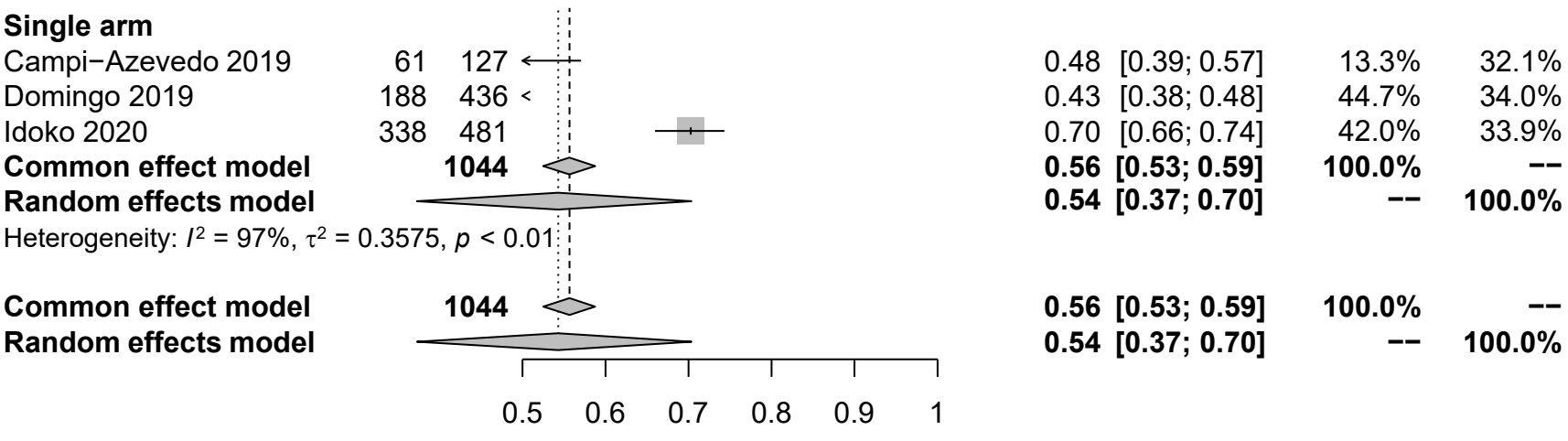
021

Design / Study	Events	Total	Proportion	95%−CI	Weight (common)	Weight (random)
RCT						
Campi−Azevedo 2014	56	68	0.82	[0.71; 0.91]	35.9%	31.0%
Roukens 2008	34	35	0.97	[0.85; 1.00]	3.5%	16.0%
Common effect model		**103**	**0.85**	**[0.75; 0.91]**	**39.4%**	**−−**
Random effects model			**0.91**	**[0.60; 0.99]**	**−−**	**47.0%**
Heterogeneity: I^2 = 71%, τ^2 = 1.4066, p = 0.06						
Non−randomised comparative study						
Roukens 2011	14	14	1.00	[0.77; 1.00]	1.8%	10.4%
Roukens 2011	22	22	1.00	[0.85; 1.00]	1.8%	10.4%
Common effect model		**36**	**0.97**	**[0.83; 1.00]**	**3.5%**	**−−**
Random effects model			**0.97**	**[0.83; 1.00]**	**−−**	**20.8%**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.83						
Single arm						
Kareko 2020	62	83	0.75	[0.64; 0.84]	57.0%	32.2%
Common effect model		**83**	**0.75**	**[0.64; 0.83]**	**57.0%**	**−−**
Random effects model			**0.75**	**[0.64; 0.83]**	**−−**	**32.2%**
Heterogeneity: not applicable						
Common effect model		**222**	**0.81**	**[0.74; 0.86]**	**100.0%**	**−−**
Random effects model			**0.89**	**[0.74; 0.96]**	**−−**	**100.0%**



Heterogeneity: I^2 = 63%, τ^2 = 0.8869, p = 0.03
Test for subgroup differences (fixed effect): χ^2_2 = 7.32, df = 2 (p = 0.03)
Test for subgroup differences (random effects): χ^2_2 = 6.91, df = 2 (p = 0.03)

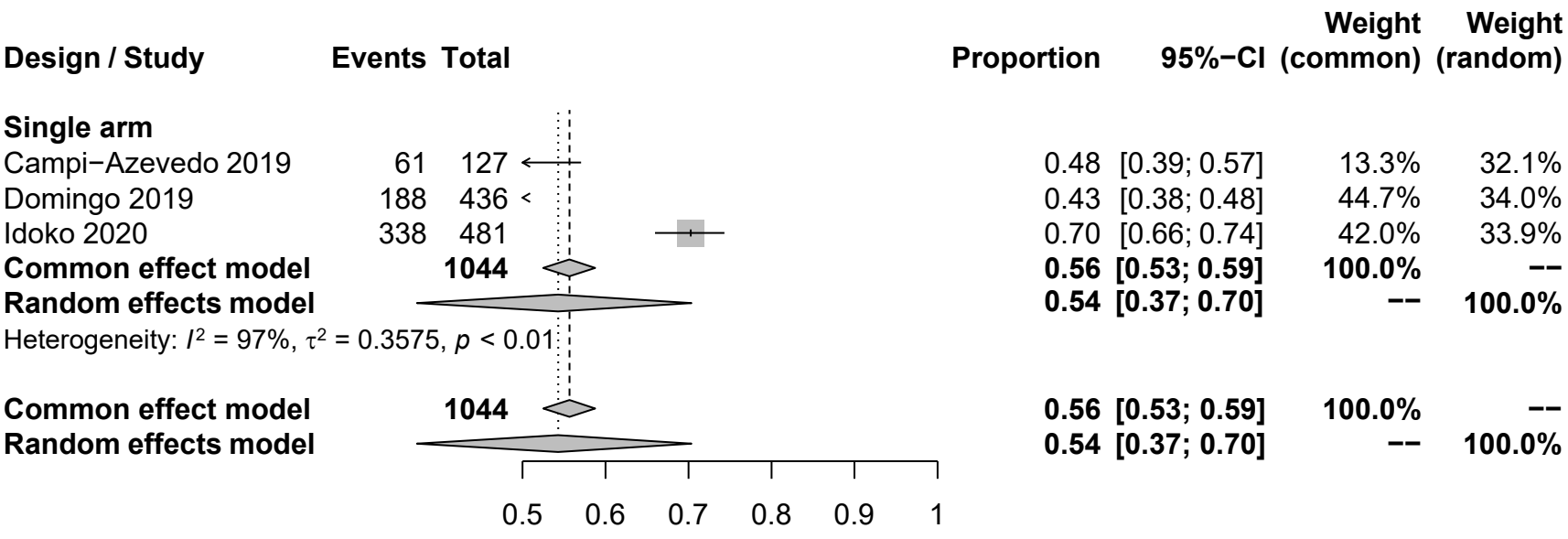
022



Heterogeneity: I^2 = 97%, τ^2 = 0.3575, p < 0.01
Test for subgroup differences (fixed effect): χ^2_0 = 0.00, df = 0 (p = NA)

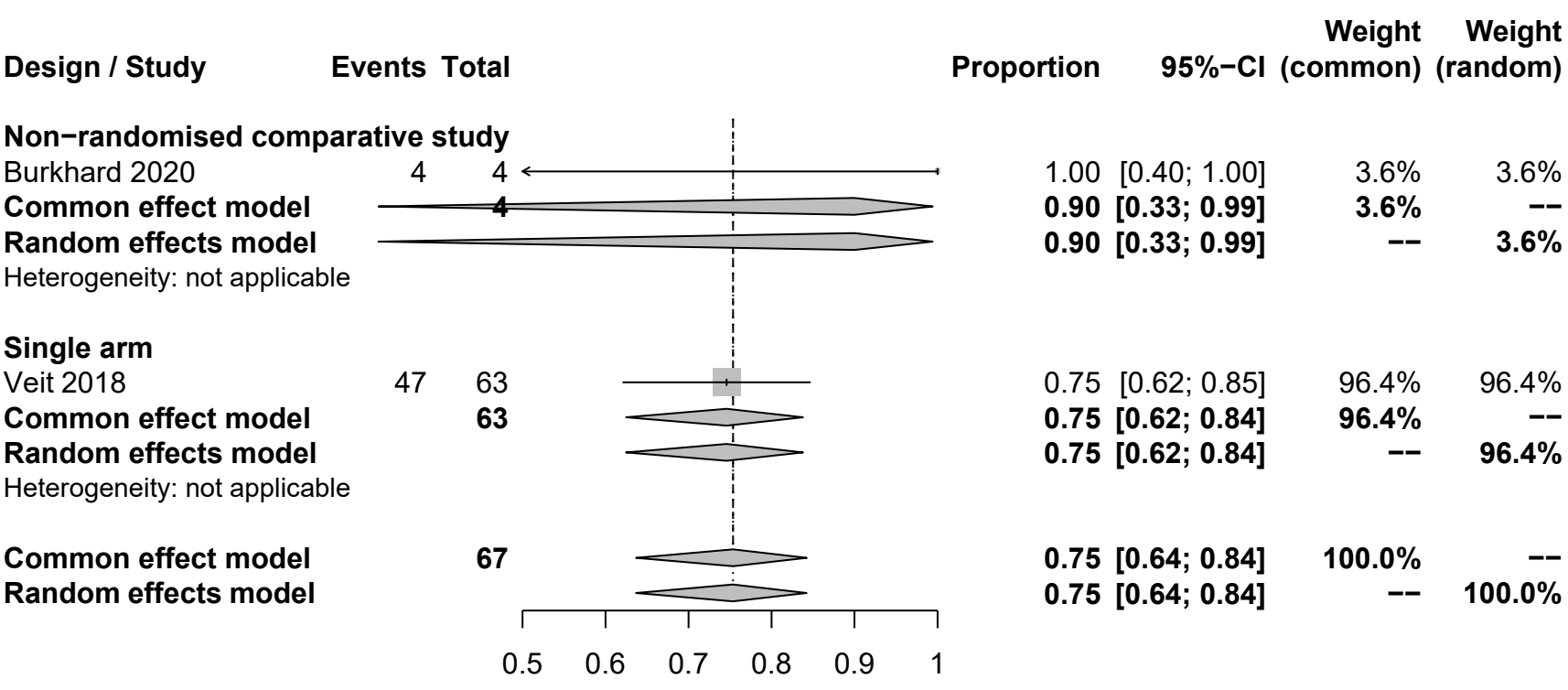
Test for subgroup differences (random effects): χ^2_0 = 0.00, df = 0 (p = NA)

023



Heterogeneity: I^2 = 97%, τ^2 = 0.3575, p < 0.01
Test for subgroup differences (fixed effect): χ^2_0 = 0.00, df = 0 (p = NA)

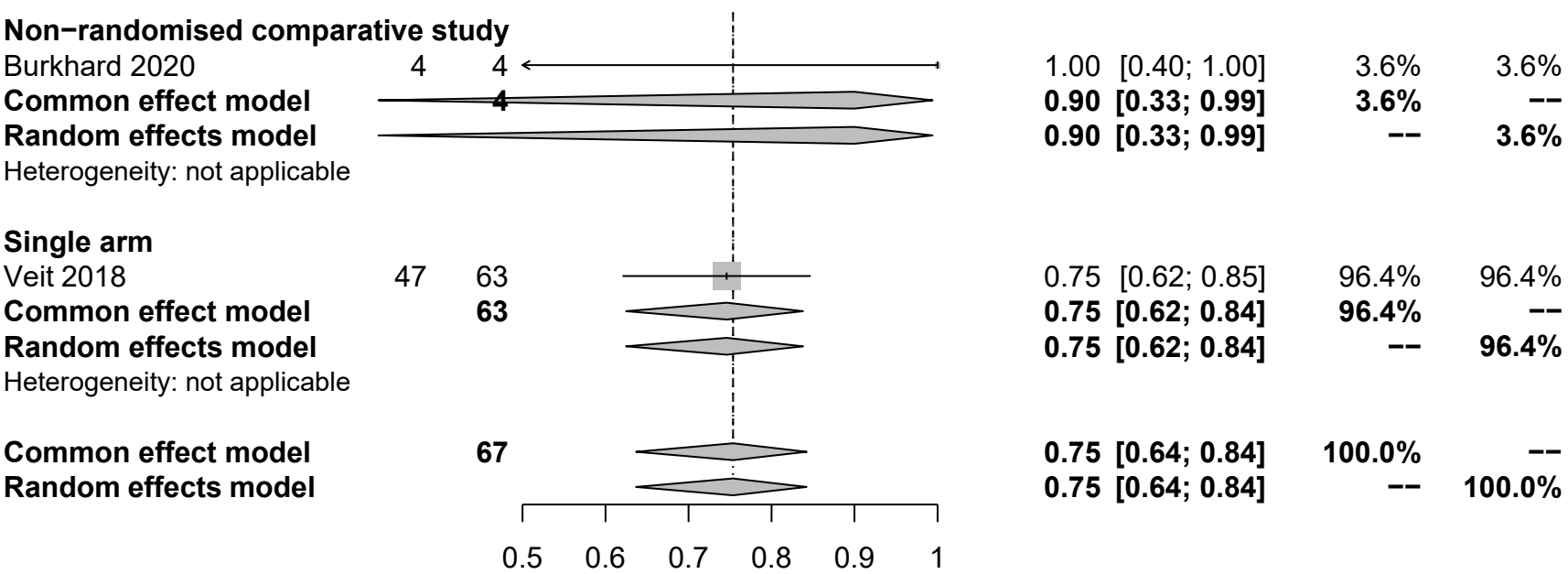
Test for subgroup differences (random effects): χ^2_0 = 0.00, df = 0 (p = NA)



Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.46
Test for subgroup differences (fixed effect): χ^2_1 = 0.54, df = 1 (p = 0.46)

Test for subgroup differences (random effects): χ^2_1 = 0.54, df = 1 (p = 0.46)

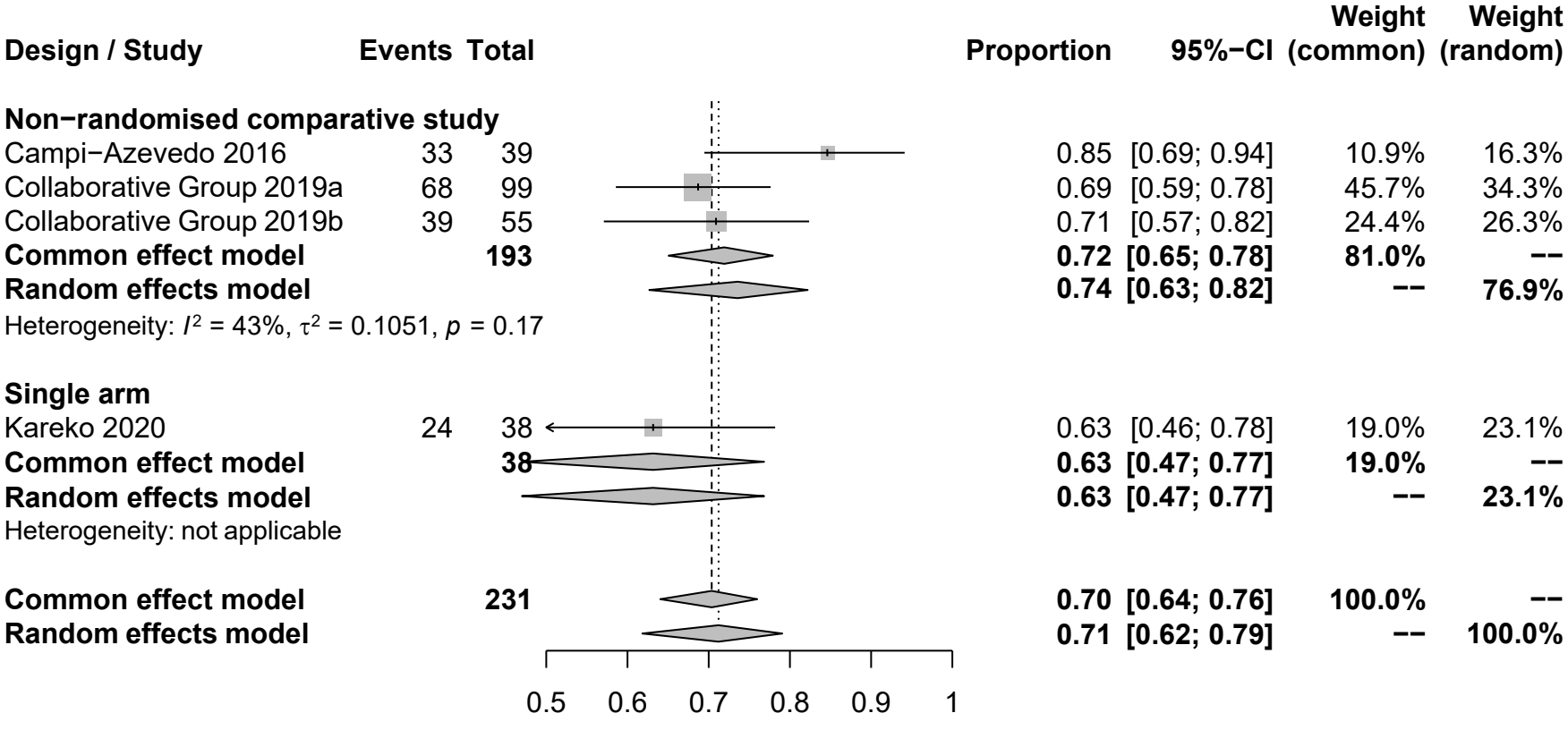
027



Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.46
Test for subgroup differences (fixed effect): χ^2_1 = 0.54, df = 1 (p = 0.46)

Test for subgroup differences (random effects): χ^2_1 = 0.54, df = 1 (p = 0.46)

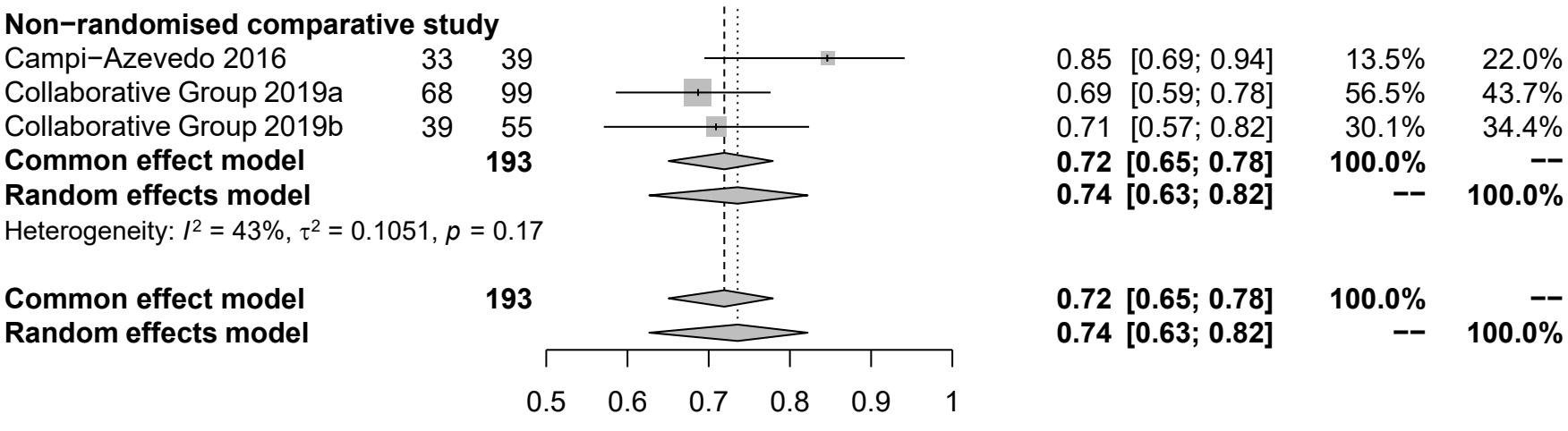
028



Heterogeneity: I^2 = 36%, τ^2 = 0.0895, p = 0.20
Test for subgroup differences (fixed effect): χ^2_1 = 1.16, df = 1 (p = 0.28)

Test for subgroup differences (random effects): χ^2_1 = 1.31, df = 1 (p = 0.25)

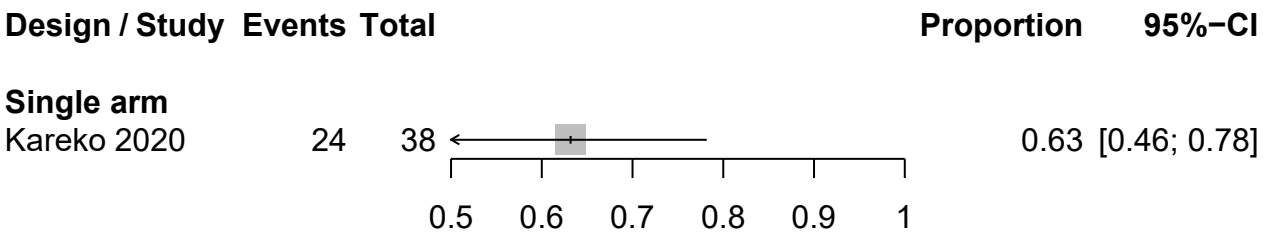
029



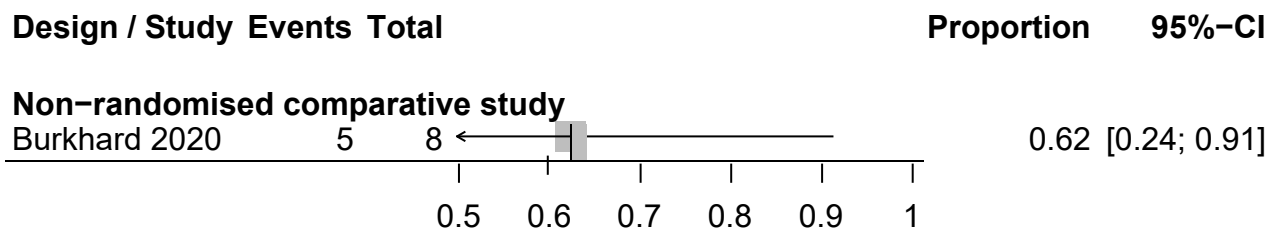
Heterogeneity: I^2 = 43%, τ^2 = 0.1051, p = 0.17
Test for subgroup differences (fixed effect): χ^2_0 = 0.00, df = 0 (p = NA)

Test for subgroup differences (random effects): χ^2_0 = 0.00, df = 0 (p = NA)

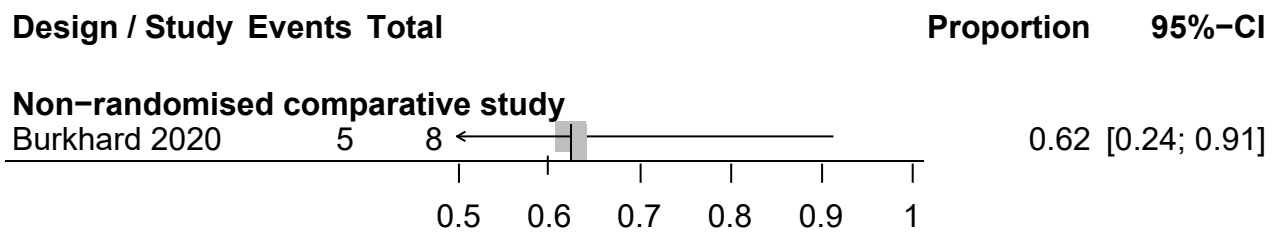
030


Design / Study Events Total Proportion 95%−CI
Single arm
Kareko 2020 24 38 0.63 [0.46; 0.78]
0.5 0.6 0.7 0.8 0.9 1

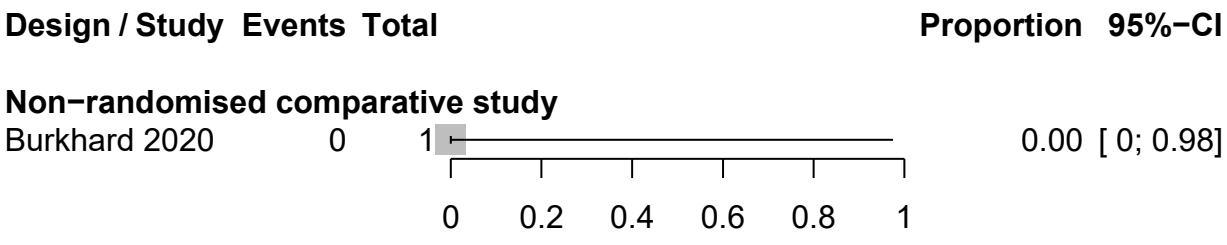
034


Design / Study Events Total
Proportion 95%−CI
Non−randomised comparative study
Burkhard 2020 5 8
0.62 [0.24; 0.91]
0.5 0.6 0.7 0.8 0.9 1

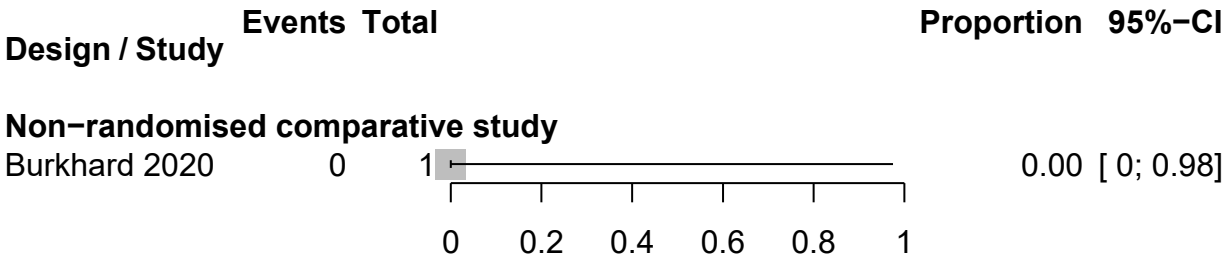
036


Design / Study Events Total
Proportion 95%−CI
Non−randomised comparative study
Burkhard 2020 5 8
0.62 [0.24; 0.91]
0.5 0.6 0.7 0.8 0.9 1

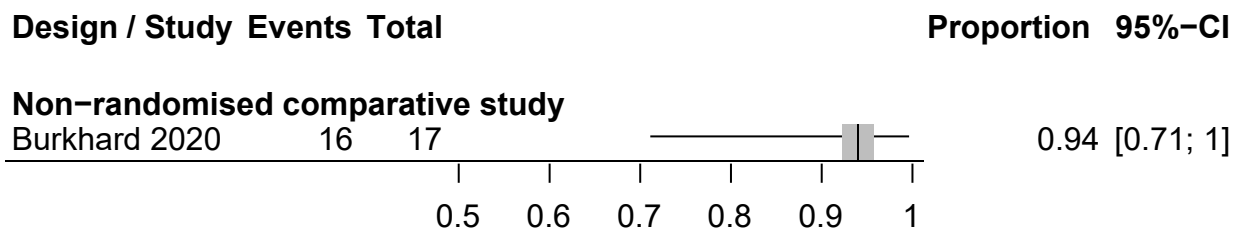
037


Design / Study Events Total
Proportion 95%−CI
Non−randomised comparative study
Burkhard 2020 0 1
0.00 [0; 0.98]
0 0.2 0.4 0.6 0.8 1

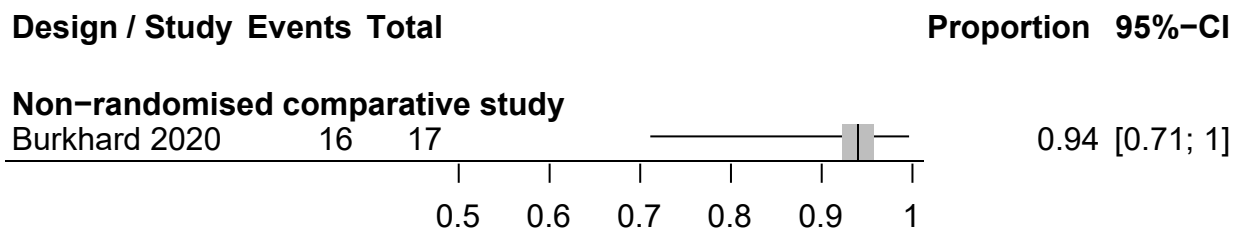
039


Design / Study
Events Total
Proportion 95%−CI
Non−randomised comparative study
Burkhard 2020 0 1 0.00 [0; 0.98]
0 0.2 0.4 0.6 0.8 1

043

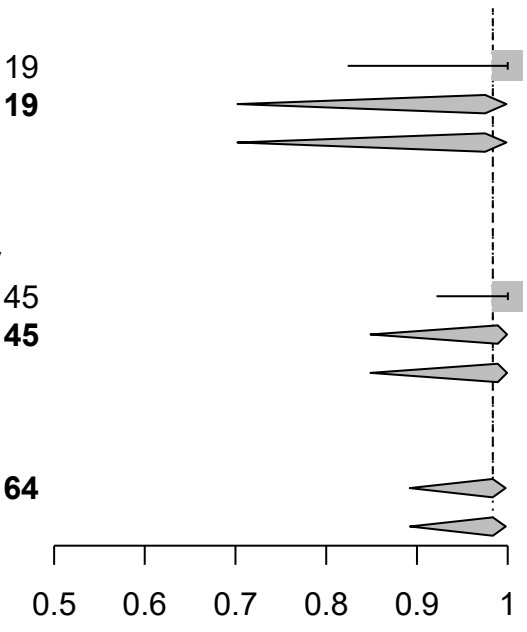

Design / Study Events Total
Proportion 95%−CI
Non−randomised comparative study
Burkhard 2020 16 17
0.94 [0.71; 1]
0.5
0.6
0.7
0.8
0.9
1

045


Design / Study Events Total
Proportion 95%−CI
Non−randomised comparative study
Burkhard 2020 16 17
0.94 [0.71; 1]
0.5
0.6
0.7
0.8
0.9
1

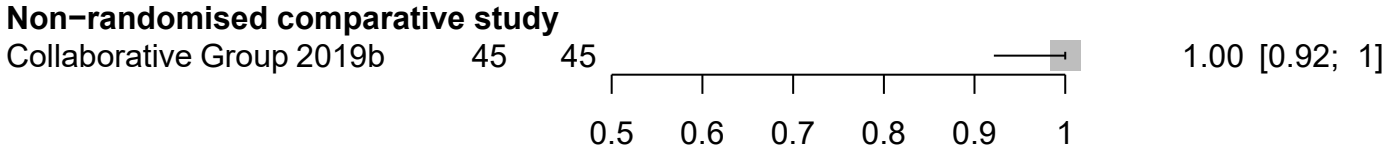
046

Design / Study	Events	Total	Proportion	95%−CI	Weight (common)	Weight (random)
RCT						
Roukens 2008	19	19	1.00	[0.82; 1]	49.6%	49.6%
Common effect model		**19**	**0.98**	**[0.70; 1]**	**49.6%**	**--**
Random effects model			**0.98**	**[0.70; 1]**	**--**	**49.6%**
Heterogeneity: not applicable						
Non−randomised comparative study						
Collaborative Group 2019b	45	45	1.00	[0.92; 1]	50.4%	50.4%
Common effect model		**45**	**0.99**	**[0.85; 1]**	**50.4%**	**--**
Random effects model			**0.99**	**[0.85; 1]**	**--**	**50.4%**
Heterogeneity: not applicable						
Common effect model		**64**	**0.98**	**[0.89; 1]**	**100.0%**	**--**
Random effects model			**0.98**	**[0.89; 1]**	**--**	**100.0%**

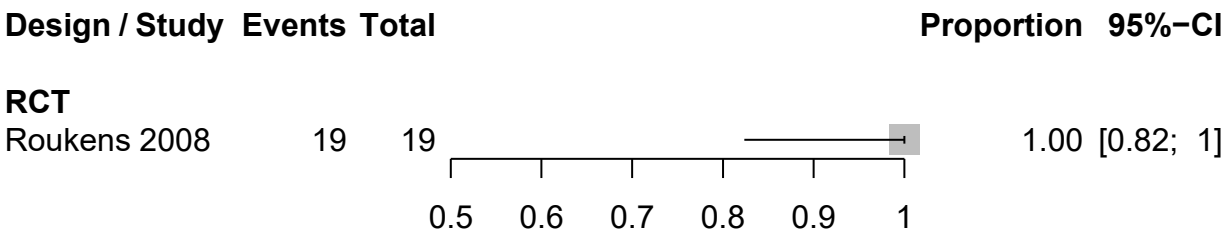


Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.67
Test for subgroup differences (fixed effect): χ^2_1 = 0.18, df = 1 (p = 0.67)
Test for subgroup differences (random effects): χ^2_1 = 0.18, df = 1 (p = 0.67)

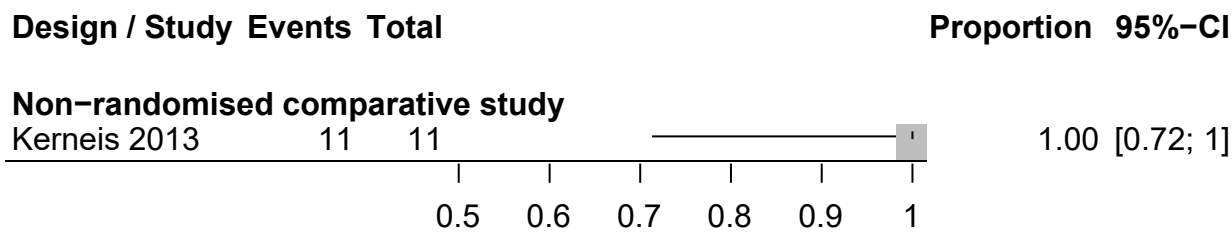
047


Design / Study
Events Total
Proportion 95%−CI
Non−randomised comparative study
Collaborative Group 2019b 45 45 1.00 [0.92; 1]
0.5 0.6 0.7 0.8 0.9 1

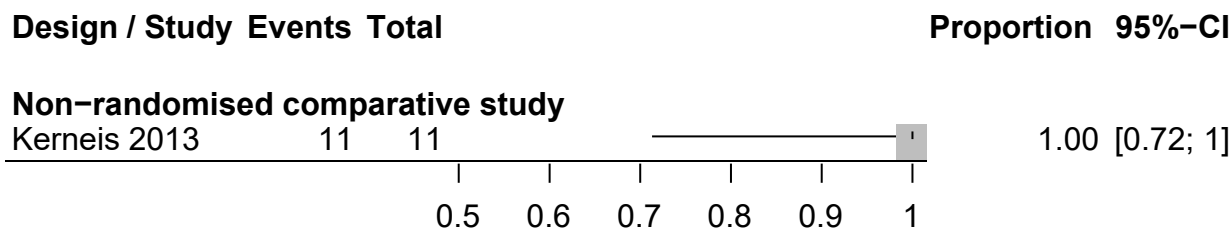
048

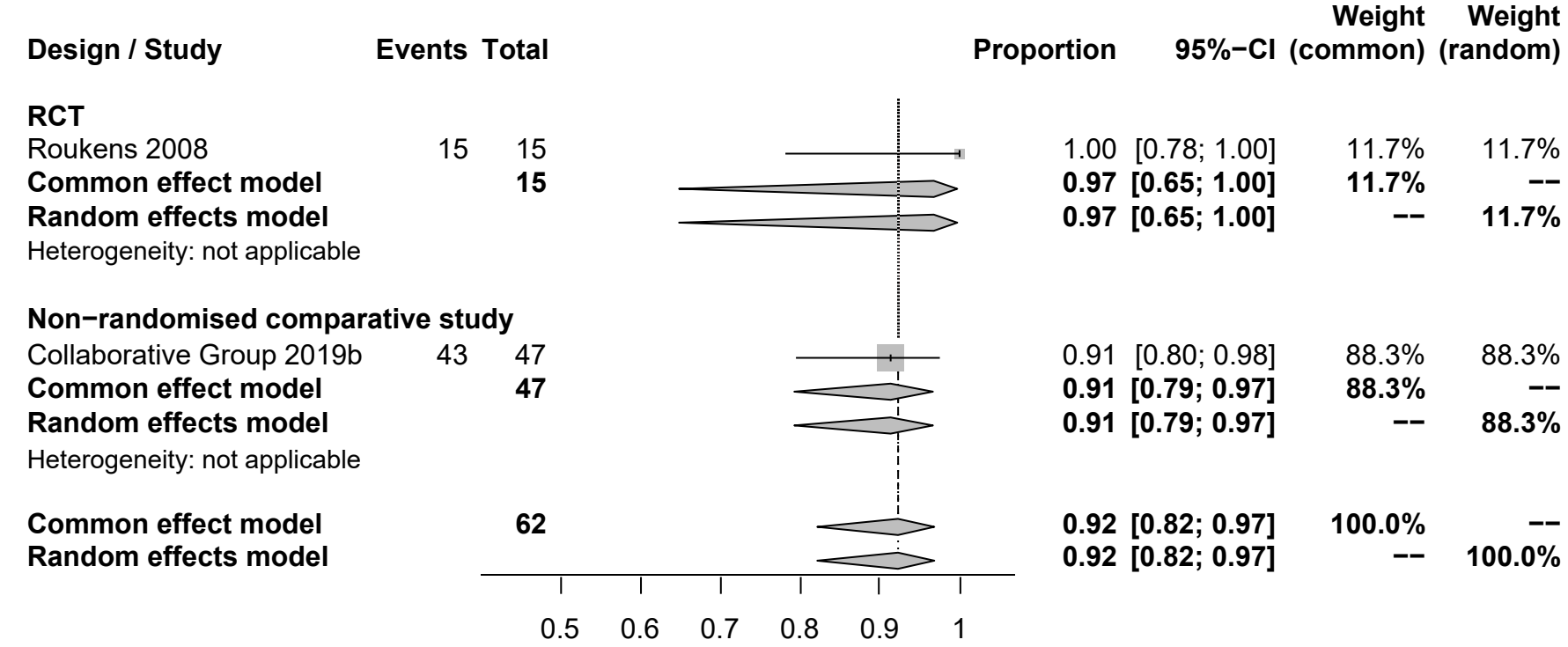

Design / Study Events Total Proportion 95%−CI
RCT
Roukens 2008 19 19 1.00 [0.82; 1]
0.5 0.6 0.7 0.8 0.9 1

052


Design / Study Events Total
Proportion 95%−CI
Non−randomised comparative study
Kerneis 2013 11 11
1.00 [0.72; 1]
0.5
0.6
0.7
0.8
0.9
1

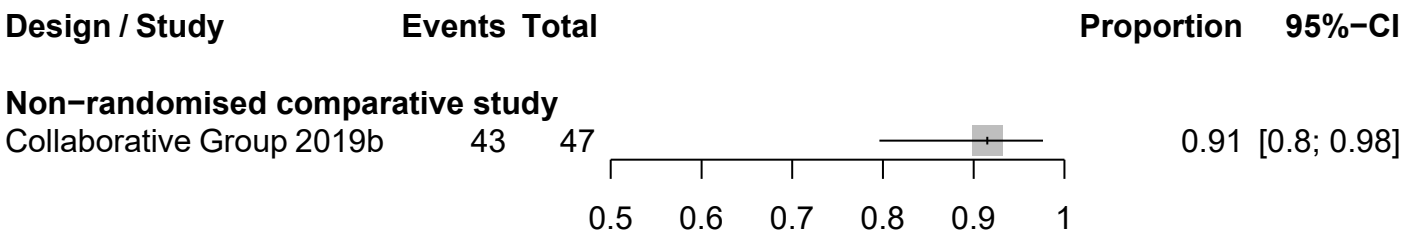
054


Design / Study Events Total
Proportion 95%−CI
Non−randomised comparative study
Kerneis 2013 11 11
1.00 [0.72; 1]
0.5
0.6
0.7
0.8
0.9
1

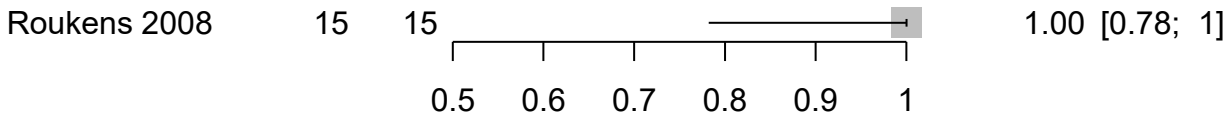


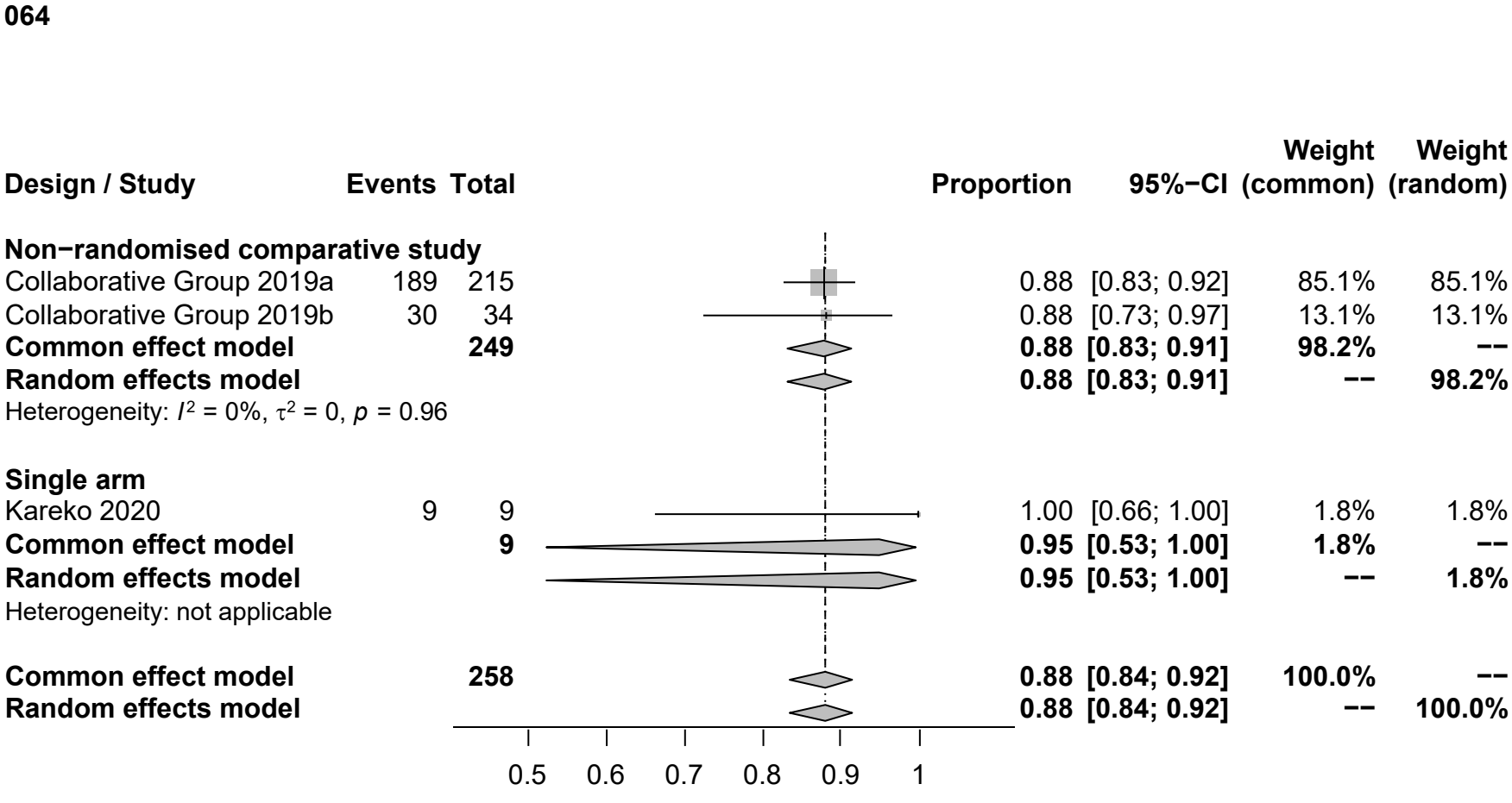
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.49
Test for subgroup differences (fixed effect): χ^2_1 = 0.48, df = 1 (p = 0.49)
Test for subgroup differences (random effects): χ^2_1 = 0.48, df = 1 (p = 0.49)

056


Design / Study
Events
Total
Proportion
95%−CI
Non−randomised comparative study
Collaborative Group 2019b
43
47
0.91
[0.8; 0.98]
0.5
0.6
0.7
0.8
0.9
1

057

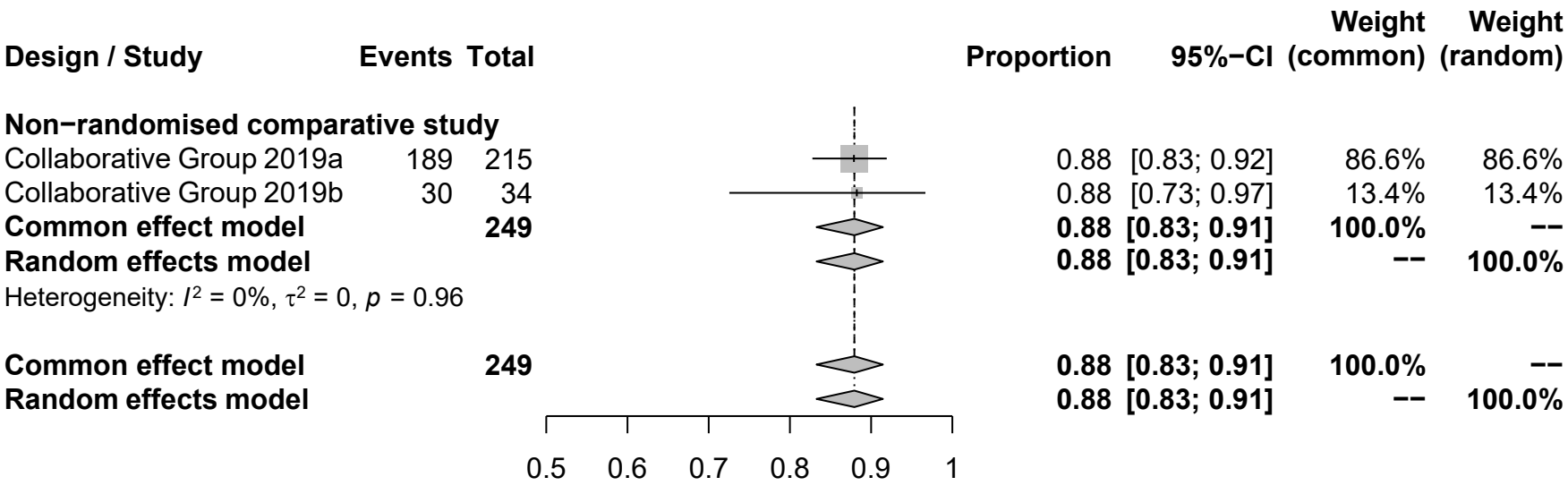

Design / Study Events Total Proportion 95%−CI
RCT
Roukens 2008 15 15 1.00 [0.78; 1]
0.5 0.6 0.7 0.8 0.9 1



Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.81
Test for subgroup differences (fixed effect): χ^2_1 = 0.43, df = 1 (p = 0.51)

Test for subgroup differences (random effects): χ^2_1 = 0.43, df = 1 (p = 0.51)

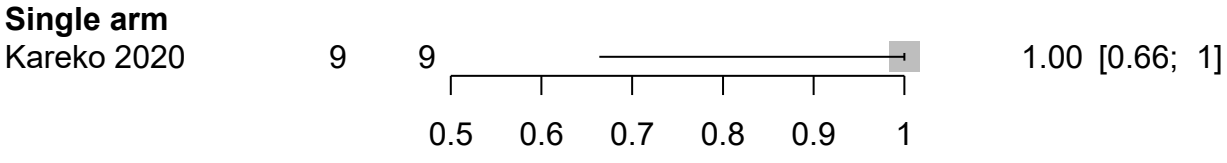
065

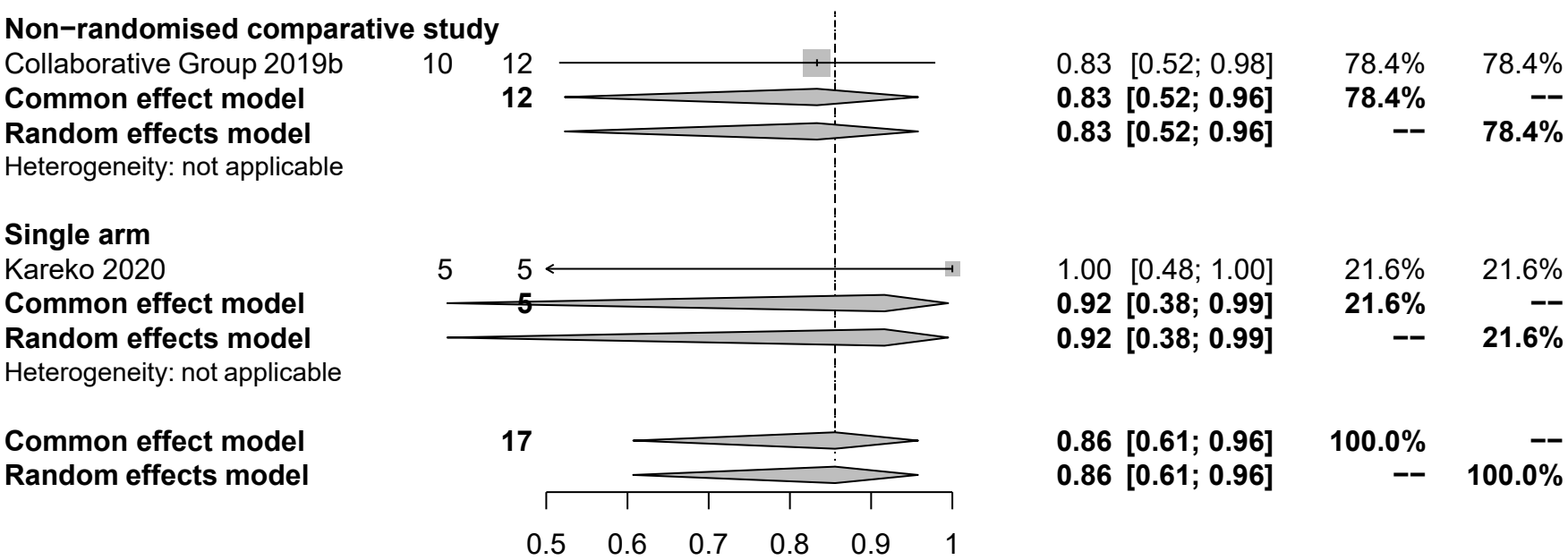


Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.96
Test for subgroup differences (fixed effect): χ^2_0 = 0.00, df = 0 (p = NA)

Test for subgroup differences (random effects): χ^2_0 = 0.00, df = 0 (p = NA)

066

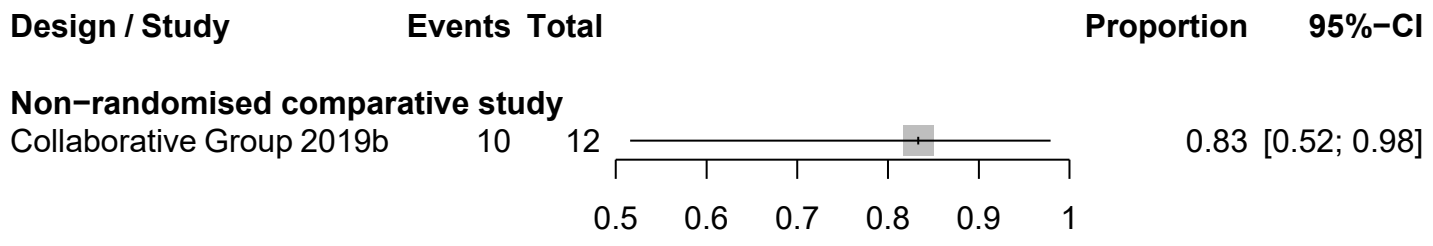

Design / Study Events Total Proportion 95%−CI
Single arm
Kareko 2020 9 9 1.00 [0.66; 1]
0.5 0.6 0.7 0.8 0.9 1



Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.64
Test for subgroup differences (fixed effect): χ^2_1 = 0.22, df = 1 (p = 0.64)

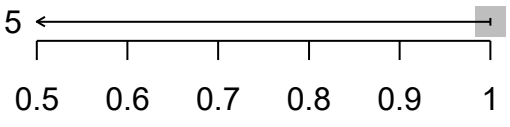
Test for subgroup differences (random effects): χ^2_1 = 0.22, df = 1 (p = 0.64)

074

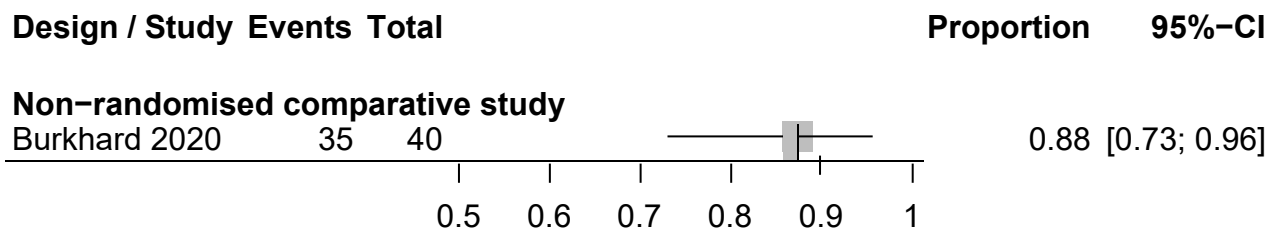

Design / Study
Events
Total
Proportion
95%−CI
Non−randomised comparative study
Collaborative Group 2019b
10
12
0.83 [0.52; 0.98]
0.5
0.6
0.7
0.8
0.9
1

075

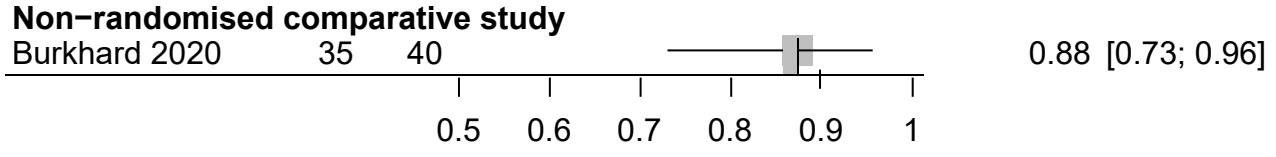
Design / Study	Events	Total	Proportion	95%−CI
Single arm				
Kareko 2020	5	5	1.00	[0.48; 1]

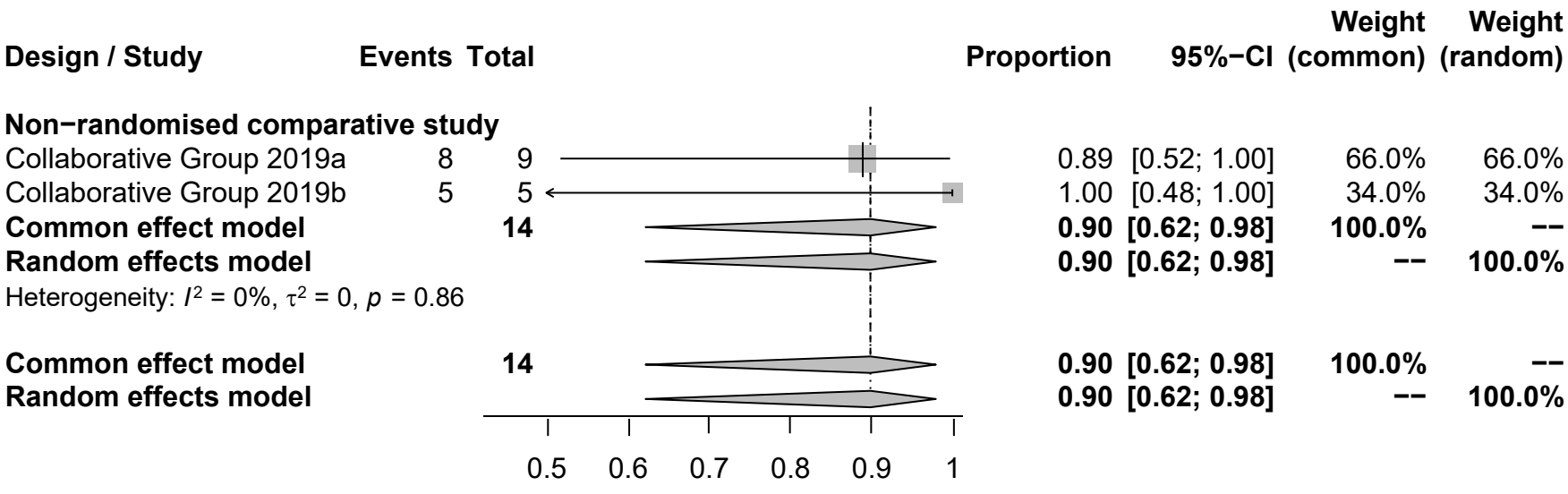


088


Design / Study Events Total
Proportion 95%−CI
Non−randomised comparative study
Burkhard 2020 35 40
0.88 [0.73; 0.96]
0.5 0.6 0.7 0.8 0.9 1

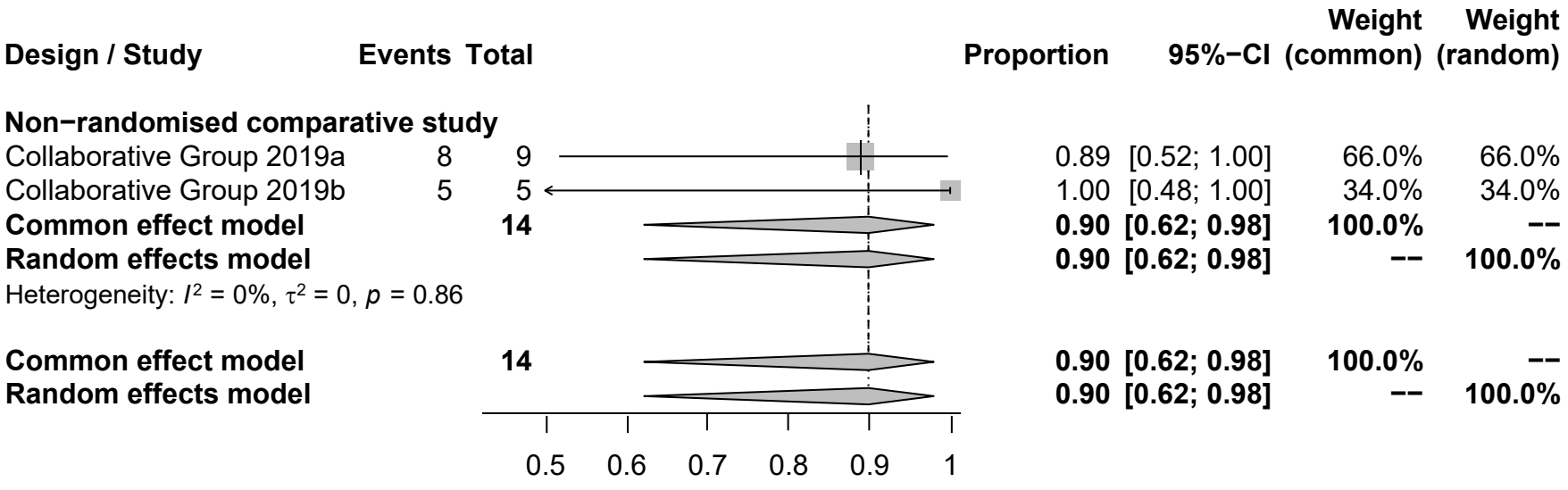
090


Design / Study Events Total
Proportion 95%−CI
Non−randomised comparative study
Burkhard 2020 35 40
0.88 [0.73; 0.96]
0.5 0.6 0.7 0.8 0.9 1



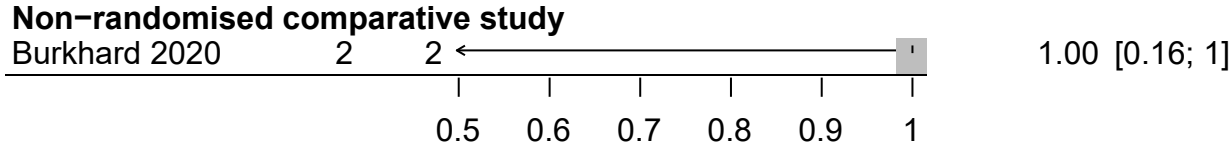
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.86
Test for subgroup differences (fixed effect): χ^2_0 = 0.00, df = 0 (p = NA)

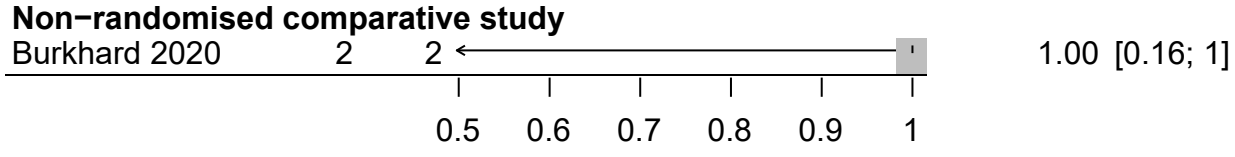
Test for subgroup differences (random effects): χ^2_0 = 0.00, df = 0 (p = NA)

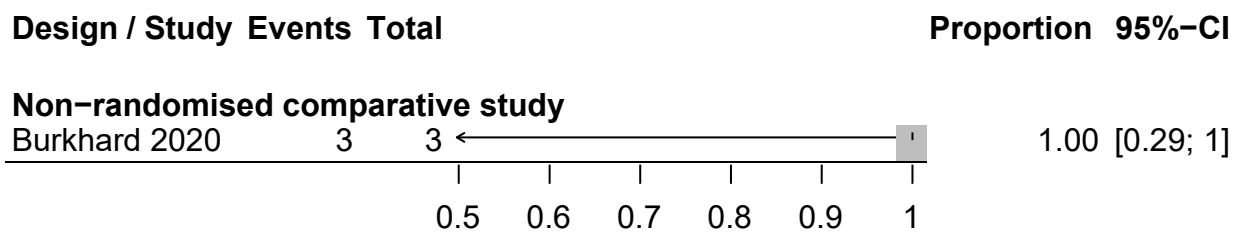


Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.86
Test for subgroup differences (fixed effect): χ^2_0 = 0.00, df = 0 (p = NA)

Test for subgroup differences (random effects): χ^2_0 = 0.00, df = 0 (p = NA)


Design / Study Events Total
Proportion 95%−CI
Non−randomised comparative study
Burkhard 2020 2 2 1.00 [0.16; 1]
0.5 0.6 0.7 0.8 0.9 1


Design / Study Events Total
Proportion 95%−CI
Non−randomised comparative study
Burkhard 2020 2 2 1.00 [0.16; 1]
0.5 0.6 0.7 0.8 0.9 1


Design / Study Events Total
Proportion 95%−CI
Non−randomised comparative study
Burkhard 2020 3 3
1.00 [0.29; 1]
0.5
0.6
0.7
0.8
0.9
1

135

Design / Study	Events	Total	Proportion	95%−CI
Non−randomised comparative study				
Burkhard 2020	3	3	1.00	[0.29; 1]