NIPH
Norwegian Institute of Public Health

REPORT

2022

RAPID REVIEW:
Prevalence of common human coronavirus (HCoV) infections

Published by	Norwegian Institute of Public Health, Division for health services
Title	Prevalence of common human coronavirus (HCoV) infections: a rapid review
Norwegian title	Forekomst av vanlige humane koronavirusinfeksjoner: en hurtigoversikt
Responsible	Camilla Stoltenberg, director
ISBN	978-82-8406-311-9
Publicationtype	Rapid review
No of pages	39 (99 including appendices)
Commissioner	Division for Infection Control and Environmental Health, the Norwegian Institute of Public Health
Keywords(MeSH)	Common coronavirus, seasonal coronavirus, human coronavirus, HCoV-229E, HCoV-HKU1, HCoV-NL63, HCoV-OC43, HumanCoV-229E, HumanCoV-HKU1, HumanCoV-NL63, HumanCoV-OC43, sCoV-229E, sCoV-HKU1, sCoV-NL63, sCoV-OC43
Citation	Flodgren GM, Steiro A, Brurberg K, Rose C. Prevalence of common human coronavirus (HCoV) infections: a rapid review [Forekomst av vanlige humane koronavirusinfeksjoner: en hurtigoversikt] –2022. Oslo: Folkehelseinstituttet, 2022.

Content

Hovedbudskap

Område for helsetjenester ved Folkehelseinstituttet (FHI) har gjennomført denne hurtigoversikten om forekomst av vanlige humane koronavirus (HCoV-OC43, HCoV-NL63, HCoV-229E og HCoV-HKU1). Hurtigoversikten var bestilt fra Område for smittevern, FHI.

Vi inkluderte 83 primærstudier som rapporterte prevalens av vanlige humane coronavirus (HCoV). Prevalens ble sett i sammenheng med bl.a. alder, geografisk region og landsøkonomi. Femten studier rapporterte om samtidig infeksjon med ulike HCoV stammer. Resultatene viser:

- Gjennomsnittlig prevalens av HCoV på tvers av ti geografiske regioner i hele verden var 4 %
- Prevalens av HCoV var kanskje noe lavere i de sørøstlige og østasiatiske geografiske regioner (2-3 %) enn i Afrika (6-14 %)
- Prevalens av HCoV blant spedbarn og barn (5 %) er muligens noe høyere enn hos voksne og eldre (3 %)
- Vi fant ingen konsistent sammenheng mellom prevalens av HCoV og lands inntektsnivå
- HCoV sees noe oftere i sammenheng med infeksjoner i øvre (6 %) enn i nedre luftveier (3 %)
- I perioden mellom 2005 og 2018 var det liten variasjon i prevalens av HCoV over tid
- Samtidig infeksjon med flere HCoV-stammer varierte fra median 0,3 % (0,2 % til 13,8 %) for OC43+HKU1 til 2,1 % (0.5 % til 10,0 %) for OC43+229E
- Samtidig infeksjon med andre luftveisvirus var vanlig (~47 % av alle HCoV-tilfeller)
- Få studier rapporterte data fra lavinntektsland. Informasjon om type lufteveisinfeksjon, innleggelser og studiested var i mange tilfeller uklart eller mangelfullt rapportert
- Ingen av de inkluderte studiene rapporterte om sosiale forhold (f.eks. minoritetsstatus og SES)

Fremtidige studier bør samle data om sosiale forhold, bruke standardiserte prosedyrer for PCR-analyse og forbedre rapporteringen generelt.

Tittel:
Forekomst av vanlige humane koronavirusinfeksjoner: en hurtigoversikt

Publikasjonstype:
Hurtigoversikt

Oppdragsgiver:
Område for smittevern, FHI

Søk oppdatert:
August 2020

Fagfellevurdering (internt):
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Key messages

Division for Health Services at the Norwegian Institute of Public Health (NIPH) conducted a rapid review of prevalence of common human coronaviruses (HCoV-OC43, HCoV-NL63, HCoV-229E, and HCoV- HKU1). This rapid review was commissioned by the Division for Infection Control, NIPH.

We included 83 original studies that reported prevalence of common HCoVs. Prevalence was analysed in association with age, geographic regions and country income levels. Fifteen studies also reported on co-infections between different HCoV strains. The results show:

- Mean prevalence og HCoV across ten geographic regions throughout the world was 4%
- Prevalence of HCoVs was possibly lower in the South-East and East Asian geographical regions (2-3%) compared to African regions (6-14%)
- Prevalence of HCoVs among infants and children (5%) was possibly lower than among adults and older adults (3%)
- We could not detect a consistant relationship between HCoV prevalence and country income level
- HCoVs are more frequently observed in association with upper respiratory tract infections (RTI) (6%) than in lower RTIs (3%)
- In the period between 2005 and 2018, there was little variations in the prevalence of HCoV over time
- Co-infections between HCoV strains ranged from median 0.3% (0.2 to 13.8) for OC43+HKU1 to median 2.1% (0.5 to 10.0) for OC43+229E
- Co-infections with other respiratory virus were common (around 47% of HCoV positive cases).
- Few studies reported data for low-income countries, and data on RTI type, admission status, and study location were in many studies unclear or lacking.
- None of the included studies reported on social determinants of health (e.g. minority status and SES), and therefore equity issues related to HCoV prevalence could not be addressed in this review.

Future studies should aim to collect data on social determinants of health, use standardized sample types for PCR analysis, and improve reporting in general.

Title:

Prevalence of common human coronavirus infections: a rapid review

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Publication type:

Rapid review

Commissioner:

Division for Infection Control, NIPH

Search Updated:

August 2020

Peer review (internal):

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Preface

This rapid review was commissioned by the Division for Infection Control at the Norwegian Institute of Public Health (NIPH).

The internal project group included the following members from the Norwegian Institute of Public Health, who's contributions to the report were as follows:

Gerd M. Flodgren (GMF), Senior researcher, project lead, data extraction, quality assessment, and responsible for drafting the report
Asbjørn Steiro (AS), Researcher, data extraction and quality assessment
Kjetil G. Brurberg (KGB), Researcher, data extraction and quality assessment
Chris Rose (CR), Statistician, statistical analyses
Elisabet Hafstad (EH), Research librarian, literature search

We wish to acknowledge Lisbeth Meyer-Næss and Fredrik Oftung, from the Division for Infection Control at NIPH, for providing expert input and internal peer review of the project.

The authors declare no conflicts of interest.

The Norwegian Institute of Public Health take full responsibility of the content of this report.

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Abbreviations

AdV	Adenovirus
CI	Confidence interval
CMV	Cytomegalovirus
COVID	Coronavirus disease
CP	Chlamydia pneumoniae
EV	Enterovirus
I^2	I-square
IFV A/B	Influenza (Flue)virus A/B
ILO	International labour organisation
NIPH	Norwegian Institute of Public Health
HBoV	Human bocavirus
HCoV	Human CoronaVirus
HCoV-HKU1	Human CoronaVirus Hong Kong University 1
HCoV-NL63	Human CoronaVirus Netherlands 63
HIC	High Income Country
HMPV	Human Meta-Pneumo Virus
HPEV	Human Parechovirus
HRV	Human Rhino Virus
LIC	Low Income Country
LMIC	Lower Middle-Income Country
LRTI	Lower Respiratory Tract Infection
MERS	Middle East Respiratory Syndrome
MIC	Middle Income Country
MP	Mycoplasma Pneumoniae
PCR	Polymerase Chain Reaction
PIC	Picornavirus
PIV-1-3	Para Influenza Virus 1-3
PM	Particular Matter
ROB	Risk of Bias

RT-PCR	Real Time-PCR
PAN-PCR	Pan-corona-virus PCR
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analyses
RNA	RiboNucleic Acid
RSV	Respiratory Syncytial Virus
RTI	Respiratory Tract Infection
SARS	Severe Acute Respiratory Syndrome
SES	Socio-Economic Status
ROB-SPEO	Risk of Bias in Studies estimating Prevalence of Exposure to Occupational risk factors
URTI	Upper Respiratory Tract Infection
WHO	World Health Organization

Background

Description of the virus

Coronaviruses belongs to the family *Coronaviridae* which includes, four genera (alpha, beta, gamma, and delta), and several subgenera and species (1). The coronavirus is a medium-sized, enveloped, positive-stranded RNA-virus. Among its specific characteristics are the spike-formed proteins that give it a crown-like resemblance, and thereby also its name (2).

Coronaviruses can cause disease in both animals and humans, and among the 46 known species there are seven human coronaviruses (hereafter HCoVs) that can infect humans (3). Common for all HCoVs is that they cause respiratory tract infections (RTIs) (3). Four of the HCoVs are common or seasonal (HCoV-OC43, HCoV-NL63, HCoV-229E, HCoV-HKU1) and typically result in milder respiratory disease (common cold), but may sometimes cause more severe infections (i.e. pneumonia)(3). HCoV-OC43 is in most surveys the most prevalent strain. The other three HCoVs (MERS, SARS-CoV, and SARS-CoV2), are considered non-seasonal and known to cause acute severe respiratory disease, and subsequently also more deaths (4). SARS-CoV-2 is the causative agent for the ongoing COVID-19 pandemic (5).

The HCoVs belong in two of the genera mentioned above: alpha (HCoV-229E and HCoV-NL63) and beta (HCoV-HKU1, HCoV-OC43, MERS-CoV, SARS-CoV, and SARS-CoV-2)(2). There may be some cross-reactivity among coronaviruses, maybe in particular between species within the same genera that are more closely related (6).

The focus of this rapid review is on the prevalence of the four common HCoVs.

Factors related to the prevalence of common HCoV infections

The four common HCoVs have been identified all over the globe. Their seasonality varies partly due to the climate, and are most prevalent in winter and early fall in temperate climates (7).

There is some evidence for higher prevalence of common HCoV infections in young children (8;9), and cross-reactive immunity after previous common HCoV infection has been put forward as one explanation as to why children are less susceptible to SARS-

CoV-2 infection, and develop less severe COVID-19 disease (10). Lower HCoV prevalence (9) was reported in the elderly (80-90 years old) in a large Swedish study, and older adults (>65 years) have been shown to lack T-lymphocytes directed at HCoV-OC43 and HCoV-NL63. Older adults may potentially also have a lower frequency of SARS-CoV-2 cross-reactive T cells, (11), which could be one reason that they often develop more severe COVID-19.

There are many other factors that may affect the prevalence of common HCoV infections, as well as other respiratory infections, which relate to the individual (e.g. smoking, comorbid conditions, poverty, etc.), but also environmental factors like exposure to ambient air pollution (12-14), which may damage the normal defense mechanisms of the human respiratory tract, thereby increasing the susceptibility to infections (15;16). Inequality in the exposure of air pollutants by socioeconomic status (SES), and/or minority status has been shown in the US, Asia and Africa, while the results for Europe have been mixed (17;18). In addition, household air pollution in low-income countries (LICs), also has the potential to affect the prevalence of RTIs due to sub-optimal cooking and heating facilities (19).

Why is it important to conduct this rapid review?

During the COVID-19 pandemic it became evident that the same virus (i.e. SARS-CoV-2) could give rise to asymptomatic, or mild disease, as well as to severe disease requiring hospital admission (20). One of many suggested mechanisms behind these differences is cross-protective immunity from previously infections with common HCoVs. By examining the prevalence of the common HCoVs, we may improve our understanding of the transmission, susceptibility and immune responses to SARS-CoV-2. In this rapid review, we have summarised results from studies reporting prevalence of the four common HCoVs, co-infections between different HCoV strains, and co-infections with other respiratory viruses.

Objectives and research questions

To assess the prevalence of common HCoVs by age group, country, geographic region, and country economy.

More specifically we aimed to answer the following research questions:

1. What is the prevalence of common HCoV infections in different *age groups, and does the prevalence differ between groups*?
2. What is the prevalence of common HCoV infections in different *countries, and does the prevalence differ between countries*?
3. What is the prevalence of common HCoV infections in different *geographic regions, and does the prevalence differ between geographic regions*?
4. What is the prevalence of common HCoVs in healthy asymptomatic people, and in people with acute upper (URTI) or lower respiratory tract infections (LRTI), and does the prevalence differ between groups?

Additional aims were, time and resources permitting, to assess the potential differences in prevalence of HCoVs by gender, minority status, socioeconomic status, and location (i.e. rural or urban/densely populated areas).

In a separate review we plan to investigate the immune responses to these common HCoVs, sequence homology with SARS-CoV-2, and the possibility of cross-reactivity/cross-protection of common HCoVs against severe SARS-CoV-2 infection.

Methods

We used a rapid review study design (21) to respond to our research questions. The rationale behind this was that we expected that new relevant studies would continuously be published at a rapid pace, why a traditional systematic review would be at risk of quickly becoming outdated. This rapid review of HCoV prevalence studies was guided by the handbook of the Johanna Briggs Institute (22). A protocol was published in PROSPERO (2020 CRD42020202574). A glossary is provided in Appendix 1.

Inclusion criteria

Participants, condition, context, localisation and outcomes

We included studies of people of all ages, with or without symptoms of upper or lower RTI, who had been tested for one or more type of common HCoV-infections (HCoV-229E, HCoV-OC43, HCoV-NL63 and HCoV-HKU1). We included studies of out- and in-patients, irrespective of country, geographic region, or location (urban/rural). The main outcome was the prevalence of common HCoVs, i.e. number and percentage (%) of tests positive for one or more (i.e. co-detection) of the four common HCoVs. We included original cross-sectional studies, cohort studies, and case-control studies.

Table 1. *Inclusion criteria*

Participants	People with symptoms of upper or lower respiratory tract infection (RTI), as well as healthy/asymptomatic people tested for HCoV infections
Condition	Common (seasonal) HCoV infections: HCoV-NL63, HCoV-OC43, HCoV-229E, and/or HCoV-HKU1
Context	People admitted to hospital (in-patients), attending primary care clinics (out-patients), and people tested in other settings (e.g. nurseries, nursing homes)
Localisation	Any country, geographic region, or location (i.e. urban or rural)
Outcomes	Prevalence: number and % of people positive for one, or more common HCoVs (i.e. co-detection)
Study design	Cross-sectional studies, cohort studies, and case-control studies

* Immune responses to HCoVs, sequence homology with SARS CoV 2, and possible cross-reactivity/cross-protection against SARS CoV 2 infection will be addressed in the second part of the review.

Exclusion criteria

We excluded the following types of studies and publications:

- Studies of specific patient groups (e.g. people with heart failure, lung disease or diabetes), as well as studies of other specific populations (e.g. air-travellers, pilgrims, and homeless).
- Studies of infections with the other three HCoVs (MERS, SARS-CoV1 or SARS-CoV2) (i.e. not common/seasonal HCoVs)
- Studies that were dissertations, conference proceedings
- Studies with no accessible full text version
- Studies with insufficient information for the analysis
- Studies with ≤12 months data collection
- Studies with data collected during outbreak and/ or epidemic seasons only
- Studies in other languages than those listed above
- Study designs other than those listed above and with date collected from other sources than registres (e.g. from electronic health journals or patient surveys)

Searching the literature

We searched MEDLINE and EMBASE for relevant studies from 1990 and up to August 2020. We used the following search terms: 'seasonal corona virus', 'human coronavirus', 'HCoV-229E', 'HCoV-HKU1', 'HCoV-NL63', 'HCoV-OC43', 'HumanCoV-229E', 'HumanCoV-HKU1', 'HumanCoV-NL63', 'HumanCoV-OC43', 'sCoV-229E', 'sCoV-HKU1', 'sCoV-NL63', 'sCoV-OC43', 'cross-reactivity', and 'cross-protection' and 'sequence homology'. The full search strategy is provided in Appendix 2.

A simplified search in PubMed was conducted by the lead author in March 2022, to find out whether any additional relevant studies had been published since the previous search date.

Study selection

One reviewer (GMF) screened the search results, by title and abstract, against the inclusion criteria and produced a long list of possible eligible studies. Uncertainties regarding the eligibility of studies were resolved through discussion among review authors. Full texts of potentially eligible articles were obtained and was further assessed for inclusion by the same reviewer (GMF). If there was uncertainty of the eligibility of a study, it was screened by a second reviewer.

Data extraction

One reviewer (from GMF, AS, KB) extracted data from each included study into a standardised and piloted data extraction form. All extractions were verified by the lead author. Uncertainties regarding individual data extractions were resolved through discussion among review authors. The following items were extracted: full citation, study design, country, geographic region, localisation (urban/rural), number and characteristics participants (e.g. age, gender, minority status, socioeconomic status, disease status, admission status, number and type of specimens/ samples analysed, methods of analysis, and outcomes (i.e. the number and percentages of people testing positive for each/any of the different HCoVs, or for all HCoVs as a group). Authors were contacted if data of importance for the analysis were missing.

Risk of bias assessment

One reviewer (from GMF, AS, and KB) used the RoB SPEO tool developed by the World Health Organisation and the International Labour Organisation (23) to assess the risk of bias of included prevalence studies. As we expected to identify a large number of eligible studies, we used what we considered were the two most relevant of the tool's eight domains for the assessment: (i) bias of selecting participants into the study, and (ii) bias due to differences in numerator and denominator. We followed the ROB SPEO guidance when judging the overall risk of bias of each study: e.g. if we judged one item to be at high risk and the other item to be at low risk, we would consider the study to, as a whole, to be at high risk. Any uncertainty regarding the risk of bias of a study, were resolved though discussion among review authors. The certainty of the included evidence was not assessed.

Data management

When feasible, the results (prevalence) of individual studies (no. and proportion of people testing positive for HCoVs) was pooled in a random effect meta-analysis following the guidance in the Cochrane Handbook (24).

Prevalence data were available for the four common human coronaviruses (HCoV-229E, HCoV-HKU1, HCoV-NL63, and HCoV-OC43), as well as for the four considered as a single group. Data were extracted as sample sizes and prevalence (i.e., percent of patients who tested positive) or number of positive tests for the following age groups (where available): 0-1 years, 1-5 years, 5-16 years, children, 16-64 years, >64 years, and all ages. The age categories "children" and "all ages" were used when no finer-grained information was available, and to provide study-level summaries. We are particularly interested in how prevalence may vary with age. To prevent double-counting of study participants and to facilitate more age-specific estimation, we discarded redundant data for the

coarser categories ("children" and "all ages") where prevalence data were available for the finer-grained categories.

To facilitate meta-analysis, we estimated prevalence and exact 95% binomial confidence intervals for each age group of each study, imputing the number of positive cases from the extracted point estimates of prevalence where necessary. For most of the included studies, data were also available on one or more of country, geographical region (e.g., Europe, Middle East), infection type (upper or lower respiratory tract, mixed or unknown), admission status (inpatients, outpatients, mixed, or unclear) and study start and end dates. We classified each country according to the World Bank income levels (low, lower middle, middle, upper middle, or high) (25).

Statistical analysis

We (CR) performed exploratory meta-analyses for each common HCoV and for all four HCoVs considered as a group, subgrouping by country, geographical region, and type of infection to explore possible differences between these variables. We then repeated that analysis, excluding all studies judged to be at high or probably high risk of bias. We present results as a single forest plot with results for the variables: region, income, age, infection type, and hospitalization, as well as forest plots for each variable, showing study-level prevalence estimates.

Using data from case-control studies that provided prevalence data on approximately corresponding age groups, we estimated the relative prevalence of each of the four viruses and all four as a group, comparing prevalence in cases and controls. We also performed meta-analyses to explore how prevalence may have varied over time. For each month from January 2000 to the present, we identified the subset of studies that had tested patients during that month. We assumed that each study had approximately constant recruitment and positive test rates and adjusted standard errors on prevalence to reflect the assumed sample size at each month. We then performed meta-analyses to estimate prevalence over time, presenting estimates graphically.

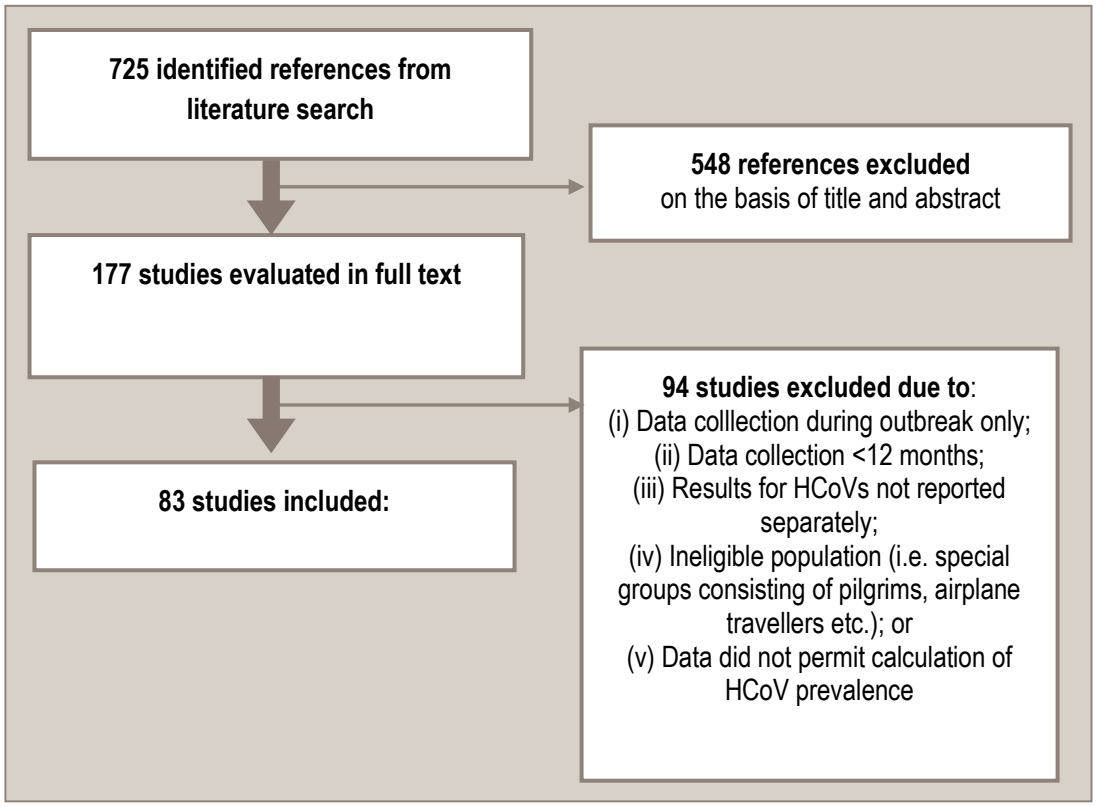
Analyses were performed using Stata 16 (StataCorp LLC, College Station, Texas, USA). Meta-analyses were performed on transformed scales as appropriate, and we back transformed to present estimates of prevalence as proportions (not percentages). We anticipated substantial heterogeneity between studies and used random effects models throughout and assessed heterogeneity using the I^2 statistic. We excluded studies that did not provide analysable data and did not attempt to impute missing values.

Results

Search results

The search of the electronic databases yielded 725 unique studies (42 duplicates were removed). Five-hundred and forty-eight of these studies were judged irrelevant and excluded at the title and abstract screening stage. The remaining 177 studies were retrieved and the full text scrutinised. Ninety-four studies were excluded after scrutiny with the most common reasons being as follows: (i) Data colllection during outbreak only;(ii) Data collection <12 months; (iii) Results for HCoVs not reported separately; (iv) Ineligible population (i.e. special group, pilgrims, airplane travellers); or (v) Data that did not permit calculation of HCoV prevalence. Eighty-three studies that reported prevalence data were subsequently included in this rapid review.

***Figure 1**. PRISMA study flow diagram (26)*



Characteristics of included studies

Study designs

We identified 83 eligible studies of HCoV prevalence published between 2005 and 2020 (Table 1). Fifty-one studies were prospective, and 32 studies were retrospective or unclear (most likely retrospective). Four were case-control studies (27-30).

Participants

A total of 336,783 participants were included in this review (median: 679; range: 119 to 74,519). The majority of studies included children, followed by studies including all ages, and lastly studies of adults only. Some of the studies also reported data for sub-groups based on age. In addition, prevalence for asymptomatic controls (N=4,036; range: 57 to 2,985) was reported in four studies (27-30).

Geographic region and country

A majority (N=42) of the 83 studies originated from Asia. Fourteen studies were conducted in Europe, of which three studies in Scandinavia: one in Norway (28), and two in Sweden (31;32). Eight studies were conducted in Africa. The remaining studies were from the other regions.

Most studies originated from China (N=23), followed by South Korea, Brazil (N=6), and USA (N=5). One to four studies provided data for the other countries (Table 1).

***Table 1**. Prevalence studies by geographic region and country (N=83)*

Geographic Area	No	Countries*
East Asia	N=31	**China (N=23)**: Cui 2015(33); Feng 2014(34); Hu 2014(35);Huang 2013(36); Huo 2012(37); Jin 2010(38); Jin 2012(39); Ju 2014(40); Li 2014 (41); Li 2019(42); Liao 2015(43); Liu 2014(44); Liu 2015(45); Liu 2019(46); Lu 2012(47); Ren 2011(48); Xin 2012(49); Ye 2017(50); Yip 2016(51); Yu 2012(52); Zeng 2018(53); Zhang 2018(54); Zhao 2019(55); **Japan**: Matoba 2015 (56); **South Korea (N=6)**: Choi 2006(57); Han 2007(58); Kim 2013(59); Kim 2018 (60); Lee 2013(61); Lee 2014 (62); **Taiwan**: Lee 2015(63)
South-East Asia	N=10	**Hong-Kong (N=4):** Chiu 2005(64); Leung 2009(65); Qu 2015(66); Sung 2009 (67); **Indonesia**: Prasetyo 2018(68); **Malaysia**: Al Khannaq 2016(69); **Thailand (N=3)**: Dare 2007(70); Soonnarong 2016 (71); Theamboonlers 2007(72); **Vietnam**: Do 2011(73)
South- Asia	N=1	**India (N=1)**: Sonawane 2019(74)
Middle East	N=6	**Kuwait:** Khadadah 2010 (75); **Quatar**: Al Romaihi 2020(76); **Saudi Arabia**: Al Hajjar 2011 (77); **Turkey (N=2)**: Goktas 2016 (78); Tuzuner 2016(79); **United Arab Emirates**: Jeon 2018 (80);
North America	N=5	**Canada** : Jean 2013(81); **USA (N=5)**: Fairchok 2010 (82); Killerby 2018(83); Talbot 2009 a(84); Talbot 2009 b(85)
South America	N=6	**Brazil (N=6)**: Cabeca 2013(86); Ferreira 2009(87); Goes 2019(88); Silva 2015 (89); Martins 2014(90); Matsuno 2019(91);
Africa	N=8	**Cameroon**: Kenmoe 2016(92); **Gabon**: Lekana-Douki 2014 (93); **Ghana (N=2)**: Berkley 2010(27); Owusu 2014(30); **Kenya (N=2)**: Kiuyka 2018(94); Sipulwa 2016(95); **South Africa (N=2)**: Nunes 2014 (96); Smuts 2008 (97)
Europe	N=14	**Belgium**: Moes 2012 (98); **Finland**: Paloniemi 2015(99); **France:** Lepiller 2013(100); **Germany**: Van der Hoek 2010(101); **Norway**: Heimdal 2019(28); **Slovenia (N=2)**: Jevsnik 2012(102); Jevsnik 2016(103); **Spain**: Cebey-Lopez 2015 (104); **Sweden(N=2)**: Brittain-Long 2012 (31); Koetz 2006 (32); **UK/Scotland (N=3)**: Gaunt 2010(105); Nickbakhsh 2016(106); Nickbakhsh 2020(107); **Mixed** (11 European countries): Jeven 2018(29)
Oceania	N=1	**Australia**: Lambert 2007(108)

*Number of studies given if >1 study provided data for a specific country.

World bank country classification (country income level)
Fifty-two studies were conducted in upper-middle income countries (UMIC), and 24 in high- income countries (HICs). Seven studies were from low- or lower-middle income countries (LMICs).

Setting
Seventy-five studies were conducted in hospitals, and a majority of these at single hospital sites. Eight studies were conducted in primary care/outpatient clinics.

Sample types and tests used for the analysis
The type of respiratory samples that most often were used in the included studies were nasopharyngeal swabs (NPS) (N=45). The remaining studies used a number of different sample types (e.g. throat swabs, nasal swabs, bronchoalveolar lavage, sputum, etc.). Polymerase chain reaction (i.e. RT-PCR, Multiplex PCR, and PAN-RCT) were in most studies used for the analysis.

Duration of studies
The median duration of included studies was 24 months (range: 12 to 294). All included studies had a duration of 12 months or more.

Prevalence of all HCoVs

Mean prevalence of all HCoV (all) by country and region

Norway and Vietnam had the third highest mean HCoV prevalence (about 9%) among the 24 countries (See Figure 1 in Appendix 3). The highest mean prevalence was found in Ghana (about 14%), and in France (about 11%), and the lowest (about 1%) in Hong Kong and Taiwan, although the estimate for Taiwan is quite imprecise (i.e., it has a wide CI). East and South-East Asia had, like in the main analysis, lower HCoV prevalence (around 3%), and African regions higher prevalence (6-14%). Also, South America and Europe had higher prevalence (around 6 %).

Prevalence of common HCoVs (all)

Geographic region

The prevalence (95%CI) of HCoVs varied across 10 geographic regions from 2% (2% to 4%; N=20) in the South-East Asian region to 14% (11% to 17%; N=1) in West Africa (Figure 2). The mean HCoV prevalence across regions was 4%, while in Europe it was 6% (N=11). Based on these results, average HCoV prevalence is unlikely to be above 10% during the period in which the studies were performed.

HCoV prevalence estimates tended to be lower in studies from Asia, especially in the East- and South-East Asian regions (range: 2% to 3%; N=79), and higher in studies from Africa (range: 6% to 14%; N=8) and South America (7%; 95% CI: 5%-10%; N=6), however some studies are imprecise and have wide confidence intervals. These findings are robust to sensitivity analyses in which we removed studies judged to be at high or potentially high risk of bias (Appendix 3, Figure 6).

Country income level

Estimates of mean HCoV (all) prevalence (95%CI) varied from 3% (95% CI 3% to 4%; N=78) in studies from lower middle-income countries (LMICs), to 8 % (95% CI 5% to 12%; N=8) in studies from middle-income countries (MICs). Mean prevalence was estimated to be lower in high income countries (HICs; 4%; 95% CI 3% to 6%; N=29) than in MICs (Figure 2). It should be noted that no studies from low-income countries (LICs) were included in the analysis.

Age group

Mean HCoV prevalence (95%CI) ranged from 3% (2% to 5%; N=34) in adults and older adults to 5% in infants (3% to 7%; N=11), and children (3% to 7%; N=14), with little or no difference between sub-groups (Figure 2). It is possible that mean HCoV prevalence is generally higher in children, but there was no statistically significant difference between age groups, so this apparent pattern may be misleading.

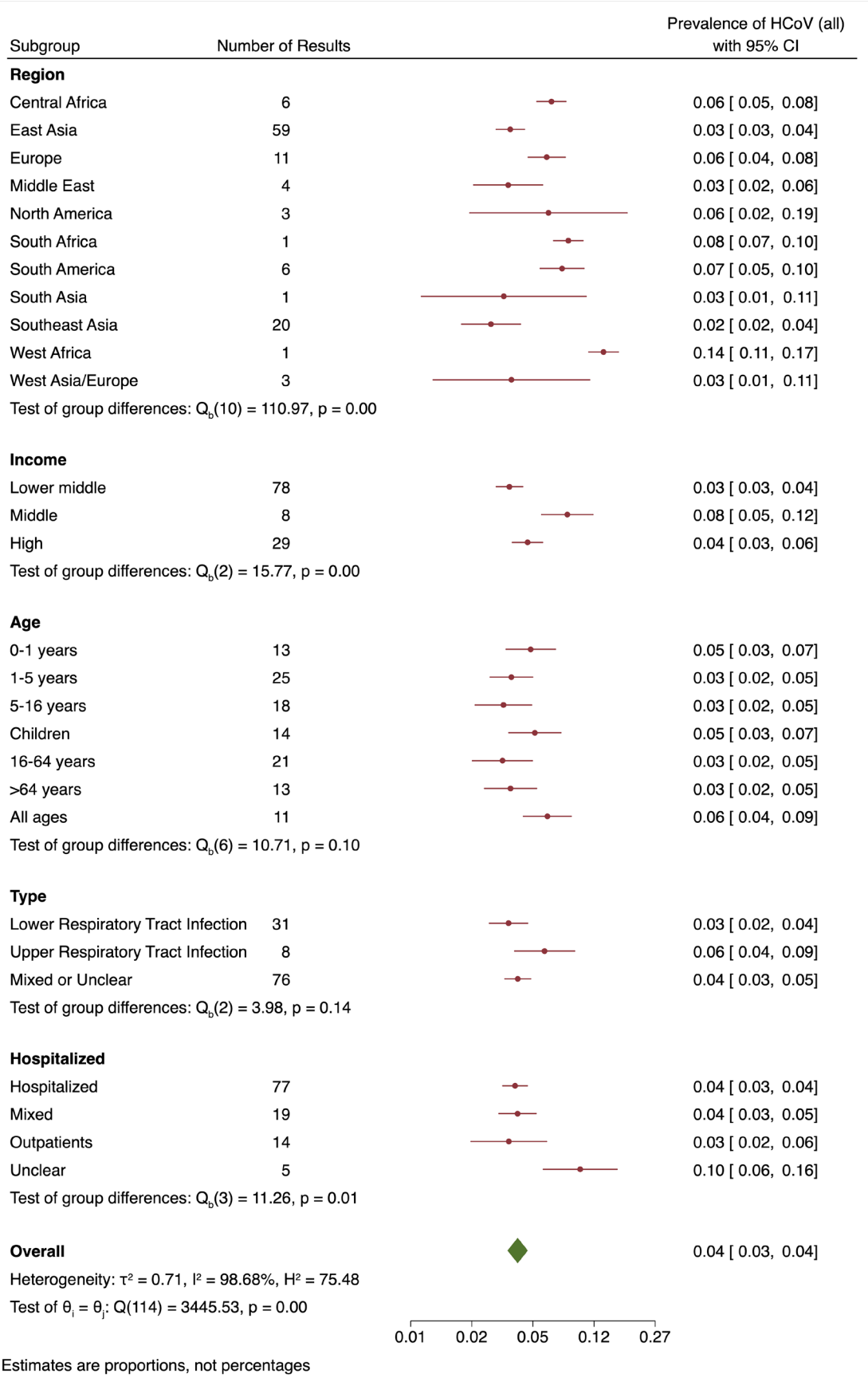
Type of RTI

Mean HCoV prevalence (95%CI) was estimated to be 3% in studies of lower respiratory tract infections (LRTI) (2% to 4%; N=31) and 6% (4% to 9%; N=8) in studies of upper RTIs (URTI) (i.e., we estimate that mean HCoV prevalence is likely higher in URTI compared to LRTI). However, RTI type was mixed or unclear in a majority of the included datasets (N=78).

Admission status

We estimate mean HCoV prevalence (95%CI) to be 3% (2% to 6%; N=14) in outpatients and 4% (3% to 4%; N=77) in patients admitted to hospital (Figure 2). Many studies, however, either reported results for mixed groups only (N=19) or did not report the admission status (N=5) of included patients.

***Figure 2**. Results for HCoV prevalence (as a group) by geographic region, country economy, age, type of RTI, and admission status*



Prevalence of individual HCoVs

Mean prevalence of individual HCoVs

Mean HCoV-229E prevalence was about 1% in most geographical regions. Three exceptions are East (N=2) and West Africa (N=8), which both had a mean prevalence of about 6%, and South America (N=3), which had a mean prevalence of about 3%. LICs had higher mean HCoV-229E prevalence (6%; 4% to 10%; N=2), than HICs (1%; 0% to 1%; N=18), but this trend was not consistent across all income levels. The pattern of mean HCoV-229E prevalence is plausibly similar to that for all HCoVs with respect to age group. There is little compelling evidence that mean HCoV-229E prevalence differs with respect to RTI type or admission status (Appendix 3, Figure 2).

Mean HCoV-NL63 prevalence ranged from 1% (in 7 of 13 regions) to 5% in West Africa (N=1). There was no clear association between mean prevalence and country income level, with estimates differing considerably across level. However, mean prevalence was highest in LICs (N=2) and lowest in HICs (N=18). Mean prevalence followed patterns similar to those for all HCoVs with respect to age group. There was no clear difference between URTI and LRTI. There was a tendency for mean prevalence to be higher in outpatients compared to patients admitted to hospital (Appendix 3, Figure 3).

Mean HCoV-OC43 prevalence ranged from 0% (0% to 3%; N=1) in North-East Asia to 4% (3% to 5%; N=1) in South Africa. There is little variation with respect to country income level, age group, RTI type, and admission status (Appendix 3, Figure 4).

Mean HCoV-HKU1 prevalence ranged from about 1% to 2% across geographic regions. Mean prevalence is plausibly similar across age groups, RTI types, and admission statuses (Appendix 3, Figure 5).

Mean prevalence of individual HCoVs by country and region

Mean HCoV-229E prevalence ranged from about 0% (in studies from Belgium, Hong Kong, Scotland, South Africa, and Sweden) to about 6% in studies from Ghana and Kenya. The regions with the highest HCoV-229E prevalence were East and West Africa (about 6%), and the region with the lowest prevalence was South Africa (about 1%), although as with the other estimates of HCoV prevalence, confidence intervals are wide and overlapping in many cases (Appendix 3, Figure 11).

Mean HCoV-NL63 prevalence ranged from about 1% in China (N=18) and 12 other countries, to about 5% in Ghana (N=1). Mean prevalence was estimated to be lowest in the East Asian region (about 1%; N=21) and highest (about 5%; N=1) in the West African region (Appendix 3, Figure 12).

Mean HCoV-OC43 prevalence ranged from about 1% in 12 of the 22 countries that provided data for HCoV-OC43 to about 4% in South Africa (N=1). Mean prevalence across regions also ranged from about 1% to 4 % (Appendix 3, Figure 13).

Mean HCoV-HKU1 prevalence was highest in France (about 4%; N=1) and Slovenia (about 3%; N=3), followed by South Africa, Japan, and Brazil (all about 2%). In 13 of the 18 countries with data on HCoV-HKU1 mean prevalence was about 1%. Mean prevalence varied between about 1% to 2% across 11 regions (Appendix 3, Figure 14).

Prevalence of HCoVs by age

There was a tendency for higher mean HCoV (all) prevalence in children (about 5%) than in adults (about 3%). For HCoV-229E, and HCoV-NL63, the prevalence was plausible similar to that of all HCoVs, i.e. a tendency to higher prevalence in children. For HCoV-OC43, and HCoV-HKU1 however, the prevalence was plausible similar across age groups. See Appendix 3, Figure 15 to 19 for details.

Prevalence of HCoVs by RTI type

There was a trend for higher mean HCoV (all) prevalence in URTI (about 6%) compared to LRTI (about 3%). For individual HCoVs however, there was little compelling evidence for a difference in prevalence between RTI types (HCoV-229E, and -NL63), and plausible similar prevalence across RTI types for HCoV-OC43 and-HKU1. See Appendix 3, Figure 20-24 for details.

Prevalence of HCoVs by country income level

Estimates did not show any consistent trends in mean HCoV (all) prevalence, or for individual HCoVs when analysed by country income level. See Appendix 3, Figure 25-29 for details.

Prevalence of HCoV infections over time

Estimates of mean prevalence for all and individual HCoVs appear relatively stable or perhaps slowly increasing with time, although the confidence bands are too wide to be sure. Estimates of mean prevalence prior to 2005 are less stable and characterized by much wider confidence intervals due to the paucity of data available. It appears that mean prevalence is likely to be about 5% between about January 2005 and January 2018. See Appendix 3, Figure 30-34 for details.

Relative HCoV prevalence: cases with RTI vs asymptomatic controls

HCoVs (all): Meta-analysis (MA) of three case-control studies ((109) infants 0-1 yrs; (29) 16-64 yrs; (30), all ages), which included a total of 7,165 cases and 3, 979 controls, estimated mean HCoV (all) prevalence to be 1.89 (95% CI 0.63 to 5.26) times higher in cases than controls. However, there was substantial heterogeneity (I^2=97.1%) that was driven by the data from the Ieven 2018 study (29), which estimated prevalence to be substantially *higher in cases* than did the other two studies. It may be of interest to know that this study included prevalence data from 11 different countries. Estimates from the other two studies are consistent with prevalence being *lower, the same, or higher in cases* than in controls (Appendix 3, Figure 35).

HCoV-229E: Meta-analysis of two studies ((27) children, (30) all ages), which included a total of 1,448 cases and 677 controls, estimate mean HCoV-229E prevalence to be 4.11(95% CI 2.09 to 8.09; I^2=0%) times *higher in cases* than controls (Appendix 3, Figure 36).

HCoV-HKU1: Data reported by Berkely 2010 (27) gives an estimate of the relative prevalence of HCoV-HKU1 that is plausibly *lower, the same, or higher in cases* than controls (relative prevalence 0.20; 95% CI 0.02 to 1.89). See Appendix 3, Figure 37 for details.

HCoV-NL63: Data reported by Owusu 2014 (30) gives an estimate of the relative prevalence of HCoV-NL63 that is *lower in cases* than controls (relative prevalence 0.59; 95% CI 0.38 to 0.91). See Appendix 3, Figure 38 for details.

HCoV-OC43: Meta-analysis of HCoV-OC43 prevalence data from two studies (27;30), including 1,448 cases and 677 controls, exhibited substantial heterogeneity (I^2=93.2%), with one study (27) reporting that prevalence is *lower in cases* (relative prevalence

0.27; 95% CI 0.09 to 0.77; children), and the other (30) that prevalence is *higher in cases* (relative prevalence 6.27; 95% CI 1.86 to 21.2; all ages), compared to controls (Appendix 3, Figure 39).

Co-detection of different HCoV strains

Fifteen studies reported on co-infections that involved two or more HCoV strains. The proportion of these co-infections of the total number of HCoV positive cases varied from median 0.3% for OC43+HKU1 to 2.1% for OC43+229E. Two of the 15 studies detected no co-infections between different HCoV strains (Table 2). See Appendix 4, and Table 2 for details.

***Table 2**. Number (%) co-infections between different HCoV strains*

Author Year	Samples tested	No (%) HCoV+	OC43+ 229E	OC43+ NL63	OC43+ HKU1	HKU1+ 229E	HKU1+ NL63	229E+ NL63
Al Khannaq 2015	2,060	48 (2.3)	-	-	-	-	-	-
Gaunt 2010	11,661	280 (2.4)	-	2 (0.7)	-	-	-	-
Heimdal 2019 (cases)	3,458	313 (9.1)	-	-	-	-	-	2(0.6)
Heimdal 2019 (controls)	38	38	-	-	-	-	-	1(2.6)
Hu 2014	559	70 (12.5) *OC43 only*	-	-	2 (2.8)	-	-	-
Jean 2013 (cases)	3,847	68 (1.7) *OC43 only*	-	-	-	-	-	-
Jean 2013 (controls)	136	136 *OC43 only*	-	-	-	-	-	-
Killerby 2018	20,806	1,538 (7.8)	8 (0.5);	8 (0.5):	4 (0.25)	-	5 (0.3);	3 (0.2)
Lepiller 2013	6,014	291(4.8)	-	-	-	1(0.34)	-	-
Liu 2014	4,242	231 (5.4)	5 (2.2)	2 (0.8)	-	-	1(0.4)	:2(0.8)
Liu 2019	445	36 (8.1)	-	-	: 5 (13.8)	-	-	-
Lu 2012*	981	157 (16.0)	3 (1.9)	-	-	-	-	1 (0.6) *+ OC43*
Nunes 2014	509	77(15.1)	-	1 (1.3)	-	-	1 (1.3)	-
Owusu 2014	1,213	150 (12.4)	3 (2.0)	-	-	-	-	:1(0.67)
Theamboonlers 2006	226	10 (4.4)	1(10.0)	-	-	-	-	-
Zeng 2018	11.399	489 (4.3)	15 (3.1)	2 (0.4)	1 (0.2)	-	1(0.2)	2 (0.4)
Zhang 2018 (79)	13,048	294 (2.2)	-	-	1(0.3)	-	-	-
Median (%)	2,060	8.6	2.1	0.7	0.3	0.34	0.35	0.6
Range (%):	38 to 20,806	2.2 to 16.0	0.5 to 10	0.4 to 1.3	0.2 to 13.8	0.34	0.2 to 1.3	0.2 to 2.6

*Double HCoV+ additional virus (with IFV A:5; hRSV:1; RV:2)

Co-detection of HCoVs and other respiratory viruses

Forty-two studies reported on HCoV co-infections (either any HCoV or a single HCoV strain) with other respiratory viruses. The frequency of these co-infections among HCoV positive cases varied across studies from 10% up to 89.7% (median 47%). Some of the most common co-infecting viruses were IFV, HRV, RSV, and PIV. It should be noted that the number and type of HCoV viruses, and other viruses assessed, varied somewhat across the included studies (Appendix 4).

Quality of included studies- results of the ROB-SPEO tool

For details on the ratings and judgements See Appendix 5. Briefly, 39 of the 83 included studies were judged to be at 'probably high' or 'high' risk of selection bias, and 35 studies were judged to be at 'probably high' or 'high' risk of numerator/denominator bias. Thirty-nine studies were at overall 'probably high risk' or 'high risk' of bias, and 44 studies were judged to be at 'probably low risk' or 'low risk' of bias. Sensitivity analyses removing studies with high risk of bias did not change the results (Appendix 3, Figures 6-10).

Discussion

Summary of main results

This rapid review on prevalence of common HCoVs, included 83 original studies, and in total 336,783 participants from 33 countries and 10 geographic regions. The quality of the included evidence was poor in around half of the included studies. The main results of the review show:

- A tendency to lower HCoV prevalence in the East and South-East Asian region, and possibly higher prevalence in African regions and South America
- A tendency to higher HCoV prevalence in children, as compared to adults and older adults
- No consistent trend for a relationship between HCoV prevalence and country income level
- Potentially higher HCoV prevalence in URTI than in LRTI
- No clear trend for a relationship between HCoV prevalence and admission status
- Relatively stable HCoV infection rate (~5%) from 2005 to 2018), possibly with a tendency to increasing prevalence over time
- No consistent trend for a relationship between HCoV prevalence and symptomatic disease or asymptomatic carriers
- Co-infections-between HCoV strains varied across studies and different combinations of co-infecting HCoV strains
- Co-infections between HCoVs and other viruses were common (around 47%)

It should be noted that results for HCoVs as a group were sometimes, but not always supported by the results for individual HCoVs, for which fewer studies provided data.

Overall completeness and applicability of the findings

None of the included studies provided any information on minority status or socioeconomic status (SES) of included participants (or any other social determinants of health). There is strong evidence from the literature for a relationship between minority status/low SES, and higher rate of respiratory tract infections, other infections, as well as an overall poorer health (17;18;110;111). Since none of the included studies provided comparative data for disadvantaged groups, we could not address equity aspects on HCoV prevalence in our review. However, collecting information on social determinants of health is crucial to find ways to address and mitigate inequities in health (112).

A majority of included studies only reported HCoVs as a group and did not provide separate data for individual HCoVs, which may have been useful in order to assess potential differences between strains, and between different genera. Due to the potential role of common beta-HCoVs in cross-protection, since they are more similar to SARS-CoV 2 (SARS CoV and MERS) than alpha-HCoVs, there is good reason for reporting results for individual HCoVs separately.

The information on RTI type, admission status, and study location (urban/rural) were also incomplete in many of the included studies, which may have affected our results

Very few studies were conducted in LICs, and due to the scarcity of data it was difficult to make a just comparison of HCoV prevalence in LICs with that of HICs.

Around half of the included studies used nasopharyngeal swabs for the PCR analysis, while the other half used various sample types (e.g. sputum, throat swabs, BAL). We could not identify any studies that reported on optimal sample types for analysis of common HCoVs using PCR. In any case, the different sample types used for analysis in the included studies may have affected the results of this review.

Quality of the evidence

Around 47% of included studies had a plausible risk of selection bias, due to for example no defined selection criteria, unclear exclusions, and not all eligible patients were tested. A little less, around 42% were judged to have a risk of numerator-denominator bias, mainly due to number of samples and number of patients not being the same. Sufficient information was typically lacking in order accurately judge the risk of bias, resulting in a judgement of 'probably high', especially if the reporting was poor throughout.

Strengths and limitations with this rapid review

Some limitations with this rapid review were the limited number of data bases searched, and that screening, data extraction, and quality assessment was not done in duplicate (and only two of the ROB-SPEO items were used in the assessment). The ROB-SPEO tool was in addition new to all reviewers, which may have affected our judgements.

The search was at publication of this review more than one year old and must thus be considered somewhat out of date. However, a simplified search conducted in March 2022 revealed that that during the course of the pandemic, focus of most publications have been on COVID-19-related issues, with few studies on the prevalence of common HCoVs been published since our previous search. We therefore believe that the results of this review stand fairly well.

Studies excluded after full text review were not screened for information on co-infections. The results for co-infections should therefore be interpreted with caution, since around 50 % of seemingly relevant studies ended up being excluded.

A strength of this review is the extensive statistical analyses, however, we applied heuristics to extracted descriptions of age groups to define subgroups and used Stata's default meta-analytical transform for proportions (logit) rather than the planned method, which may be seen as a limitation with the analysis. Another strength with this review, was the peer review by experts in the field from the Division for Infection Control and Environmental Health at NIPH. However, the review was not subjected to external peer review by experts not affiliated to NIPH.

Agreement and disagreements with other studies or reviews

Geographical region

Evidence from studies on different coronaviruses suggest that factors like low temperature and little sunlight favor survival of the virus (113), which in turn suggests lower prevalence in warmer regions, and higher prevalence in temperate climates. Our review showed a tendency for lower HCoV prevalence in East- and South-East Asia, where the climate is monsoonal and mostly tropical respectively, and a tendency to higher prevalence in some African regions with a tropical climate. There are however many co-variates (e.g. age, place of residence, poverty/SES, indoor air quality, smoking, crowded housing, underlying chronic diseases, air pollution, etc.) that may have an impact on the HCoV prevalence.

It may be noted that South-East Asia is one of the regions that have suffered most deaths during the COVID19 pandemic[1]), while the death toll in most regions in Africa has been comparatively low (114). It has however, been debated whether the low death rate due to COVID-19 may be due to the low age of the African population, and to underreporting[2]

Age

The results of our review indicate potentially (non-significant) higher HCoV prevalence in young children than in adults, and older adults (>65 years). Evidence from one systematic review (8), and one large original study (9) support our findings. However, the systematic review in question (8) included only 22 studies, and no meta-analysis, and the original study was retrospective with 80% of available children tested for common HCoVs, as compared to only 40% of available older patients.

[1] SEAR COVID-19 - Dashboard (arcgis.com)
[2] Morgue data hint at COVID's true toll in Africa (nature.com)

Results of one large (>74,000 samples) included study from Scotland (115) suggests different age incidence patterns of individual HCoVs, with higher HCoV-OC43 prevalence in children between 1-5 years old, and older adults (>65 years), higher HCoV-229E prevalence in adults (>18 years), and higher prevalence of HCoV-NL63 in infants (<1 years old). This can be compared with the results of a recent large (>55,000 samples) Swedish study, in which HCoV-NL63 and HCoV-HKU1prevalence showed a tendency to decline with age, while HCoV-229E and HCoV-OC43 were more similar across the age strata. These age incidence patterns for individual HCoVs were not supported by the overall findings of our review.

Country economy

We found no consistent trend for a relationship between HCoV prevalence and country economy in our review, but very few of the included studies were from LICs and most of them reported data for a single HCoV. We did not identify any systematic reviews, or original studies, that assessed this relationship that we could compare our results to.

Type of RTI infection

In many of the studies included in our review information on type of RTI was lacking, and it is possible that this lack of data may have affected our results. However, the results of our review, which suggest a plausible higher prevalence of HCoV infections in URTI, than in LRTI, are in line with what is reported in the literature (116).

Admission status

In many of the studies included in our review the admission status of participants was unclear, which may have affected our results. We could not identify any systematic reviews or that reported on the relationship between HCoV-prevalence and admission status. In the largest study included in this review (115) however, the results were pointing towards higher HCoV prevalence in out-patients than in patients admitted to hospital. Our results, however, could neither confirm nor refute these results.

Symptomatic and asymptomatic disease

Seasonal HCoVs have been detected in asymptomatic people i.e. people who carry the virus but do not show any signs of illness (116), but the evidence regarding the prevalence of asymptomatic HCoV infections is scarce. The results of the four included case-control studies were mixed, with typically wide CIs that included the point of no effect.

We did not identify any systematic review or original paper that reported on age-related prevalence of asymptomatic HCov infections. Results reported for SARS-CoV-2 suggest that clinical symptoms manifest in a larger proportion (~70%) of older cases (≥70 years), and only to a lesser extent (~20%) in younger cases (10 and 19 years of age) (20;117). However, since only single studies provided data for asymptomatic infants, children, adults and mixed age groups in our review. and no study of asymptomatic older people was included, we could not say whether this age-prevalence pattern for asymptomatic SARS-CoV-2 infections would apply also for common HCoVs.

Co-infections

The proportion of co-infections among HCoV strains varied across studies and different combinations of HCoVs, and so did also the proportion of co-infections with other viruses. A recent study from China reported somewhat lower prevalence of co-infections between HCoVs and other viruses (31.3% vs. 47% in our review), and the same study reported only a single HCoV-HCoV co-infection (118). Co-infections was in a Canadian study detected only in a small proportion of patients with seasonal respiratory viruses (4.3%), and in an even smaller proportion (2.5%) of individuals with laboratory confirmed SARS-CoV-2 (119).

Conclusion

The main results of this rapid review, which included 83 studies, suggest a mean HCoV prevalence of 4% across countries and regions. There was a tendency for lower prevalence in the East- and South-East Asian regions, and higher prevalence in most African regions and in the South Americas. Prevalence also tended to be higher in young children than in adults, and older adults, and higher in URTI than in LRTI, which is in accordance with what is previously reported in the literature. Common HCoV prevalence appear to be relatively stable over time.

Few studies reported data for LICs, and data on RTI type, admission status, and study location were in many studies unclear or lacking. None of the included studies reported on social determinants of health (e.g. minority status and SES), and therefore equity issues related to HCoV prevalence could not be addressed in this review. While around half of the included studies used nasopharyngeal swabs for the PCR analysis, there was great variation in sample types used across the other studies.

Future research in the area should aim to collect data on social determinants of health, to address the inequities in respiratory diseases and general health that exist today. Future studies should make sure to provide data on RTI type, admission status, and study location, as this data should be readily available in any settings. In addition, following guidelines on which sample types to use for the detection of HCoVs, could improve the robustness of data.

References

1. Owens, Flores, Di Serio F, Li S, Pallás V, Randles J, et al. Virus Taxonomy: Ninth Report of the International Committee on Taxonomy of Viruses. I: 2012. s. 1221-34.
2. Masters PS PS. Coronaviridae. I: Knipe DM HP, Cohen JI, et al (Eds),, red. Fields Virology, 6th ed,. Vol 2. Philadelphia Lippincott Williams & Wilkins, a Wolters Kluwer business; 2013.
3. Liu DX L, JQ, Fung TS,. Human Coronavirus-229E, -OC43, -NL63, and -HKU1 (Coronaviridae). Encyclopedia of Virology. 4th edition utg. China.
4. Zhu Z, Lian X, Su X, Wu W, Marraro GA, Zeng Y. From SARS and MERS to COVID-19: a brief summary and comparison of severe acute respiratory infections caused by three highly pathogenic human coronaviruses. Respiratory Research 2020;21(1):224.
5. Khan S, Siddique R, Bai Q, Shabana, Liu Y, Xue M, et al. Coronaviruses disease 2019 (COVID-19): Causative agent, mental health concerns, and potential management options. J Infect Public Health 2020;13(12):1840-4.
6. Yaqinuddin A. Cross-immunity between respiratory coronaviruses may limit COVID-19 fatalities. Med Hypotheses 2020;144:110049.
7. Rucinski SL, Binnicker MJ, Thomas AS, Patel R. Seasonality of Coronavirus 229E, HKU1, NL63, and OC43 From 2014 to 2020. Mayo Clin Proc 2020;95(8):1701-3.
8. Park S, Lee Y, Michelow IC, Choe YJ. Global Seasonality of Human Coronaviruses: A Systematic Review. Open Forum Infectious Diseases 2020;7(11).
9. Dyrdak R, Hodcroft EB, Wahlund M, Neher RA, Albert J. Interactions between seasonal human coronaviruses and implications for the SARS-CoV-2 pandemic: A retrospective study in Stockholm, Sweden, 2009-2020. Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology 2021;136:104754-.
10. Brodin P. SARS-CoV-2 infections in children: Understanding diverse outcomes. Immunity 2022;55(2):201-9.
11. Saletti G, Gerlach T, Jansen JM, Molle A, Elbahesh H, Ludlow M, et al. Older adults lack SARS CoV-2 cross-reactive T lymphocytes directed to human coronaviruses OC43 and NL63. Scientific Reports 2020;10(1):21447.
12. Copat C, Cristaldi A, Fiore M, Grasso A, Zuccarello P, Signorelli SS, et al. The role of air pollution (PM and NO(2)) in COVID-19 spread and lethality: A systematic review. Environ Res 2020;191:110129.
13. Travaglio M, Yu Y, Popovic R, Selley L, Leal NS, Martins LM. Links between air pollution and COVID-19 in England. Environ Pollut 2021;268(Pt A):115859.
14. Veronesi G, De Matteis S, Calori G, Pepe N, Ferrario MM. Long-term exposure to air pollution and COVID-19 incidence: a prospective study of residents in the city of Varese, Northern Italy. Occupational and Environmental Medicine 2022;79(3):192-9.
15. Bourdrel T, Annesi-Maesano I, Alahmad B, Maesano CN, Bind M-A. The impact of outdoor air pollution on COVID-19: a review of evidence from in vitro, animal, and human studies. European Respiratory Review 2021;30(159):200242.

16. WHO. Ambient (outdoor) air pollution[lest].
17. Hajat A, Hsia C, O'Neill MS. Socioeconomic Disparities and Air Pollution Exposure: a Global Review. Curr Environ Health Rep 2015;2(4):440-50.
18. Jbaily A, Zhou X, Liu J, Lee T-H, Kamareddine L, Verguet S, et al. Air pollution exposure disparities across US population and income groups. Nature 2022;601(7892):228-33.
19. WHO. Household air pollution and health[lest].
20. Davies NG, Klepac P, Liu Y, Prem K, Jit M, Pearson CAB, et al. Age-dependent effects in the transmission and control of COVID-19 epidemics. Nature Medicine 2020;26(8):1205-11.
21. Tricco AC, Antony J, Zarin W, Strifler L, Ghassemi M, Ivory J, et al. A scoping review of rapid review methods. BMC Medicine 2015;13(1):224.
22. Johanna Briggs Institute J. Chapter 5: Systematic reviews of prevalence and incidence. I: Aromataris E MZE, red. JBI Manual for Evidence Synthesis JBI, 2020 Available from https://synthesismanualjbiglobal https://doiorg/1046658/JBIMES-20-01. USA: Johanna Briggs Institute; 2020.
23. Pega F, Norris SL, Backes C, Bero LA, Descatha A, Gagliardi D, et al. RoB-SPEO: A tool for assessing risk of bias in studies estimating the prevalence of exposure to occupational risk factors from the WHO/ILO Joint Estimates of the Work-related Burden of Disease and Injury. Environ Int 2020;135:105039-.
24. Cochrane collaboration. Chapter 10: Analysing data and undertaking meta-analyses. I: Higgins JPT TJ, Chandler J, Cumpston M, Li T, Page MJ, Welch VA red. Cochrane Handbook for Systematic Reviews of Interventions: Cochrane Collaboration; 2022.
25. World Bank. World Bank Country Classiciation[lest accessed in September 2020 at https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups].
26. Page MJ, McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. PLOS Medicine, 18(3), https://doiorg/101371/journalpmed1003583 2021;18(3):e1003583.
27. Berkley JA, Munywoki P, Ngama M, Kazungu S, Abwao J, Bett A, et al. Viral etiology of severe pneumonia among Kenyan infants and children. JAMA 2010;303(20):2051-7.
28. Heimdal I, Moe N, Krokstad S, Christensen A, Skanke LH, Nordbo SA, et al. Human Coronavirus in Hospitalized Children With Respiratory Tract Infections: A 9-Year Population-Based Study From Norway. J Infect Dis 2019;219(8):1198-206.
29. Ieven M, Coenen S, Loens K, Lammens C, Coenjaerts F, Vanderstraeten A, et al. Aetiology of lower respiratory tract infection in adults in primary care: a prospective study in 11 European countries. Clin Microbiol Infect 2018;24(11):1158-63.
30. Owusu M, Annan A, Corman VM, Larbi R, Anti P, Drexler JF, et al. Human coronaviruses associated with upper respiratory tract infections in three rural areas of Ghana. PLoS ONE [Electronic Resource] 2014;9(7):e99782.
31. Brittain-Long R, Andersson LM, Olofsson S, Lindh M, Westin J. Seasonal variations of 15 respiratory agents illustrated by the application of a multiplex polymerase chain reaction assay. Scand J Infect Dis 2012;44(1):9-17.
32. Koetz A, Nilsson P, Linden M, van der Hoek L, Ripa T. Detection of human coronavirus NL63, human metapneumovirus and respiratory syncytial virus in children with respiratory tract infections in south-west Sweden. Clin Microbiol Infect 2006;12(11):1089-96.
33. Cui B, Zhang D, Pan H, Zhang F, Farrar J, Law F, et al. Viral aetiology of acute respiratory infections among children and associated meteorological factors in southern China. BMC Infect Dis 2015;15:124.

34. Feng L, Li Z, Zhao S, Nair H, Lai S, Xu W, et al. Viral etiologies of hospitalized acute lower respiratory infection patients in China, 2009-2013. PLoS One 2014;9 (6) (no pagination)(e99419).
35. Hu Q, Lu R, Peng K, Duan X, Wang Y, Zhao Y, et al. Prevalence and genetic diversity analysis of human coronavirus OC43 among adult patients with acute respiratory infections in Beijing, 2012. PLoS ONE [Electronic Resource] 2014;9(7):e100781.
36. Huang G, Yu D, Mao N, Zhu Z, Zhang H, Jiang Z, et al. Viral etiology of acute respiratory infection in Gansu Province, China, 2011. PLoS ONE [Electronic Resource] 2013;8(5):e64254.
37. Huo X, Qin Y, Qi X, Zu R, Tang F, Li L, et al. Surveillance of 16 respiratory viruses in patients with influenza-like illness in Nanjing, China. J Med Virol 2012;84(12):1980-4.
38. Jin Y, Song JR, Xie ZP, Gao HC, Yuan XH, Xu ZQ, et al. Prevalence and clinical characteristics of human CoV-HKU1 in children with acute respiratory tract infections in China. J Clin Virol 2010;49(2):126-30.
39. Jin Y, Zhang RF, Xie ZP, Gao HC, Yan KL, Yuan XH, et al. [The detection and clinical feature of HcoV-nL63 in children with acute respiratory tract infection in Lanzhou city]. Chung Hua Shih Yen Ho Lin Chuang Ping Tu Hsueh 2012;26(6):409-11.
40. Ju X, Fang Q, Zhang J, Xu A, Liang L, Ke C. Viral etiology of influenza-like illnesses in Huizhou, China, from 2011 to 2013. Arch Virol 2014;159(8):2003-10.
41. Li Y, Han GY, Liu YF, Liu LF, Li Q, Qi SX. [Detection of respiratory viruses in influenza-like illness in Shijiazhuang, China in 2011]. Bingdu Xuebao 2014;30(4):391-5.
42. Li YT, Liang Y, Ling YS, Duan MQ, Pan L, Chen ZG. The spectrum of viral pathogens in children with severe acute lower respiratory tract infection: A 3-year prospective study in the pediatric intensive care unit. J Med Virol 2019;91(9):1633-42.
43. Liao X, Hu Z, Liu W, Lu Y, Chen D, Chen M, et al. New Epidemiological and Clinical Signatures of 18 Pathogens from Respiratory Tract Infections Based on a 5-Year Study. PLoS ONE [Electronic Resource] 2015;10(9):e0138684.
44. Liu WK, Liu Q, Chen DH, Liang HX, Chen XK, Chen MX, et al. Epidemiology of acute respiratory infections in children in Guangzhou: a three-year study. PLoS ONE [Electronic Resource] 2014;9(5):e96674.
45. Liu T, Li Z, Zhang S, Song S, Julong W, Lin Y, et al. Viral Etiology of acute respiratory tract infections in hospitalized children and adults in Shandong Province, China. Virol J 2015;12:168.
46. Liu GS, Li H, Zhao SC, Lu RJ, Niu PH, Tan WJ. Viral and Bacterial Etiology of Acute Febrile Respiratory Syndrome among Patients in Qinghai, China. Biomed Environ Sci 2019;32(6):438-45.
47. Lu R, Yu X, Wang W, Duan X, Zhang L, Zhou W, et al. Characterization of human coronavirus etiology in Chinese adults with acute upper respiratory tract infection by real-time RT-PCR assays. PLoS ONE [Electronic Resource] 2012;7(6):e38638.
48. Ren L, Gonzalez R, Xu J, Xiao Y, Li Y, Zhou H, et al. Prevalence of human coronaviruses in adults with acute respiratory tract infections in Beijing, China. J Med Virol 2011;83(2):291-7.
49. Xin C, Yong ZZ, Yan L, Dong ZX. Human coronavirus NL63 in hospitalized children with respiratory infection: a 2-year study from Chongqing, China. Indian Pediatr 2012;49(10):825-8.
50. Ye C, Zhu W, Yu J, Li Z, Fu Y, Lan Y, et al. Viral pathogens among elderly people with acute respiratory infections in Shanghai, China: Preliminary results from a laboratory-based surveillance, 2012-2015. J Med Virol 2017;89(10):1700-6.
51. Yip CC, Lam CS, Luk HK, Wong EY, Lee RA, So LY, et al. A six-year descriptive epidemiological study of human coronavirus infections in hospitalized patients in Hong Kong. Virol Sin 2016;31(1):41-8.

52. Yu X, Lu R, Wang Z, Zhu N, Wang W, Julian D, et al. Etiology and clinical characterization of respiratory virus infections in adult patients attending an emergency department in beijing. PLoS One 2012;7 (2) (no pagination)(e32174).
53. Zeng ZQ, Chen DH, Tan WP, Qiu SY, Xu D, Liang HX, et al. Epidemiology and clinical characteristics of human coronaviruses OC43, 229E, NL63, and HKU1: a study of hospitalized children with acute respiratory tract infection in Guangzhou, China. Eur J Clin Microbiol Infect Dis 2018;37(2):363-9.
54. Zhang SF, Tuo JL, Huang XB, Zhu X, Zhang DM, Zhou K, et al. Epidemiology characteristics of human coronaviruses in patients with respiratory infection symptoms and phylogenetic analysis of HCoV-OC43 during 2010-2015 in Guangzhou. PLoS ONE [Electronic Resource] 2018;13(1):e0191789.
55. Zhao Y, Lu R, Shen J, Xie Z, Liu G, Tan W. Comparison of viral and epidemiological profiles of hospitalized children with severe acute respiratory infection in Beijing and Shanghai, China. BMC Infect Dis 2019;19(1):729.
56. Matoba Y, Abiko C, Ikeda T, Aoki Y, Suzuki Y, Yahagi K, et al. Detection of the human coronavirus 229E, HKU1, NL63, and OC43 between 2010 and 2013 in Yamagata, Japan. Jpn J Infect Dis 2015;68(2):138-41.
57. Choi EH, Lee HJ, Kim SJ, Eun BW, Kim NH, Lee JA, et al. The association of newly identified respiratory viruses with lower respiratory tract infections in Korean children, 2000-2005. Clin Infect Dis 2006;43(5):585-92.
58. Han TH, Chung JY, Kim SW, Hwang ES. Human Coronavirus-NL63 infections in Korean children, 2004-2006. J Clin Virol 2007;38(1):27-31.
59. Kim JK, Jeon JS, Kim JW, Rheem I. Epidemiology of respiratory viral infection using multiplex rt-PCR in Cheonan, Korea (2006-2010). J Microbiol Biotechnol 2013;23(2):267-73.
60. Kim JM, Jung HD, Cheong HM, Lee A, Lee NJ, Chu H, et al. Nation-wide surveillance of human acute respiratory virus infections between 2013 and 2015 in Korea. J Med Virol 2018;90(7):1177-83.
61. Lee WJ, Chung YS, Yoon HS, Kang C, Kim K. Prevalence and molecular epidemiology of human coronavirus HKU1 in patients with acute respiratory illness. J Med Virol 2013;85(2):309-14.
62. Lee J, Storch GA. Characterization of human coronavirus OC43 and human coronavirus NL63 infections among hospitalized children <5 years of age. Pediatr Infect Dis J 2014;33(8):814-20.
63. Lee CY, Chang YF, Lee CL, Wu MC, Ho CL, Chang YC, et al. Molecular viral epidemiology and clinical characterization of acute febrile respiratory infections in hospitalized children in Taiwan. J Med Virol 2015;87(11):1860-6.
64. Chiu SS, Chan KH, Chu KW, Kwan SW, Guan Y, Poon LL, et al. Human coronavirus NL63 infection and other coronavirus infections in children hospitalized with acute respiratory disease in Hong Kong, China. Clin Infect Dis 2005;40(12):1721-9.
65. Leung TF, Li CY, Lam WY, Wong GW, Cheuk E, Ip M, et al. Epidemiology and clinical presentations of human coronavirus NL63 infections in hong kong children. J Clin Microbiol 2009;47(11):3486-92.
66. Qu JX, Gu L, Pu ZH, Yu XM, Liu YM, Li R, et al. Viral etiology of community-acquired pneumonia among adolescents and adults with mild or moderate severity and its relation to age and severity. BMC Infect Dis 2015;15:89.
67. Sung RY, Chan PK, Tsen T, Li AM, Lam WY, Yeung AC, et al. Identification of viral and atypical bacterial pathogens in children hospitalized with acute respiratory infections in Hong Kong by multiplex PCR assays. J Med Virol 2009;81(1):153-9.
68. Prasetyo AA, Desyardi MN, Tanamas J, Suradi, Reviono, Harsini, et al. Respiratory viruses and torque teno virus in adults with acute respiratory infections. Intervirology 2015;58(1):57-68.
69. Al-Khannaq MN, Ng KT, Oong XY, Pang YK, Takebe Y, Chook JB, et al. Molecular epidemiology and evolutionary histories of human coronavirus OC43 and HKU1

among patients with upper respiratory tract infections in Kuala Lumpur, Malaysia. Virol J 2016;13:33.
70. Dare RK, Fry AM, Chittaganpitch M, Sawanpanyalert P, Olsen SJ, Erdman DD. Human coronavirus infections in rural Thailand: a comprehensive study using real-time reverse-transcription polymerase chain reaction assays. J Infect Dis 2007;196(9):1321-8.
71. Soonnarong R, Thongpan I, Payungporn S, Vuthitanachot C, Vuthitanachot V, Vichiwattana P, et al. Molecular epidemiology and characterization of human coronavirus in Thailand, 2012-2013. Springerplus 2016;5(1):1420.
72. Theamboonlers A, Samransamruajkit R, Thongme C, Amonsin A, Chongsrisawat V, Poovorawan Y. Human coronavirus infection among children with acute lower respiratory tract infection in Thailand. Intervirology 2007;50(2):71-7.
73. Do AH, van Doorn HR, Nghiem MN, Bryant JE, Hoang TH, Do QH, et al. Viral etiologies of acute respiratory infections among hospitalized Vietnamese children in Ho Chi Minh City, 2004-2008. PLoS ONE [Electronic Resource] 2011;6(3):e18176.
74. Sonawane AA, Shastri J, Bavdekar SB. Respiratory Pathogens in Infants Diagnosed with Acute Lower Respiratory Tract Infection in a Tertiary Care Hospital of Western India Using Multiplex Real Time PCR. Indian J Pediatr 2019;86(5):433-8.
75. Khadadah M, Essa S, Higazi Z, Behbehani N, Al-Nakib W. Respiratory syncytial virus and human rhinoviruses are the major causes of severe lower respiratory tract infections in Kuwait. J Med Virol 2010;82(8):1462-7.
76. Al-Romaihi HE, Smatti MK, Al-Khatib HA, Coyle PV, Ganesan N, Nadeem S, et al. Molecular epidemiology of influenza, RSV, and other respiratory infections among children in Qatar: A six years report (2012-2017). Int J Infect Dis 2020;95:133-41.
77. Al Hajjar S, Al Thawadi S, Al Seraihi A, Al Muhsen S, Imambaccus H. Human metapneumovirus and human coronavirus infection and pathogenicity in Saudi children hospitalized with acute respiratory illness. Ann Saudi Med 2011;31(5):523-7.
78. Goktas S, Sirin MC. Prevalence and Seasonal Distribution of Respiratory Viruses During the 2014 - 2015 Season in Istanbul. Jundishapur j 2016;9(9):e39132.
79. Tuzuner U, Akkaya O, Ozdemir M, Kurtoglu MG. Prevalence and Concomitancy of Respiratory Viruses in Children with Acute Respiratory Tract Infections. Journal of Pediatric Infectious Diseases 2016;11(1):1-5.
80. Jeon JH, Han M, Chang HE, Park SS, Lee JW, Ahn YJ, et al. Incidence and seasonality of respiratory viruses causing acute respiratory infections in the Northern United Arab Emirates. J Med Virol 2019;91(8):1378-84.
81. Jean A, Quach C, Yung A, Semret M. Severity and outcome associated with human coronavirus OC43 infections among children. Pediatr Infect Dis J 2013;32(4):325-9.
82. Fairchok MP, Martin ET, Chambers S, Kuypers J, Behrens M, Braun LE, et al. Epidemiology of viral respiratory tract infections in a prospective cohort of infants and toddlers attending daycare. J Clin Virol 2010;49(1):16-20.
83. Killerby ME, Biggs HM, Haynes A, Dahl RM, Mustaquim D, Gerber SI, et al. Human coronavirus circulation in the United States 2014-2017. J Clin Virol 2018;101:52-6.
84. Talbot HK, Crowe JE, Jr., Edwards KM, Griffin MR, Zhu Y, Weinberg GA, et al. Coronavirus infection and hospitalizations for acute respiratory illness in young children. J Med Virol 2009;81(5):853-6.
85. Talbot HK, Shepherd BE, Crowe JE, Jr., Griffin MR, Edwards KM, Podsiad AB, et al. The pediatric burden of human coronaviruses evaluated for twenty years. Pediatr Infect Dis J 2009;28(8):682-7.
86. Cabeca TK, Passos AM, Granato C, Bellei N. Human coronavirus ocurrence in different populations of Sao Paulo: A comprehensive nine-year study using a pancoronavirus RT-PCR assay. Braz J Microbiol 2013;44(1):335-9.

87. Ferreira H, Costa KLP, Cariolano MS, Oliveira GS, Felipe KKP, Silva ESA, et al. High incidence of rhinovirus infection in children with community-acquired pneumonia from a city in the Brazilian pre-Amazon region. J Med Virol 2019;91(10):1751-8.
88. Goes LGB, Zerbinati RM, Tateno AF, de Souza AV, Ebach F, Corman VM, et al. Typical epidemiology of respiratory virus infections in a Brazilian slum. J Med Virol 2019;26:26.
89. Silva RC, Mendes Gda S, Rojas MA, Amorim AR, Couceiro JN, Lupi O, et al. Frequency of viral etiology in symptomatic adult upper respiratory tract infections. Braz J Infect Dis 2015;19(1):30-5.
90. Martins Junior RB, Carney S, Goldemberg D, Bonine L, Spano LC, Siqueira M, et al. Detection of respiratory viruses by real-time polymerase chain reaction in outpatients with acute respiratory infection. Mem Inst Oswaldo Cruz 2014;109(6):716-21.
91. Matsuno AK, Gagliardi TB, Paula FE, Luna LKS, Jesus BLS, Stein RT, et al. Human coronavirus alone or in co-infection with rhinovirus C is a risk factor for severe respiratory disease and admission to the pediatric intensive care unit: A one-year study in Southeast Brazil. PLoS ONE [Electronic Resource] 2019;14(6):e0217744.
92. Kenmoe S, Tchendjou P, Vernet MA, Moyo-Tetang S, Mossus T, Njankouo-Ripa M, et al. Viral etiology of severe acute respiratory infections in hospitalized children in Cameroon, 2011-2013. Influenza Other Respi Viruses 2016;10(5):386-93.
93. Lekana-Douki SE, Nkoghe D, Drosten C, Ngoungou EB, Drexler JF, Leroy EM. Viral etiology and seasonality of influenza-like illness in Gabon, March 2010 to June 2011. BMC Infect Dis 2014;14:373.
94. Kiyuka PK, Agoti CN, Munywoki PK, Njeru R, Bett A, Otieno JR, et al. Human Coronavirus NL63 Molecular Epidemiology and Evolutionary Patterns in Rural Coastal Kenya. J Infect Dis 2018;217(11):1728-39.
95. Sipulwa LA, Ongus JR, Coldren RL, Bulimo WD. Molecular characterization of human coronaviruses and their circulation dynamics in Kenya, 2009-2012. Virol J 2016;13:18.
96. Nunes MC, Kuschner Z, Rabede Z, Madimabe R, Van Niekerk N, Moloi J, et al. Clinical epidemiology of bocavirus, rhinovirus, two polyomaviruses and four coronaviruses in HIV-infected and HIV-uninfected South African children. PLoS ONE [Electronic Resource] 2014;9(2):e86448.
97. Smuts H. Human coronavirus NL63 infections in infants hospitalised with acute respiratory tract infections in South Africa. Influenza Other Respi Viruses 2008;2(4):135-8.
98. Moes E, Vijgen L, Keyaerts E, Zlateva K, Li S, Maes P, et al. A novel pancoronavirus RT-PCR assay: frequent detection of human coronavirus NL63 in children hospitalized with respiratory tract infections in Belgium. BMC Infect Dis 2005;5:6.
99. Paloniemi M, Lappalainen S, Vesikari T. Commonly circulating human coronaviruses do not have a significant role in the etiology of gastrointestinal infections in hospitalized children. J Clin Virol 2015;62:114-7.
100. Lepiller Q, Barth H, Lefebvre F, Herbrecht R, Lutz P, Kessler R, et al. High incidence but low burden of coronaviruses and preferential associations between respiratory viruses. J Clin Microbiol 2013;51(9):3039-46.
101. van der Hoek L, Ihorst G, Sure K, Vabret A, Dijkman R, de Vries M, et al. Burden of disease due to human coronavirus NL63 infections and periodicity of infection. J Clin Virol 2010;48(2):104-8.
102. Jevsnik M, Ursic T, Zigon N, Lusa L, Krivec U, Petrovec M. Coronavirus infections in hospitalized pediatric patients with acute respiratory tract disease. BMC Infect Dis 2012;12:365.
103. Jevsnik M, Steyer A, Pokorn M, Mrvic T, Grosek S, Strle F, et al. The Role of Human Coronaviruses in Children Hospitalized for Acute Bronchiolitis, Acute Gastroenteritis, and Febrile Seizures: A 2-Year Prospective Study. PLoS ONE [Electronic Resource] 2016;11(5):e0155555.

104. Cebey-Lopez M, Herberg J, Pardo-Seco J, Gomez-Carballa A, Martinon-Torres N, Salas A, et al. Viral co-infections in pediatric patients hospitalized with lower tract acute respiratory infections. PLoS One 2015;10 (9) (no pagination)(e0136526).
105. Gaunt ER, Hardie A, Claas EC, Simmonds P, Templeton KE. Epidemiology and clinical presentations of the four human coronaviruses 229E, HKU1, NL63, and OC43 detected over 3 years using a novel multiplex real-time PCR method. J Clin Microbiol 2010;48(8):2940-7.
106. Nickbakhsh S, Thorburn F, B VONW, Mc MJ, Gunson RN, Murcia PR. Extensive multiplex PCR diagnostics reveal new insights into the epidemiology of viral respiratory infections. Epidemiol Infect 2016;144(10):2064-76.
107. Nickbakhsh S, Ho A, Marques DFP, McMenamin J, Gunson RN, Murcia PR. Epidemiology of Seasonal Coronaviruses: Establishing the Context for the Emergence of Coronavirus Disease 2019. J Infect Dis 2020;222(1):17-25.
108. Lambert SB, Allen KM, Druce JD, Birch CJ, Mackay IM, Carlin JB, et al. Community epidemiology of human metapneumovirus, human coronavirus NL63, and other respiratory viruses in healthy preschool-aged children using parent-collected specimens. Pediatrics 2007;120(4):e929-37.
109. Heimdal I, Valand J, Krokstad S, Moe N, Christensen A, Risnes K, et al. Hospitalized Children With Common Human Coronavirus Clinical Impact of Codetected Respiratory Syncytial Virus and Rhinovirus. Pediatr Infect Dis J 2022;41(3):e95-e101.
110. WHO. WHO. Ambient (outdoor) air pollution[WHO [lest].
111. WHO. Household air pollution and health: WHO [lest].
112. Biermann O, Mwoka M, Ettman CK, Abdalla SM, Shawky S, Ambuko J, et al. Data, Social Determinants, and Better Decision-making for Health: the 3-D Commission. Journal of Urban Health 2021;98(1):4-14.
113. Nichols GL, Gillingham EL, Macintyre HL, Vardoulakis S, Hajat S, Sarran CE, et al. Coronavirus seasonality, respiratory infections and weather. BMC Infectious Diseases 2021;21(1):1101.
114. Osei SA, Biney RP, Anning AS, Nortey LN, Ghartey-Kwansah G. Low incidence of COVID-19 case severity and mortality in Africa; Could malaria co-infection provide the missing link? BMC Infectious Diseases 2022;22(1):78.
115. Nickbakhsh S, Ho A, Marques DFP, McMenamin J, Gunson RN, Murcia PR. Epidemiology of Seasonal Coronaviruses: Establishing the Context for the Emergence of Coronavirus Disease 2019. The Journal of infectious diseases 2020;222(1):17-25.
116. Liu DX, Liang JQ, Fung TS. Human Coronavirus-229E, -OC43, -NL63, and -HKU1 (Coronaviridae). Encyclopedia of Virology 2021:428-40.
117. Sah P, Fitzpatrick MC, Zimmer CF, Abdollahi E, Juden-Kelly L, Moghadas SM, et al. Asymptomatic SARS-CoV-2 infection: A systematic review and meta-analysis. Proceedings of the National Academy of Sciences 2021;118(34):e2109229118.
118. Kong D, Zheng Y, Hu L, Chen J, Wu H, Teng Z, et al. Epidemiological and co-infection characteristics of common human coronaviruses in Shanghai, 2015-2020: a retrospective observational study. Emerging microbes & infections 2021;10(1):1660-8.
119. Peci A, Tran V, Guthrie JL, Li Y, Nelson P, Schwartz KL, et al. Prevalence of Co-Infections with Respiratory Viruses in Individuals Investigated for SARS-CoV-2 in Ontario, Canada. Viruses 2021;13(1):130.

Appendices

Appendix 1. Glossary

Ambient air	Is atmospheric air in its natural state, and what we breathe when the atmosphere is not contaminated by airborne pollutants
Asymptomatic	Is when a person is infected with a disease (or develops a disease; diagnosed) but fails to display any noticeable symptoms
Broncoalveolar lavage (BAL)	Also known as bronchoalveolar washing, is a method performed to diagnose pathogenic infections of the lower respiratory airways, in which a bronchoscope is passed through the mouth or nose into an appropriate airway in the lungs, with a measured amount of fluid introduced and then collected for examination
Co-infection	Is the simultaneous infection of a host by multiple pathogen species
Common human corona virus (cHCoV)	Also seasonal HCoVs, or endemic HCoVs, consist of four viruses (HCoV-229E, -HKU1, -NL63, OC43), which typically results in less severe disease
Corona virus	Any of a family (*Coronaviridae*) of large single-stranded RNA viruses that have a lipid envelope studded with club-shaped spike proteins, infect birds and many mammals including humans, and include the causative agents of MERS, SARS, and COVID-19
Country classification by income level	The World Bank assigns the world's economies to four income groups—low, lower-middle, upper-middle, and high-income countries; the classifications are based on GNI per capita in current USD of the previous year (i.e. 2021 in this case)
Cross-reactivity	Is the extent to which different antigens appear similar to the immune system (in a general sense, cross-reactivity is the reactivity of an observed agent which initiates reactions outside the main reaction expected)
Cross-protection	is a type of induced resistance against viruses. Its basis is that prior infection with one virus affords protection against closely related ones

Denominator	Is the bottom number in a fraction that shows the number of equal parts an item is divided into; the divisor of a fraction.
Endemic	A pathogen or disease that is regularly found among particular people or in a certain area
Genus	A principal taxonomic category that ranks above species and below family, and is denoted by a capitalized Latin name, e.g. *Alpha*
Heterogeneity	Is the quality or state of consisting of dissimilar or diverse elements (e.g. different populations)
Human corona-virus (HCoVs)	Are the types of coronaviruses that are known to infect humans (HCoV-229E, -HKU1, -NL63, OC43, MERS, SARS CoV1 and SARS-CoV2)
Immune response	Is a reaction which occurs within an organism for the purpose of defending against foreign invaders (i.e. microorganisms like viruses, bacteria, parasites, and fungi)
Inpatient	A person who stays one or more nights in a hospital in order to receive medical care
Lower respiratory tract infection (LRTI)	An infection that affects the airways (below the level of the larynx), including the trachea and the alveolar sacs
Meta-analysis (MA)	Is a statistical analysis that combines the results of multiple scientific studies that can be performed when there are multiple studies addressing the same question
Minority	Is a group of people of the same race, culture, or religion who live in a place where most of the people around them are of a different race, culture, or religion
Multiplex Polymerase chain reaction	Multiplex PCR, a method in which two or more primer sets designed for amplification of different targets are included in the same reaction mixture
Nasal aspiration	A sample is taken by inserting a small tube into the nostril, and through the use of a suction device, remove (aspirate) secretions from the nose
Nasal swab	Is a test that checks for viruses and bacteria that cause respiratory infections. It may be taken from (I) Front part of the nostrils (anterior nares); (ii) Back of the nostrils, in a procedure known as nasal mid-turbinate (NMT) swab, or (iii) from the nasopharynx (i.e. the uppermost part of the nose and throat)
Nasopharyngeal swab	As (iii) above
Numerator	Is the top part of a fraction

Outpatient	A patient who attends a hospital for treatment without staying there overnight
PAN-PCR	Is a tool which enables the exploitation of available genome sequence data to design highly discriminatory PCR assays
Particular matter	Also called particle pollution, is a term for a mixture of solid particles and liquid droplets found in the air
Pathogen	Is a term that describes viruses, bacteria, and other types of germs that can cause some kind of disease
Pathogenicity	Refers to the ability of an organism to cause disease (i.e., harm the host)
Percentage	Is a ratio or a fraction whose denominator is always 100. It can be written as a fraction
Pneumonia	A severe inflammation of the lungs in which the alveoli (tiny air sacs) are filled with fluid
Prevalence	Is the proportion of a population who have a specific characteristic in a given time period
Proportion	Is the relation or the equality between two ratios or fractions; it can be written as a fraction; the proportion is out of any given total
Rapid review	Is a form of knowledge synthesis in which components of the systematic review process are simplified or omitted to produce information in a timely manner
Respiratory system	Is the system of the body involved in breathing, such as the sinuses, throat, airways and lungs
Respiratory tract infection (RTI)	Is an infection of parts of the body involved in breathing, such as the sinuses, throat, airways or lungs
Real time-PCR	Is a technique of collecting data throughout the PCR process as it occurs, thus combining amplification and detection into a single step, which is achieved using a variety of different fluorescent chemistries that correlate PCR product concentration to fluorescence intensity
Risk of bias	Is the likelihood that features of the study design or conduct of the study will give misleading results
Seasonal	Is relating to, or varying in occurrence according to the season
Sequence homology	Is the biological homology between DNA, RNA, or protein sequences, defined in terms of shared ancestry in the evolutionary history of life

Socio-economic status (SES)	Is the social standing or class of an individual or group. It is often measured as a combination of education, income and occupation.
Spieces	A group of living organisms consisting of similar individuals capable of exchanging genes or interbreeding
Strain	A genetic variant, a subtype or a culture within a biological species
Sputum test	A test mainly used to diagnose a bacterial infection, which is taken by asking the patients to take a deep breath, and then cough deeply to produce a sample of sputum.
Throat swab	A cotton stick is used to swab the area near the tonsils, which typically is used to determine if Group A Streptococcus bacteria is the cause of pharyngitis in a patient
Upper respiratory tract infection (URTI)	An infection that affects the upper part of the respiratory system, including the sinuses and throat
Variant	A subtype of a microorganism that is genetically distinct from a main strain, but not sufficiently different to be termed a distinct strain
Virulence	The degree of pathogenicity of a pathogen (bacteria, fungi, or viruses) and is determined by its ability to invade and multiply within the host

Appendix 2. Search strategy

Note that this search was conducted to identify relevant studies for both parts of this rapid review: Part 1 (prevalence and co-detection), and Part 2 (cross-reactivity, immune responses, and sequence homology).

Databaser: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to June 16, 2020, Embase 1974 to 2020 June 16 **Søkegrensesnitt:** Advanced search **Søkedato:** 2020-06-17		
1	(Coronavirus 229E, Human/ or Coronavirus NL63, Human/ or Coronavirus OC43, Human/) use ppezv or (Human coronavirus 229E/ or Human coronavirus NL63/ or Human coronavirus OC43/) use oemezd or (HCoV-229E or HCoV-HKU1 or HCoV-NL63 or HCoV-OC43 or HumanCoV-229E or HumanCoV-HKU1 or HumanCoV-NL63 or HumanCoV-OC43 or sCoV-229E or sCoV-HKU1 or sCoV-NL63 or sCoV-OC43).tw,kw,kf. or ((seasonal or human or endemic or common cold) adj coronavirus*).tw,kw,kf	3156
2	(Cross Protection/ or Immunity, cellular/ or Immunity, humoral/ or Immunity, mucosal/ or im.fs.) use ppezv or (Cross Protection/ or Cellular Immunity/ or Humoral Immunity/ or Mucosal Immunity/) use oemezd or (cross-protect* or crossprotect* or cross-react* or cross-react* or cross-neutral* or ((immune or B-cell* or T-cell* or antibod* or IgG or IgM or immunoglobulin* or immune globulin*) adj response*)).tw,kw,kf. or (((cell-mediated or cellular or humoral or mucosal) adj immunity) or antibody formation).tw,kw,kf	2165403
3	exp Epidemiologic Studies/ use ppezv or exp Epidemiology/ use oemezd or ep.fs. or (prevalence or epidemiolog*).ti,kw,kf	7563302
4	(1 and (2 or 3))	1286
5	(conference abstract or conference paper).pt use oemezd	4568452
6	(Animal/ not (Animal/ and Human/)) use ppezv or ((Animal/ or exp Nonhuman/ or Animal Experiment/) not ((Animal/ or exp Nonhuman/ or Animal Experiment/) and exp Human/)) use oemezd	10666044

7	4 not (5 or 6)	1128
8	**remove duplicates from 7 [MEDLINE: 605; Embase: 183]**	**788**
9	Sequence Homology/ use ppezv or Sequence Homology/ use oemezd or ((sequence or DNA or gene or protein) adj3 (compar* or homolog* or analys*)).tw,kw,kf.	894995
10	(2019-ncov or ncov19 or ncov-19 or "2019-novel CoV" or sars-cov2 or sars-cov-2 or sarscov2 or sars-coronavirus2 or sars-coronavirus-2).tw,kw,kf.	14401
11	**1 and 9 and 10**	**18**

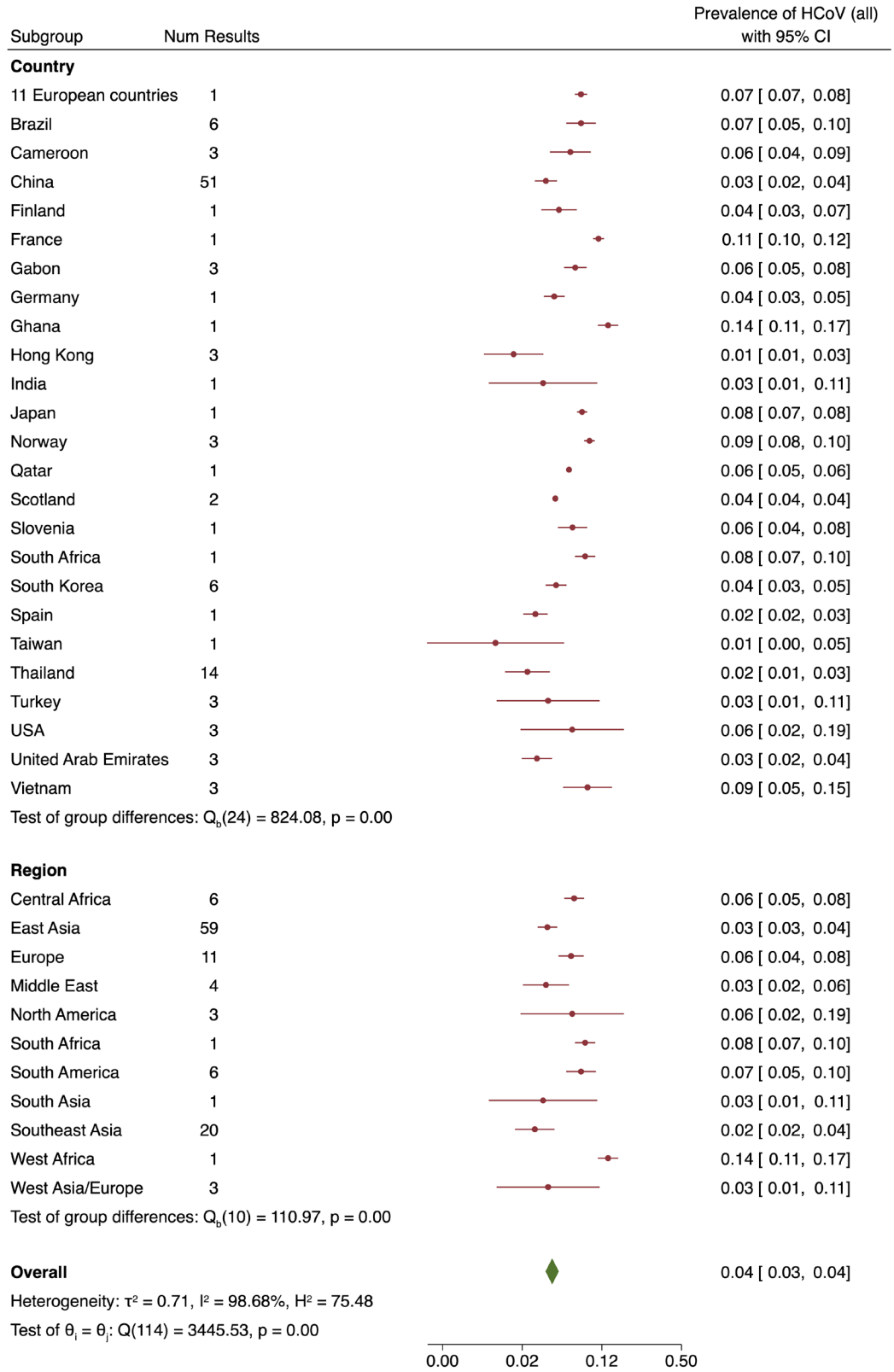
Koder og symboler	
exp "xxx"/	Angitt term og hierarkisk underordnede termer fra det kontrollerte vokabularet
"xxx"/	Term fra databasens kontrollerte vokabular
ppezv	Kode for deldatabasen av MEDLINE som er søkt
oemezd	Kode for deldatabasen av Embase som er søkt
adjx	Nærhetsoperator hvor x angir antall tillatte ord (-1) mellom to søkeord
*	Trunkeringstegn
.tw	Søk i tittel og sammendrag
.kf	MEDLINE: Søk etter ord i feltet keyword heading
.kw	Embase: Søk etter ord i feltet keyword heading
ep.fs	Floating subheading: epidemiology. For eksempel Coronavirus 229E, Human/epidemiology
im.fs.	Floating subheading: immunology. For eksempel Coronavirus 229E, Human/immunology

Appendix 3. Results from meta-analyses of HCoV prevalence

This document presents present the results of meta-analyses and meta-regressions. These sections prioritize the presentation of main results. For example, the first plot summarizes meta-analytical estimates with respect to geographical region, income, age, and infection type; subsequent plots present meta-analytical results and study level estimates.

Prevalence of all HCoVs by country and region

Figure 1. *Prevalence of HCoV (all) by country and region*



Prevalence by region, income, age, infection type, and admission status

Figure 2. *Prevalence of HCoV-229E by region, income, age, infection type, and hospitalization*

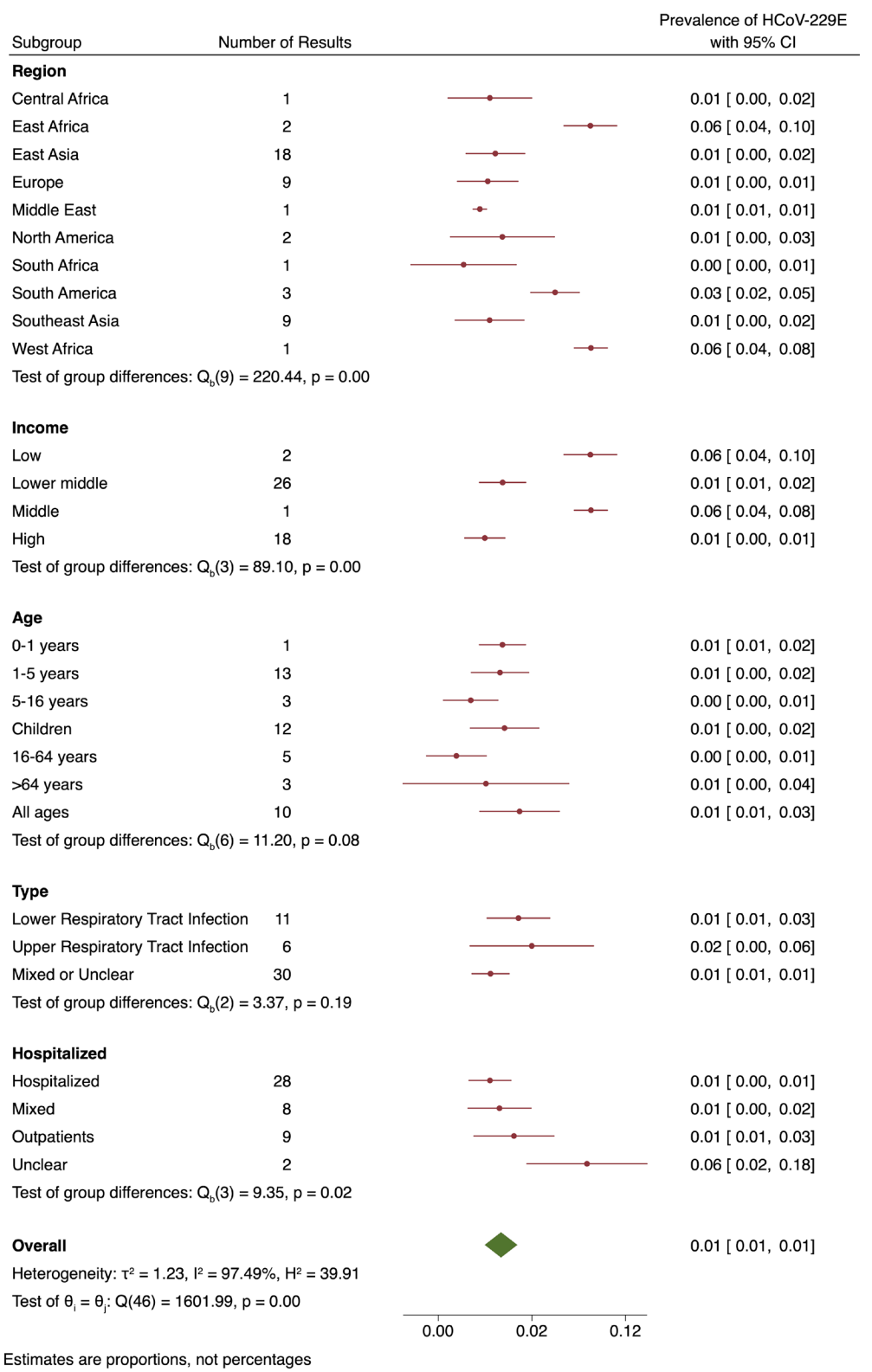


Figure 3. *Prevalence of HCoV-NL63 by region, income, age, infection type, and hospitalization*

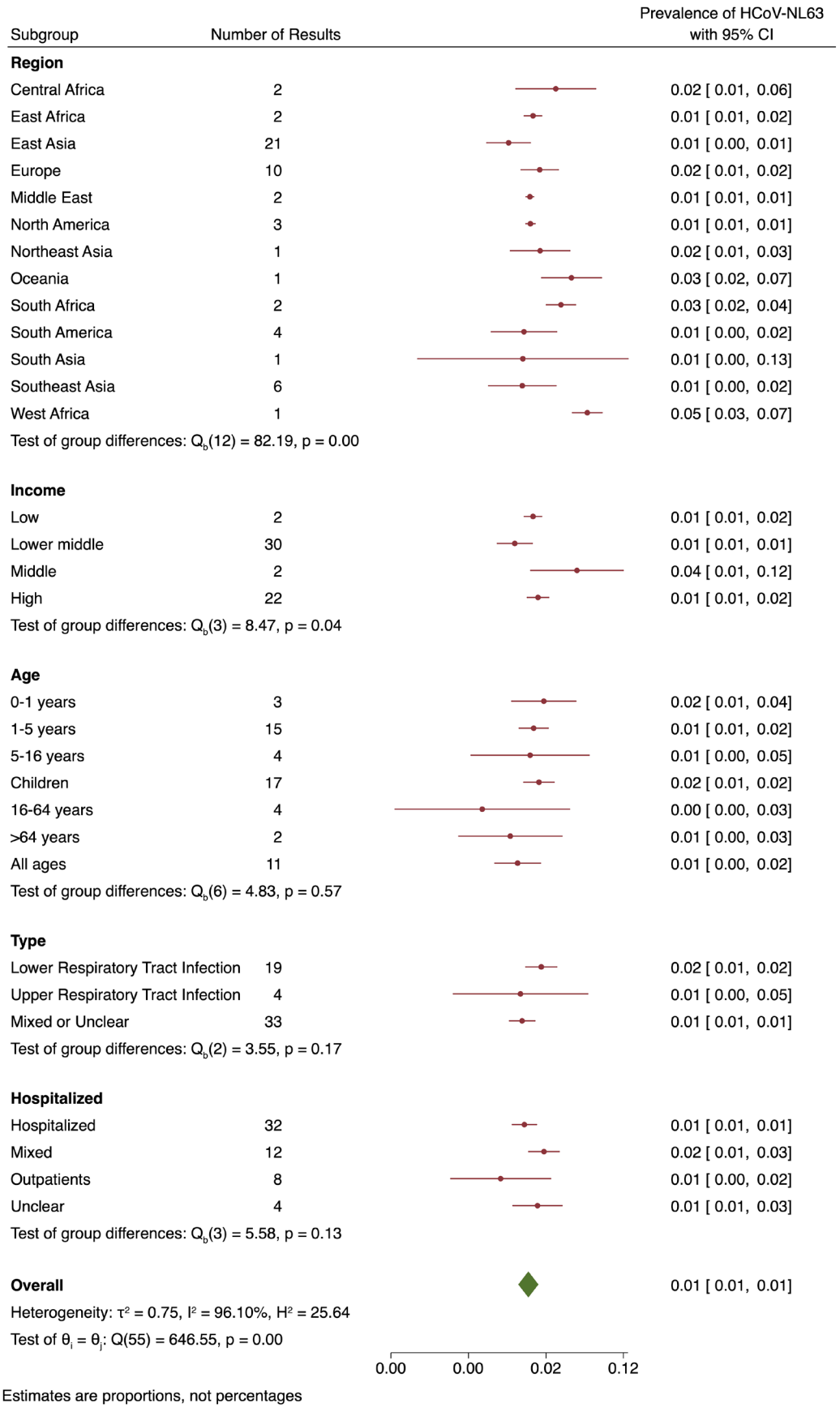


Figure 4. *Prevalence of HCoV-OC43 by region, income, age, infection type, and hospitalization*

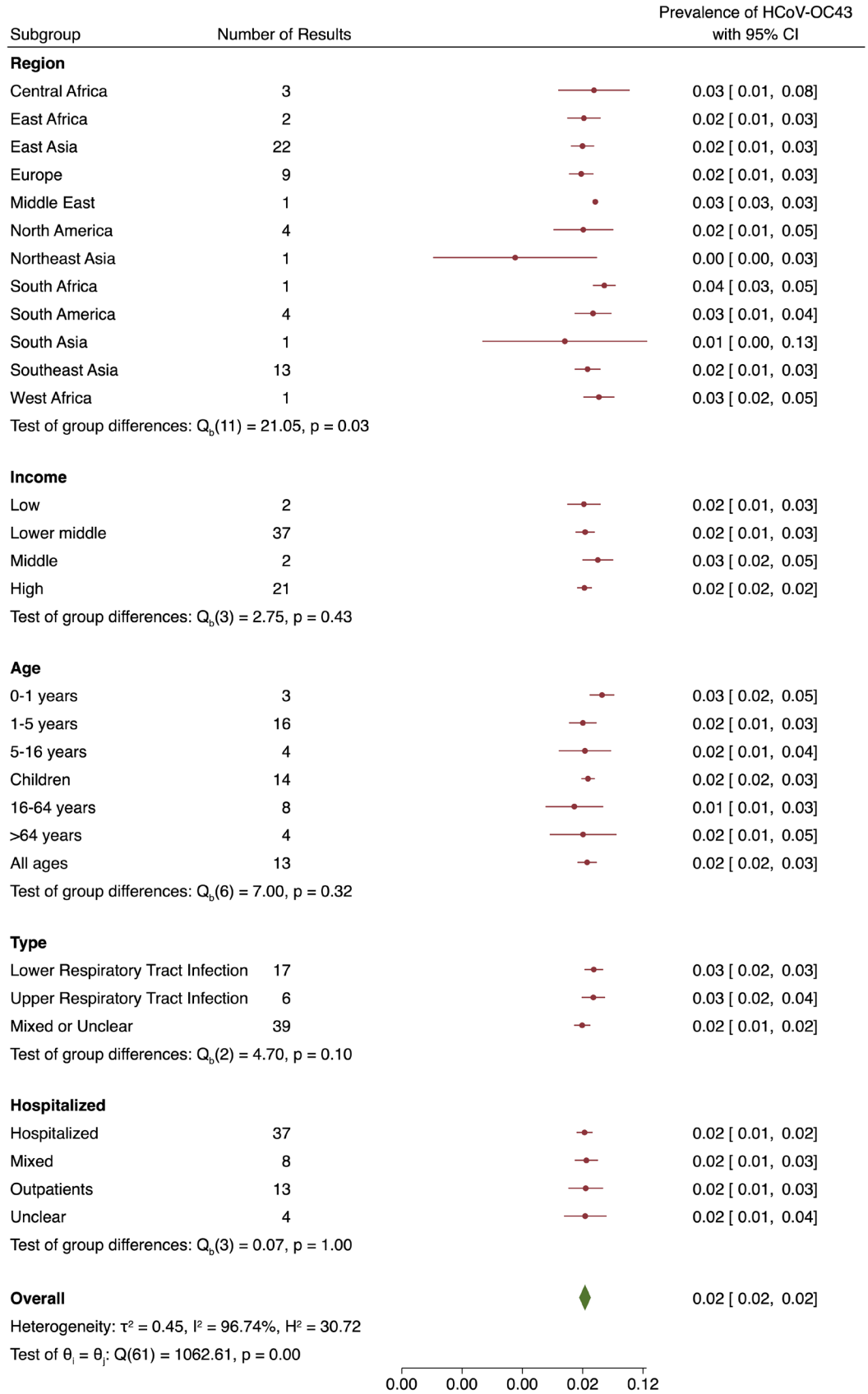


Figure 5. *Prevalence of HCoV-HKU1 by region, income, age, infection type, and hospitalization*

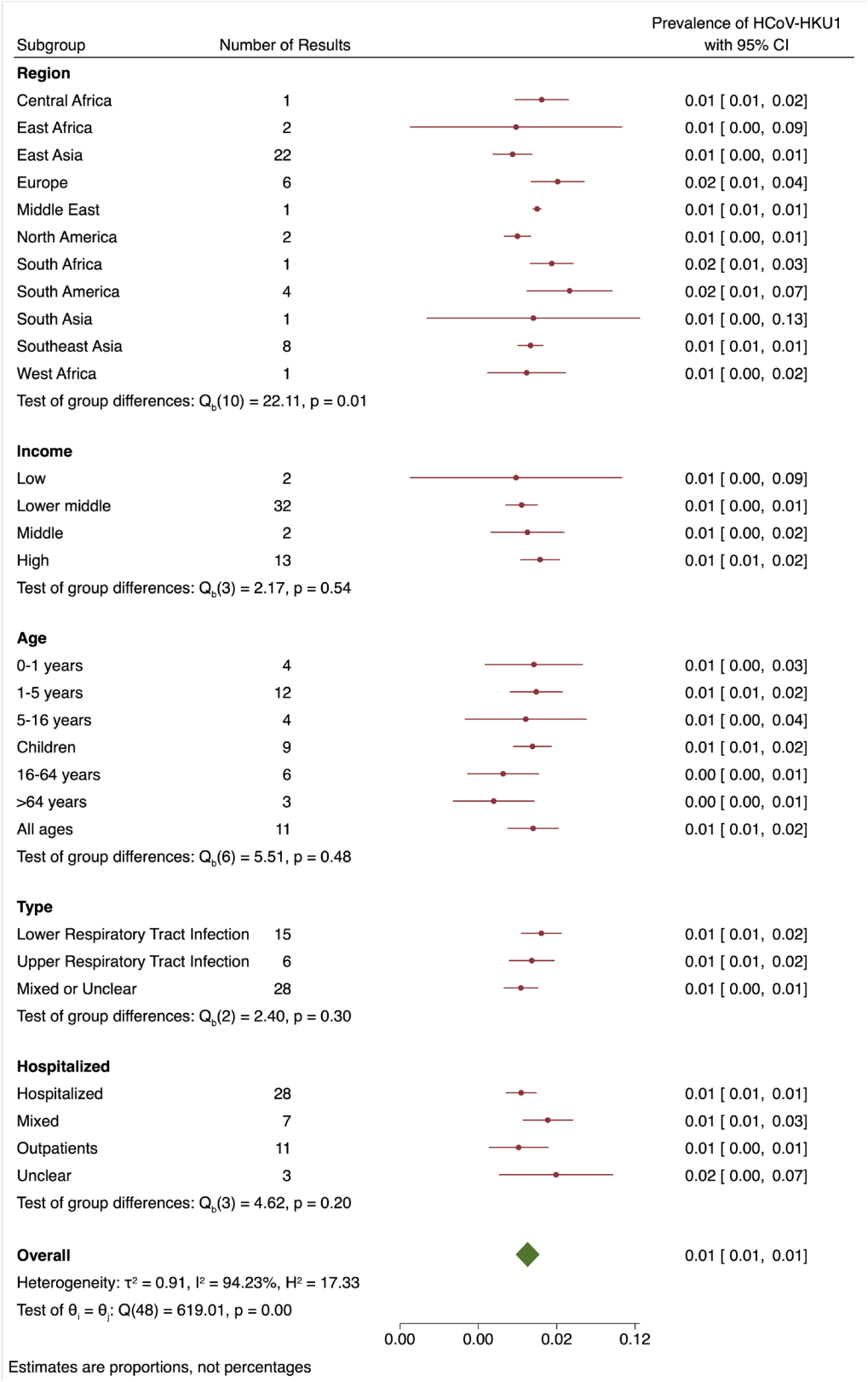


Figure 6. *Prevalence of HCoV (all) by region, income, age, infection type, and hospitalization (excluding studies judged to be at high or probably high risk of bias)*

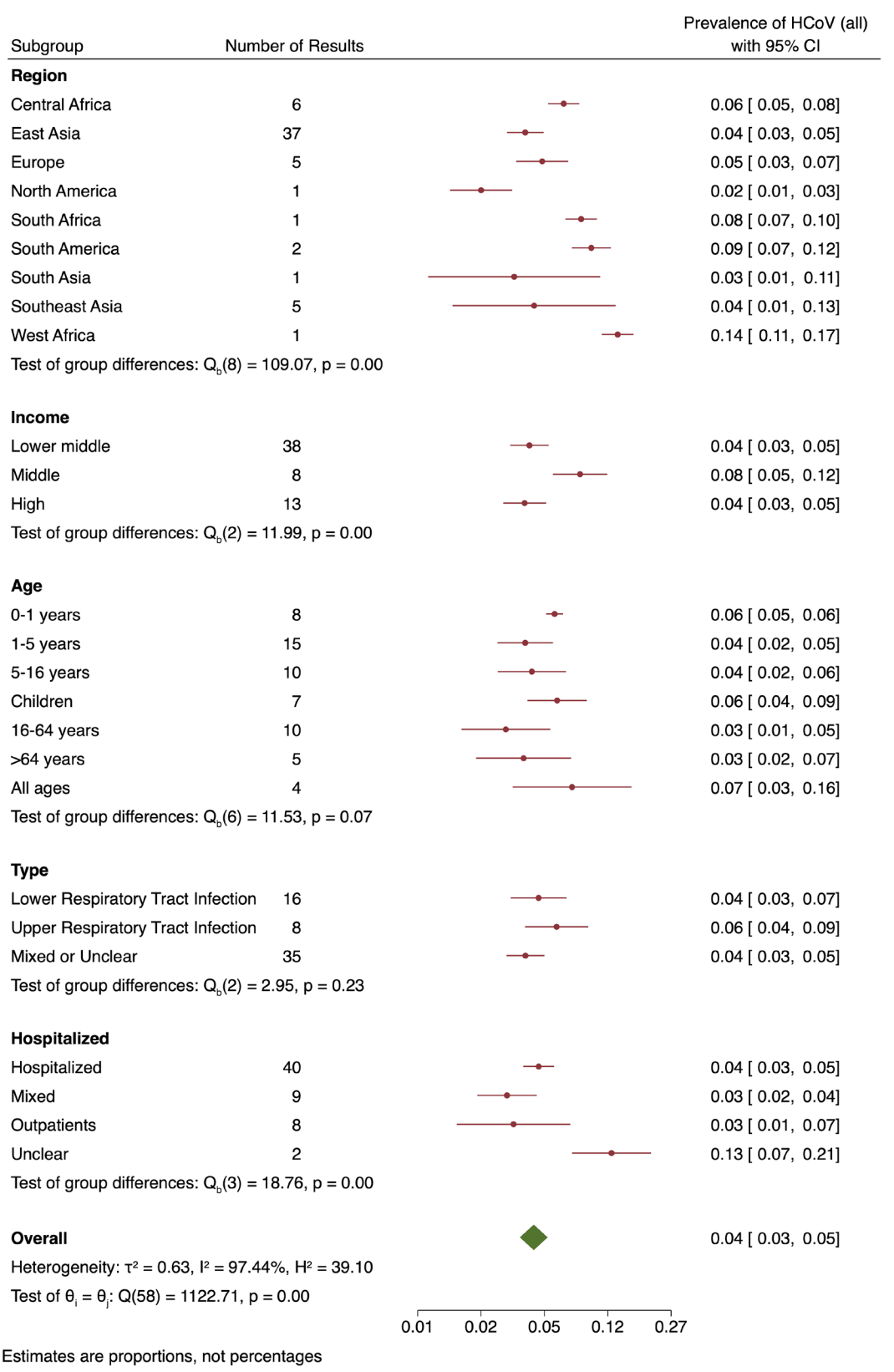


Figure 7. *Prevalence of HCoV-229E by region, income, age, infection type, and hospitalization (excluding studies judged to be at high or probably high risk of bias)*

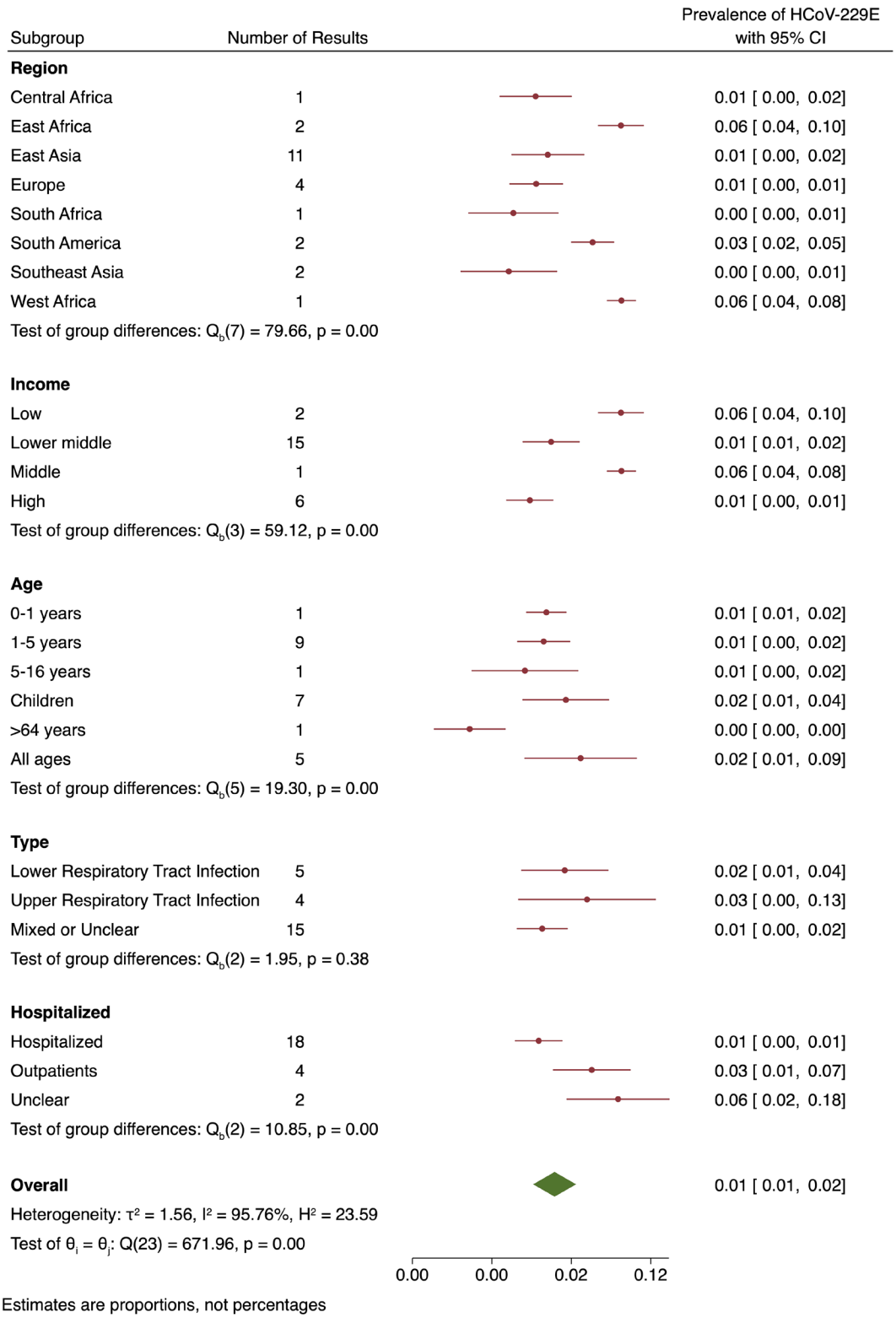


Figure 8. *Prevalence of HCoV-HKU1 by region, income, age, infection type, and hospitalization (excluding studies judged to be at high or probably high risk of bias)*

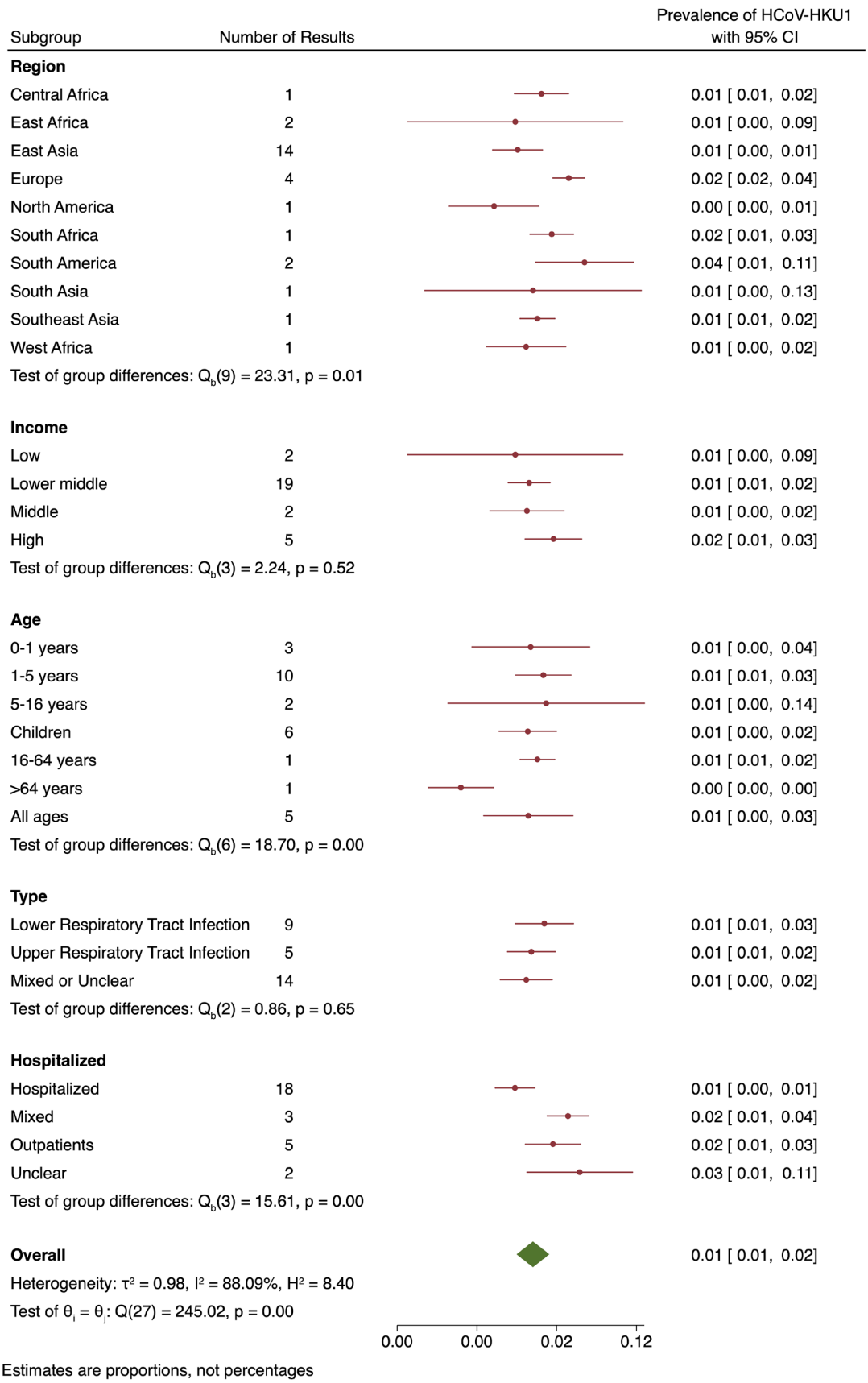


Figure 9. *Prevalence of HCoV-NL63 by region, income, age, infection type, and hospitalization (excluding studies judged to be at high or probably high risk of bias)*

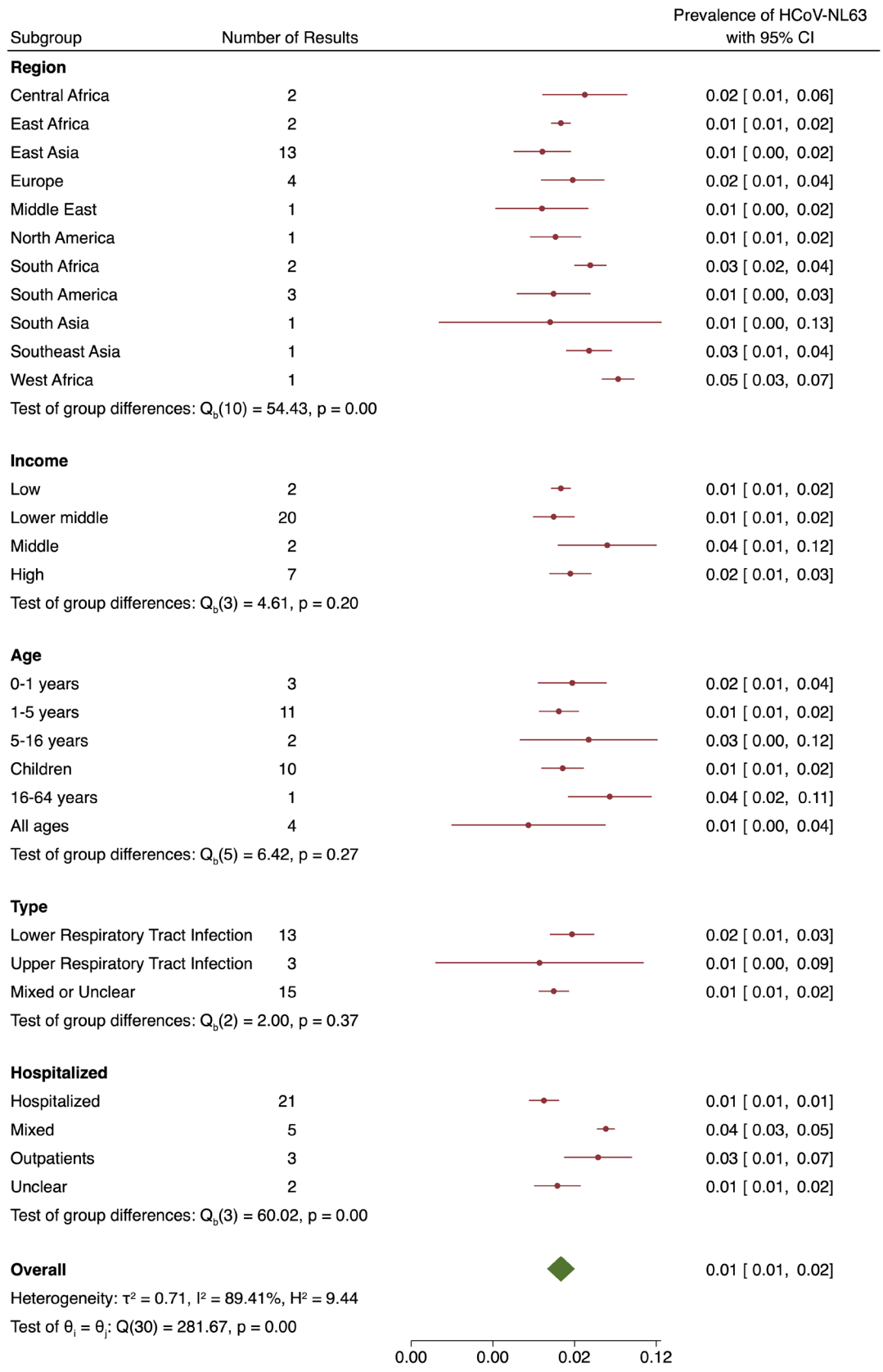
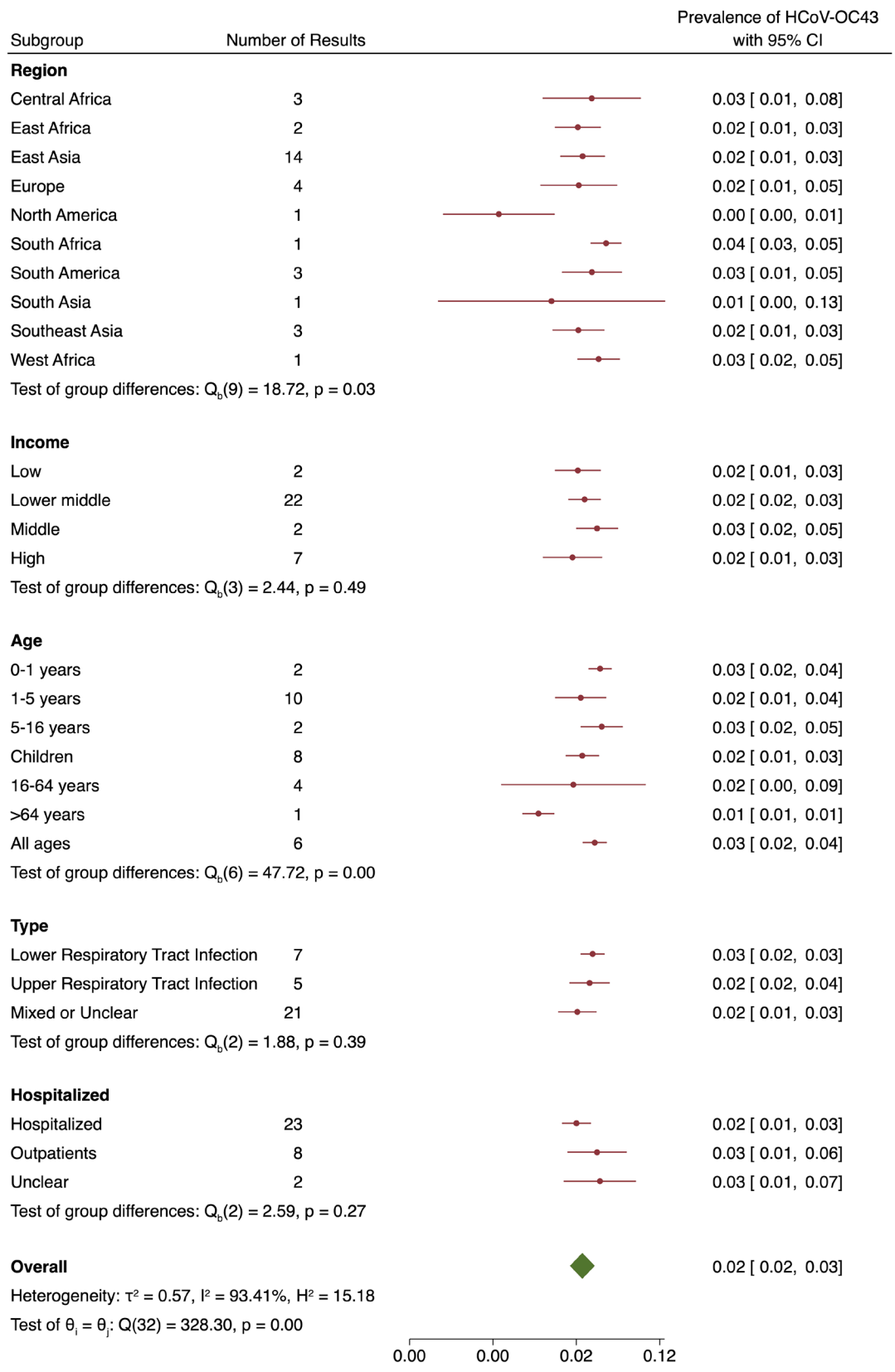


Figure 10. *Prevalence of HCoV-OC43 by region, income, age, infection type, and hospitalization (excluding studies judged to be at high or probably high risk of bias)*



Prevalence by country and region

The following forest plots show the results for the meta-analyses of prevalence, sub-grouped by country and region.

Figure 11. *Prevalence of HCoV-229E by country and region*

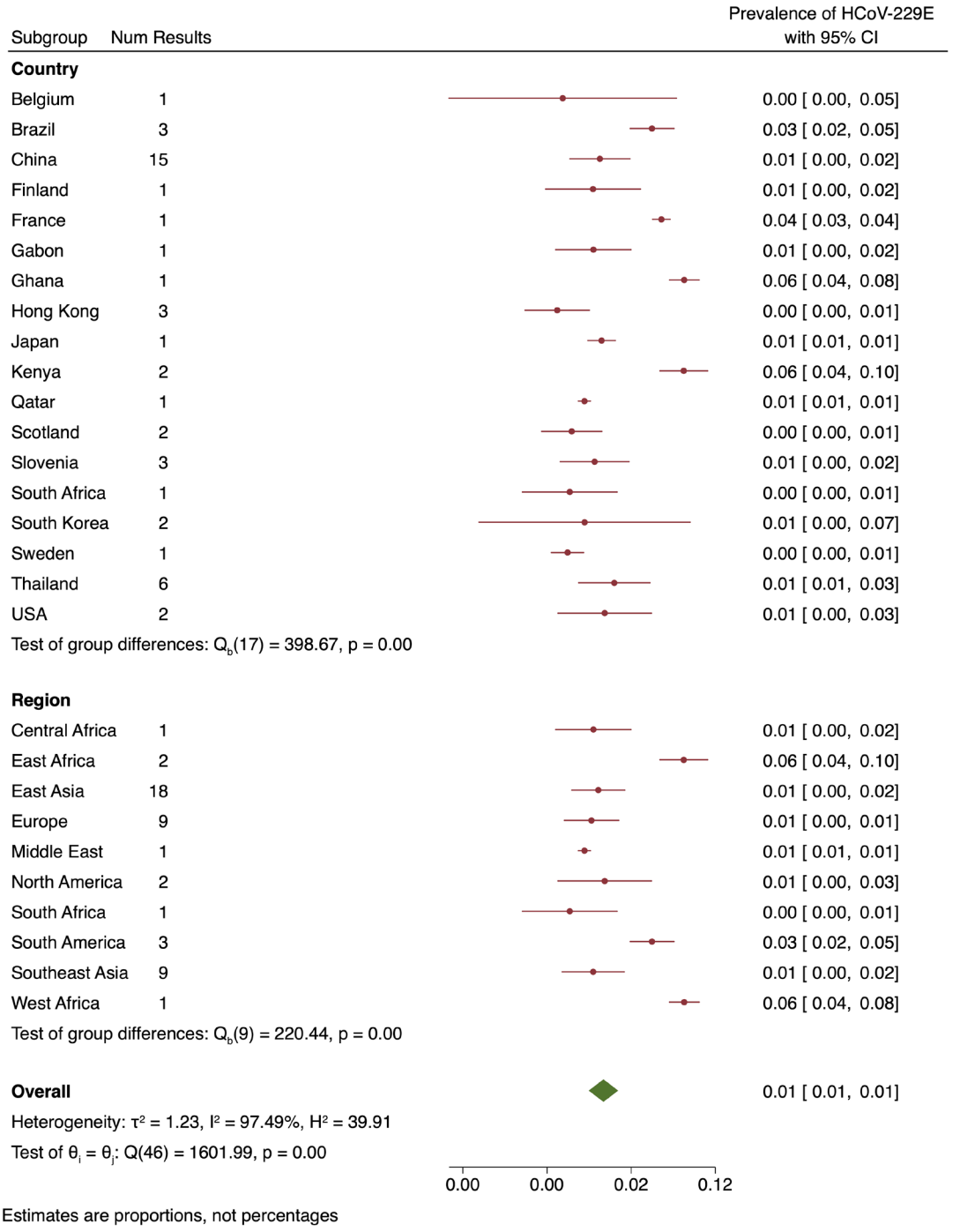


Figure 12. *Prevalence of HCoV-NL63 by country and region*

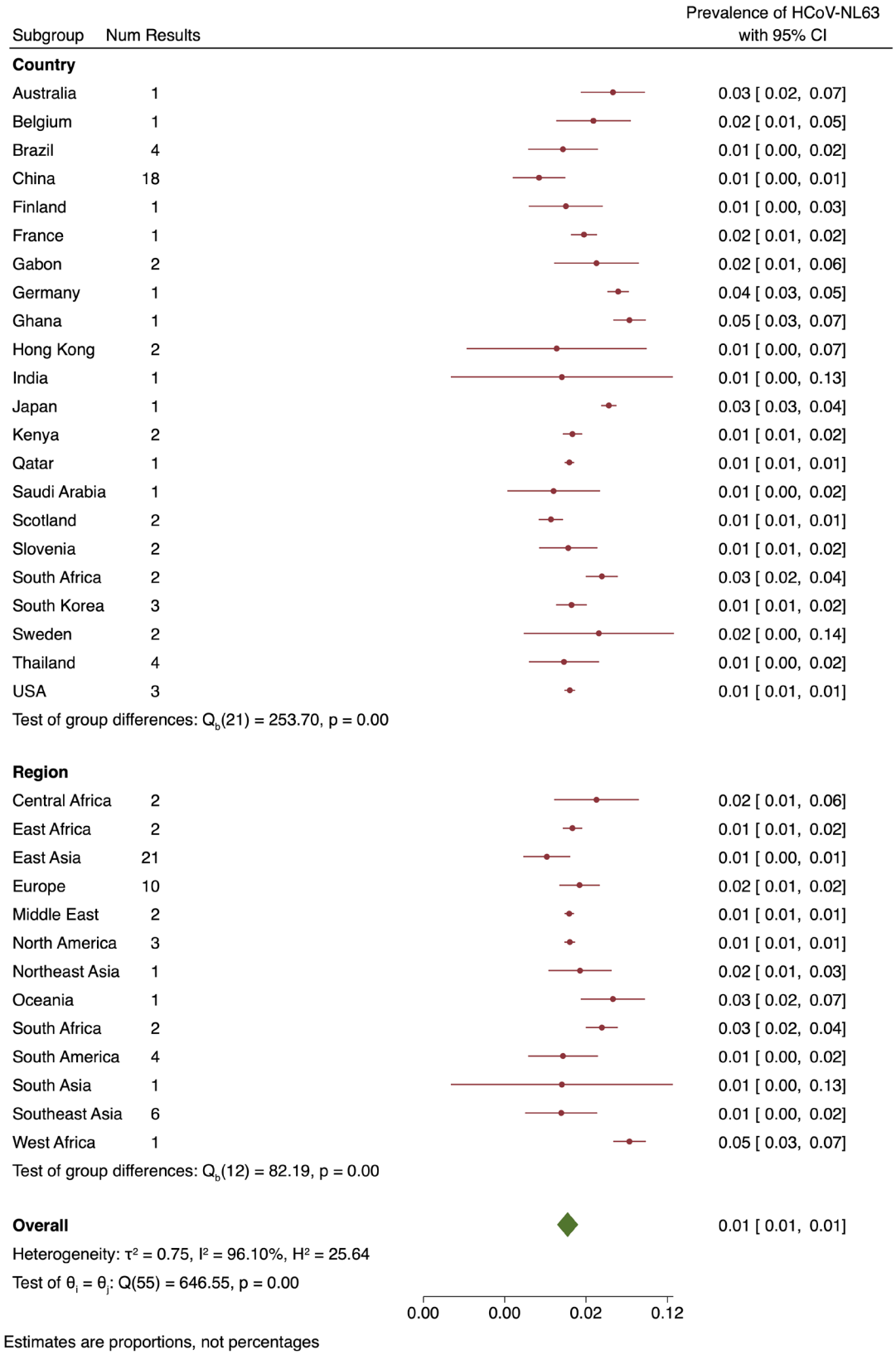


Figure 13. *Prevalence of HCoV-OC43 by country and region*

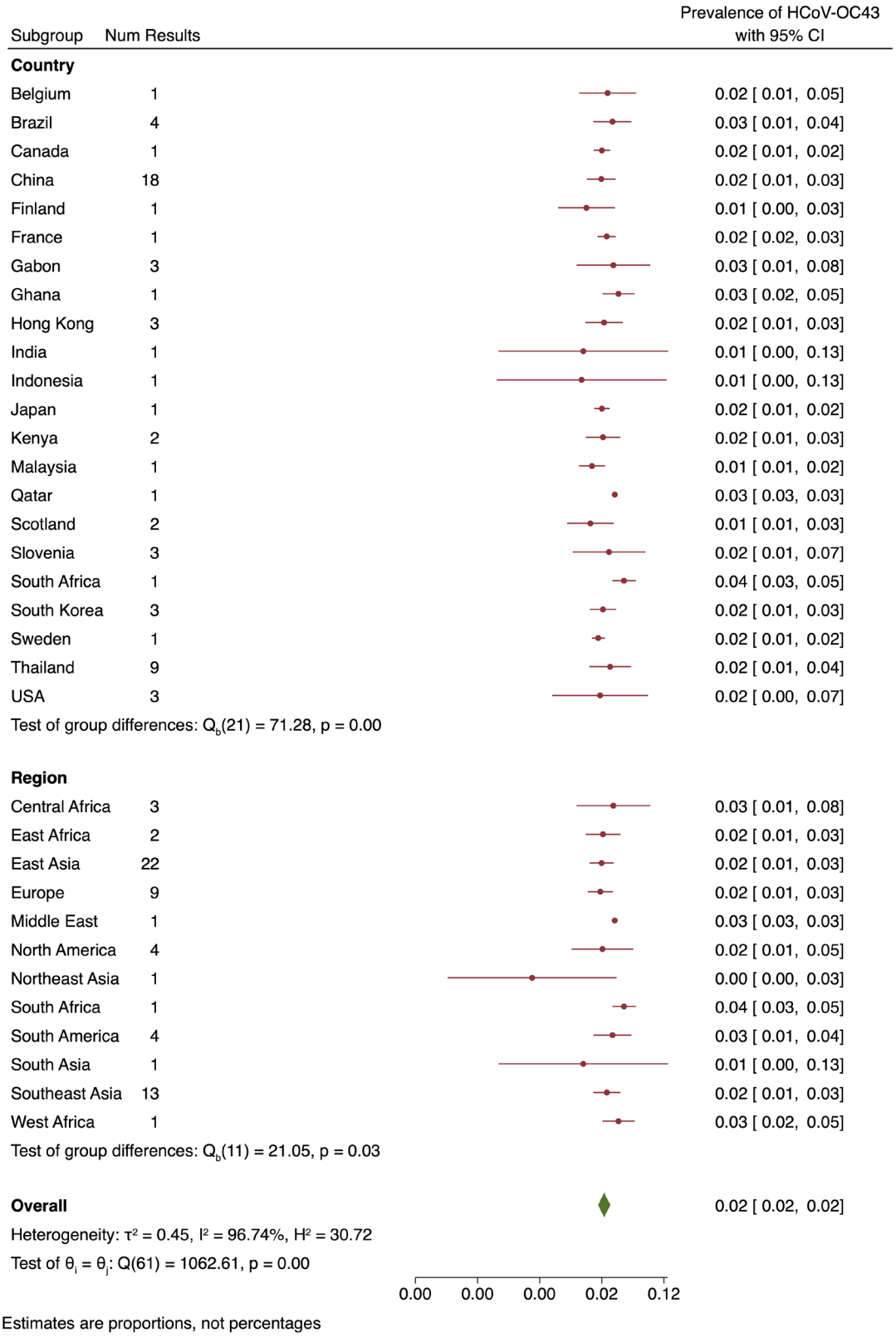
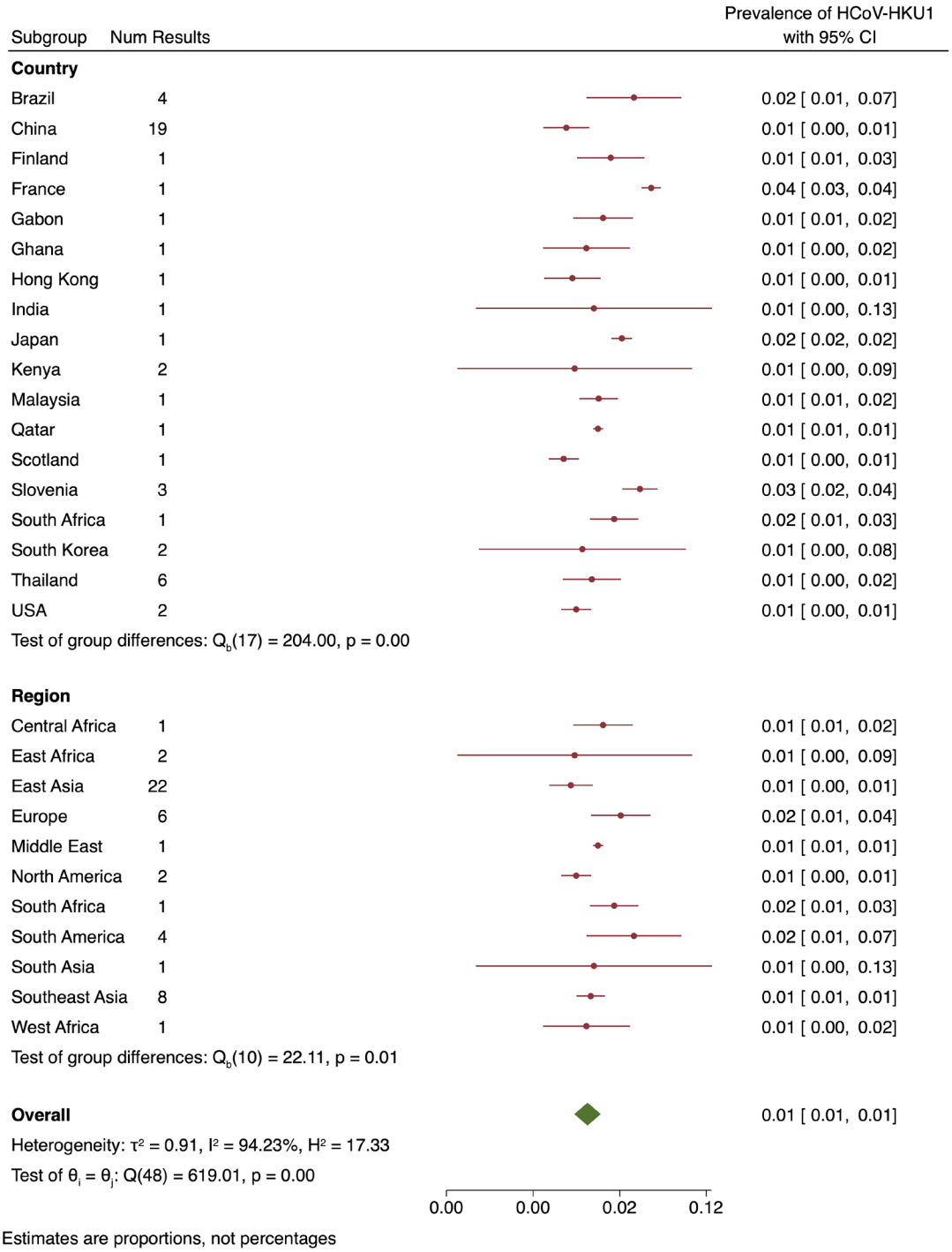


Figure 14. *Prevalence of HCoV-HKU1 by country and region*



Prevalence by age group

The following forest plots show the results for the meta-analyses of prevalence, sub-grouped by age group.

Figure 15. *Prevalence of HCoV (all) by age group*

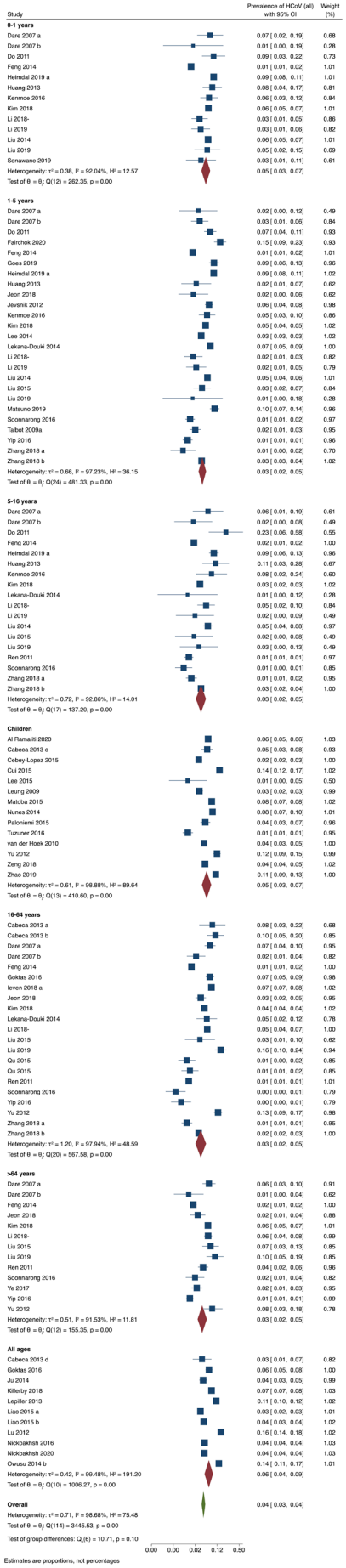

Study
Prevalence of HCoV (all) with 95% CI
Weight (%)
0-1 years
Dare 2007 a 0.07 [0.02, 0.19] 0.68
Dare 2007 b 0.01 [0.00, 0.19] 0.28
Do 2011 0.09 [0.03, 0.22] 0.73
Feng 2014 0.01 [0.01, 0.02] 1.01
Heimdal 2019 a 0.09 [0.08, 0.11] 1.01
Huang 2013 0.08 [0.04, 0.17] 0.81
Kenmoe 2016 0.06 [0.03, 0.12] 0.84
Kim 2018 0.06 [0.05, 0.07] 1.01
Li 2018- 0.03 [0.01, 0.05] 0.86
Li 2019 0.03 [0.01, 0.06] 0.82
Liu 2014 0.06 [0.05, 0.07] 1.01
Liu 2019 0.05 [0.02, 0.15] 0.69
Sonawane 2019 0.03 [0.01, 0.11] 0.61
Heterogeneity: τ² = 0.38, I² = 92.04%, H² = 12.57 0.05 [0.03, 0.07]
Test of θi = θj: Q(12) = 262.35, p = 0.00
1-5 years
Dare 2007 a 0.02 [0.00, 0.12] 0.49
Dare 2007 b 0.03 [0.01, 0.06] 0.84
Do 2011 0.07 [0.04, 0.11] 0.93
Fairchok 2020 0.15 [0.09, 0.23] 0.93
Feng 2014 0.01 [0.01, 0.02] 1.01
Goes 2019 0.09 [0.06, 0.13] 0.96
Heimdal 2019 a 0.09 [0.08, 0.11] 1.02
Huang 2013 0.02 [0.01, 0.07] 0.62
Jeon 2018 0.02 [0.00, 0.06] 0.62
Jevsnik 2012 0.06 [0.04, 0.08] 0.98
Kenmoe 2016 0.05 [0.03, 0.10] 0.86
Kim 2018 0.05 [0.04, 0.05] 1.02
Lee 2014 0.03 [0.03, 0.03] 1.02
Lekana-Douki 2014 0.07 [0.05, 0.09] 1.00
Li 2018- 0.02 [0.01, 0.03] 0.82
Li 2019 0.02 [0.01, 0.05] 0.79
Liu 2014 0.05 [0.04, 0.06] 1.01
Liu 2015 0.03 [0.02, 0.07] 0.84
Liu 2019 0.01 [0.00, 0.18] 0.28
Matsuno 2019 0.10 [0.07, 0.14] 0.96
Soonnarong 2016 0.01 [0.01, 0.02] 0.97
Talbot 2009a 0.02 [0.01, 0.03] 0.95
Yip 2016 0.01 [0.01, 0.01] 0.96
Zhang 2018 a 0.01 [0.00, 0.02] 0.70
Zhang 2018 b 0.03 [0.03, 0.04] 1.02
Heterogeneity: τ² = 0.66, I² = 97.23%, H² = 36.15 0.03 [0.02, 0.05]
Test of θi = θj: Q(24) = 481.33, p = 0.00
5-16 years
Dare 2007 a 0.06 [0.01, 0.19] 0.61
Dare 2007 b 0.02 [0.00, 0.08] 0.49
Do 2011 0.23 [0.06, 0.58] 0.55
Feng 2014 0.02 [0.01, 0.02] 1.00
Heimdal 2019 a 0.09 [0.06, 0.13] 0.96
Huang 2013 0.11 [0.03, 0.28] 0.67
Kenmoe 2016 0.08 [0.02, 0.24] 0.60
Kim 2018 0.03 [0.02, 0.03] 1.02
Lekana-Douki 2014 0.01 [0.00, 0.12] 0.28
Li 2018- 0.05 [0.02, 0.10] 0.84
Li 2019 0.02 [0.00, 0.09] 0.49
Liu 2014 0.05 [0.04, 0.08] 0.97
Liu 2015 0.02 [0.00, 0.08] 0.49
Liu 2019 0.03 [0.00, 0.13] 0.49
Ren 2011 0.01 [0.01, 0.01] 0.97
Soonnarong 2016 0.01 [0.00, 0.01] 0.85
Zhang 2018 a 0.01 [0.01, 0.02] 0.95
Zhang 2018 b 0.03 [0.02, 0.04] 1.00
Heterogeneity: τ² = 0.72, I² = 92.86%, H² = 14.01 0.03 [0.02, 0.05]
Test of θi = θj: Q(17) = 137.20, p = 0.00
Children
Al Ramaiti 2020 0.06 [0.05, 0.06] 1.03
Cabeca 2013 c 0.05 [0.03, 0.08] 0.93
Cebey-Lopez 2015 0.02 [0.02, 0.03] 1.00
Cui 2015 0.14 [0.12, 0.17] 1.02
Lee 2015 0.01 [0.00, 0.05] 0.50
Leung 2009 0.03 [0.02, 0.03] 0.99
Matoba 2015 0.08 [0.07, 0.08] 1.02
Nunes 2014 0.08 [0.07, 0.10] 1.01
Paloniemi 2015 0.04 [0.03, 0.07] 0.96
Tuzuner 2016 0.01 [0.01, 0.01] 0.95
van der Hoek 2010 0.04 [0.03, 0.05] 1.00
Yu 2012 0.12 [0.09, 0.15] 0.99
Zeng 2018 0.04 [0.04, 0.05] 1.02
Zhao 2019 0.11 [0.09, 0.13] 1.00
Heterogeneity: τ² = 0.61, I² = 98.88%, H² = 89.64 0.05 [0.03, 0.07]
Test of θi = θj: Q(13) = 410.60, p = 0.00
16-64 years
Cabeca 2013 a 0.08 [0.03, 0.22] 0.68
Cabeca 2013 b 0.10 [0.05, 0.20] 0.85
Dare 2007 a 0.07 [0.04, 0.10] 0.95
Dare 2007 b 0.02 [0.01, 0.04] 0.82
Feng 2014 0.01 [0.01, 0.02] 1.00
Goktas 2016 0.07 [0.05, 0.09] 0.98
Ieven 2018 a 0.07 [0.07, 0.08] 1.02
Jeon 2018 0.03 [0.02, 0.05] 0.95
Kim 2018 0.04 [0.04, 0.04] 1.02
Lekana-Douki 2014 0.05 [0.02, 0.12] 0.78
Li 2018- 0.05 [0.04, 0.07] 1.00
Liu 2015 0.03 [0.01, 0.10] 0.62
Liu 2019 0.16 [0.10, 0.24] 0.94
Qu 2015 0.01 [0.00, 0.02] 0.85
Qu 2015 0.01 [0.01, 0.02] 0.85
Ren 2011 0.01 [0.01, 0.01] 1.01
Soonnarong 2016 0.00 [0.00, 0.01] 0.79
Yip 2016 0.00 [0.00, 0.01] 0.79
Yu 2012 0.13 [0.09, 0.17] 0.98
Zhang 2018 a 0.01 [0.01, 0.01] 0.95
Zhang 2018 b 0.02 [0.02, 0.03] 1.00
Heterogeneity: τ² = 1.20, I² = 97.94%, H² = 48.59 0.03 [0.02, 0.05]
Test of θi = θj: Q(20) = 567.58, p = 0.00
>64 years
Dare 2007 a 0.06 [0.03, 0.10] 0.91
Dare 2007 b 0.01 [0.00, 0.04] 0.62
Feng 2014 0.02 [0.01, 0.02] 1.00
Jeon 2018 0.02 [0.01, 0.04] 0.88
Kim 2018 0.06 [0.05, 0.07] 1.01
Li 2018- 0.06 [0.04, 0.08] 0.99
Liu 2015 0.07 [0.03, 0.13] 0.85
Liu 2019 0.10 [0.05, 0.19] 0.85
Ren 2011 0.04 [0.02, 0.06] 0.96
Soonnarong 2016 0.02 [0.01, 0.04] 0.82
Ye 2017 0.02 [0.01, 0.03] 0.95
Yip 2016 0.01 [0.01, 0.01] 0.99
Yu 2012 0.08 [0.03, 0.18] 0.78
Heterogeneity: τ² = 0.51, I² = 91.53%, H² = 11.81 0.03 [0.02, 0.05]
Test of θi = θj: Q(12) = 155.35, p = 0.00
All ages
Cabeca 2013 d 0.03 [0.01, 0.07] 0.82
Goktas 2016 0.06 [0.05, 0.08] 1.00
Ju 2014 0.04 [0.03, 0.05] 0.99
Kilerby 2018 0.07 [0.07, 0.08] 1.03
Lepiller 2013 0.11 [0.10, 0.12] 1.02
Liao 2015 a 0.03 [0.02, 0.03] 1.01
Liao 2015 b 0.04 [0.03, 0.04] 1.02
Lu 2012 0.16 [0.14, 0.18] 1.02
Nickbakhsh 2016 0.04 [0.04, 0.04] 1.03
Nickbakhsh 2020 0.04 [0.04, 0.04] 1.03
Owusu 2014 b 0.14 [0.11, 0.17] 1.01
Heterogeneity: τ² = 0.42, I² = 99.48%, H² = 191.20 0.06 [0.04, 0.09]
Test of θi = θj: Q(10) = 1006.27, p = 0.00
Overall 0.04 [0.03, 0.04]
Heterogeneity: τ² = 0.71, I² = 98.68%, H² = 75.48
Test of θi = θj: Q(114) = 3445.53, p = 0.00
Test of group differences: Qb(6) = 10.71, p = 0.10
0.00 0.00 0.02 0.12 0.50
Estimates are proportions, not percentages

Figure 16. *Prevalence of HCoV-229E by age group*

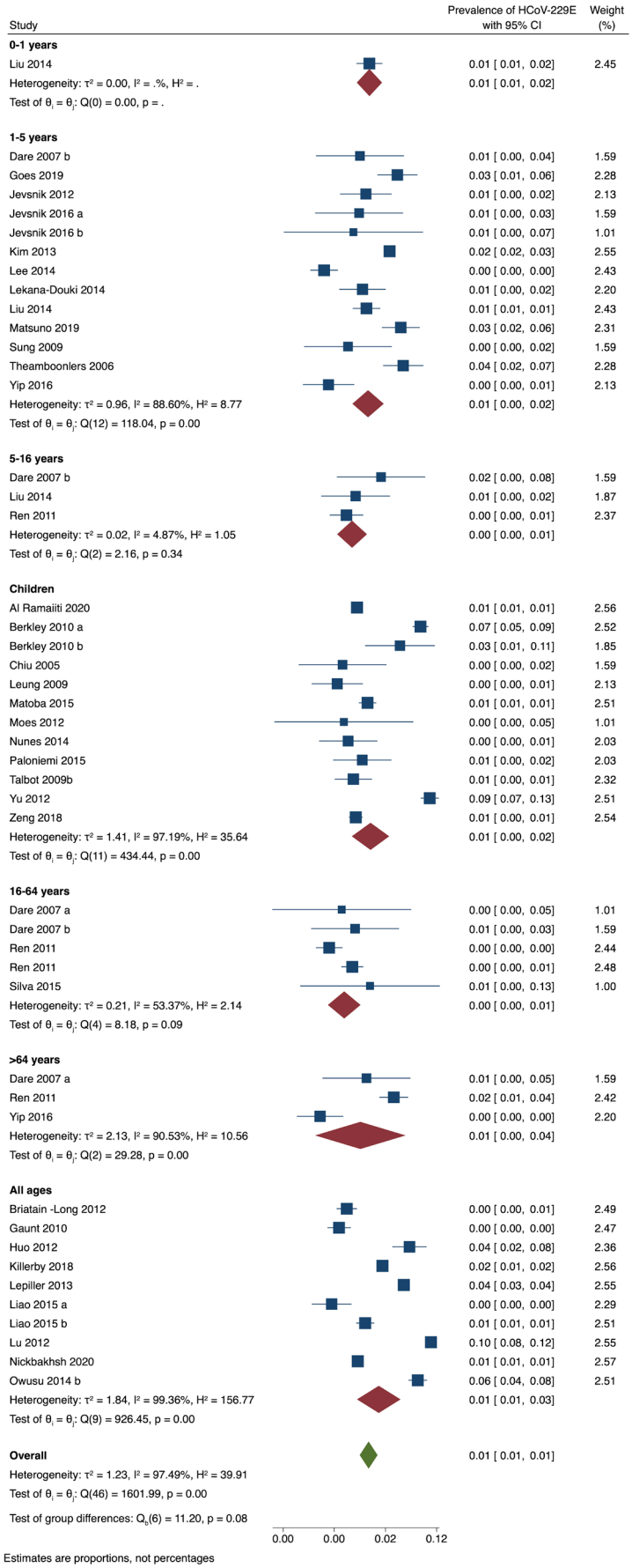


Figure 17. *Prevalence of HCoV-HKU1 by age group*

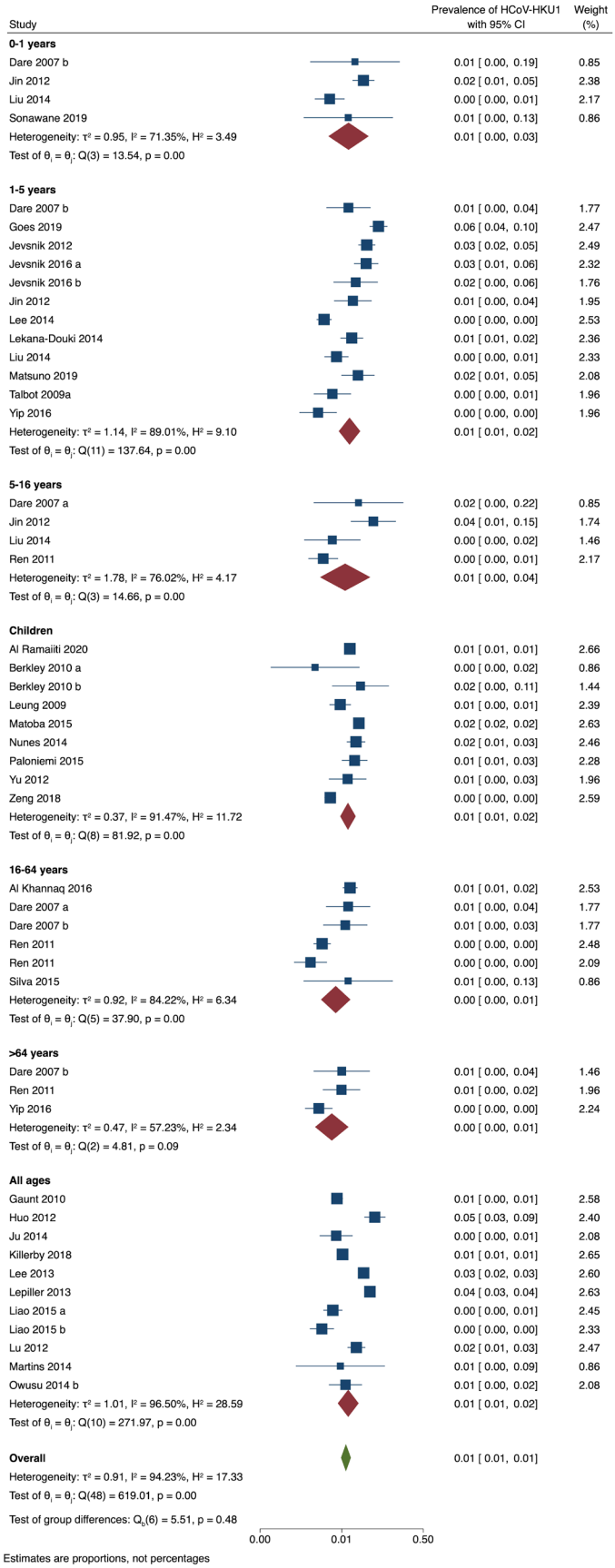


Figure 18. *Prevalence of HCoV-NL63 by age group*

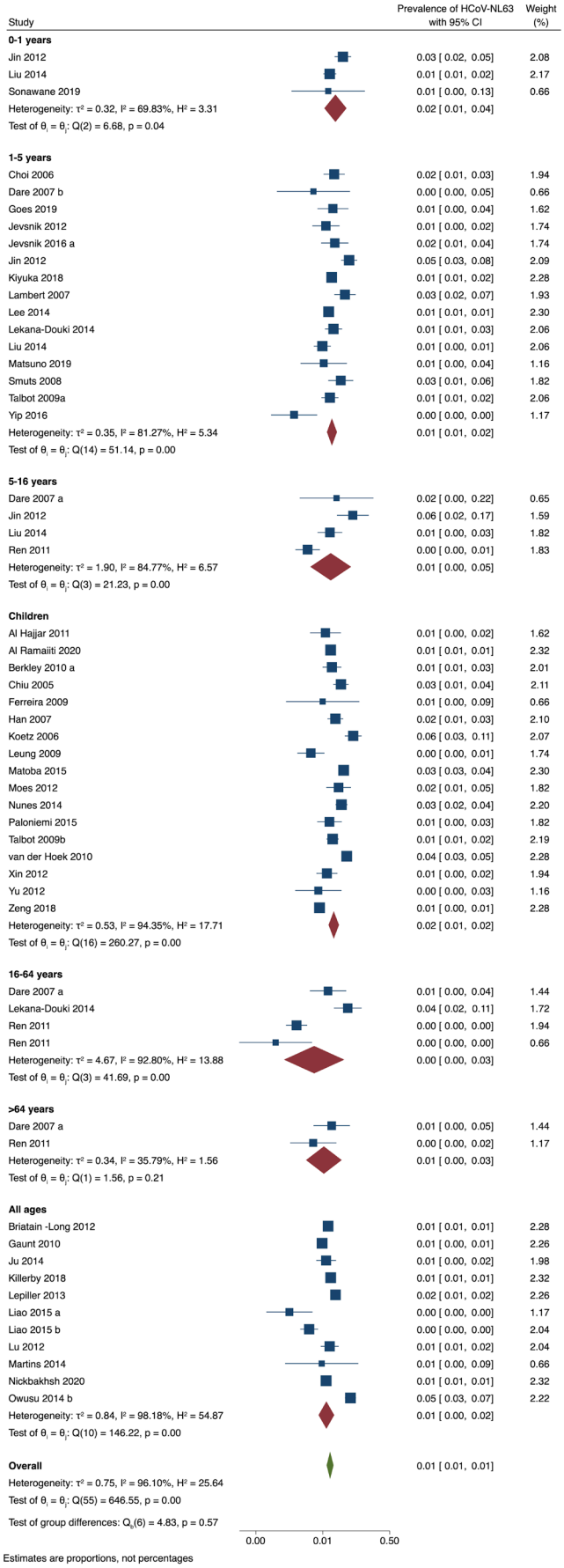
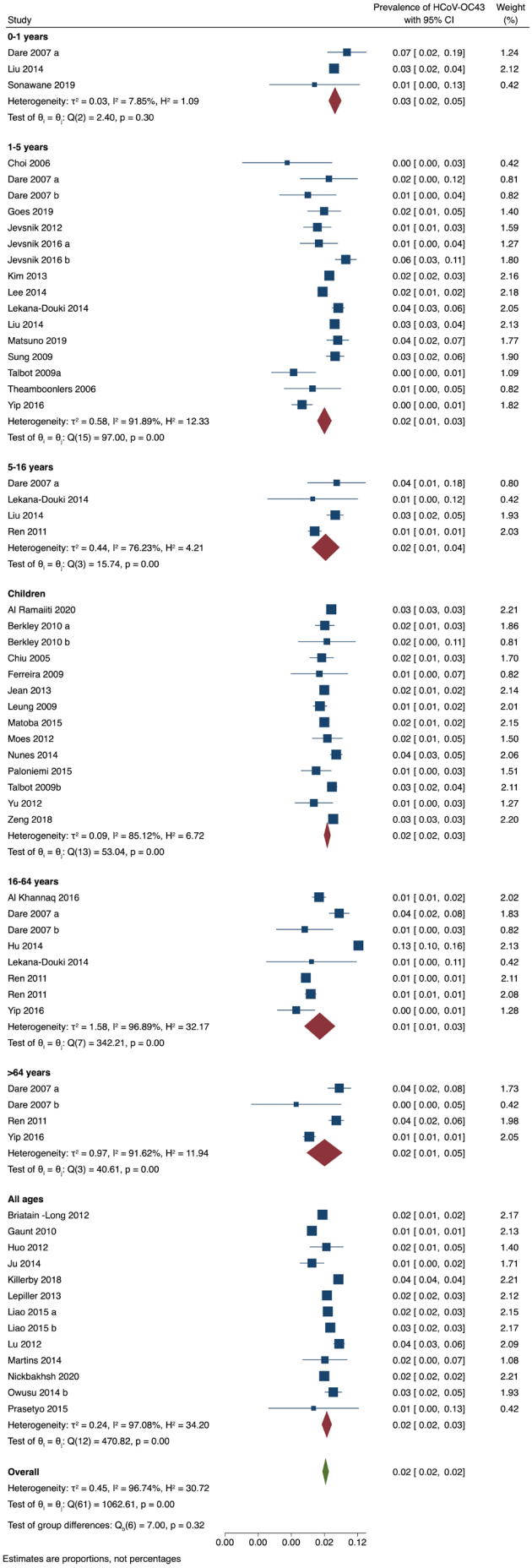


Figure 19. *Prevalence of HCoV-OC43 by age group*



Prevalence by infection type

The following forest plots show the results for the meta-analyses of prevalence, sub-grouped by infection type.

Figure 20. *Prevalence of HCoV (all) by infection type*

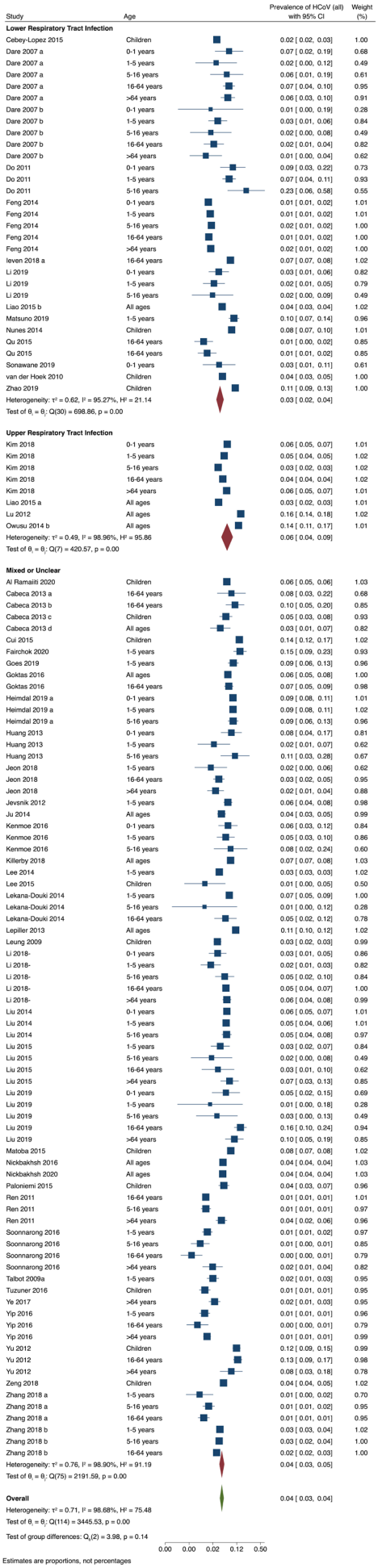

Study
Age
Prevalence of HCoV (all) with 95% CI
Weight (%)
Lower Respiratory Tract Infection
Cebey-Lopez 2015 Children 0.02 [0.02, 0.03] 1.00
Dare 2007 a 0-1 years 0.07 [0.02, 0.19] 0.68
Dare 2007 a 1-5 years 0.02 [0.00, 0.12] 0.49
Dare 2007 a 5-16 years 0.06 [0.01, 0.19] 0.61
Dare 2007 a 16-64 years 0.07 [0.04, 0.10] 0.95
Dare 2007 a >64 years 0.06 [0.03, 0.10] 0.91
Dare 2007 b 0-1 years 0.01 [0.00, 0.19] 0.28
Dare 2007 b 1-5 years 0.03 [0.01, 0.06] 0.84
Dare 2007 b 5-16 years 0.02 [0.00, 0.08] 0.49
Dare 2007 b 16-64 years 0.02 [0.01, 0.04] 0.82
Dare 2007 b >64 years 0.01 [0.00, 0.04] 0.62
Do 2011 0-1 years 0.09 [0.03, 0.22] 0.73
Do 2011 1-5 years 0.07 [0.04, 0.11] 0.93
Do 2011 5-16 years 0.23 [0.06, 0.58] 0.55
Feng 2014 0-1 years 0.01 [0.01, 0.02] 1.01
Feng 2014 1-5 years 0.01 [0.01, 0.02] 1.01
Feng 2014 5-16 years 0.02 [0.01, 0.02] 1.00
Feng 2014 16-64 years 0.01 [0.01, 0.02] 1.00
Feng 2014 >64 years 0.02 [0.01, 0.02] 1.00
Ieven 2018 a 16-64 years 0.07 [0.07, 0.08] 1.02
Li 2019 0-1 years 0.03 [0.01, 0.06] 0.82
Li 2019 1-5 years 0.02 [0.01, 0.05] 0.79
Li 2019 5-16 years 0.02 [0.00, 0.09] 0.49
Liao 2015 b All ages 0.04 [0.03, 0.04] 1.02
Matsuno 2019 1-5 years 0.10 [0.07, 0.14] 0.96
Nunes 2014 Children 0.08 [0.07, 0.10] 1.01
Qu 2015 16-64 years 0.01 [0.00, 0.02] 0.85
Qu 2015 16-64 years 0.01 [0.01, 0.02] 0.85
Sonawane 2019 0-1 years 0.03 [0.01, 0.11] 0.61
van der Hoek 2010 Children 0.04 [0.03, 0.05] 1.00
Zhao 2019 Children 0.11 [0.09, 0.13] 1.00
Heterogeneity: τ² = 0.62, I² = 95.27%, H² = 21.14 0.03 [0.02, 0.04]
Test of θi = θj: Q(30) = 698.86, p = 0.00
Upper Respiratory Tract Infection
Kim 2018 0-1 years 0.06 [0.05, 0.07] 1.01
Kim 2018 1-5 years 0.05 [0.04, 0.05] 1.02
Kim 2018 5-16 years 0.03 [0.02, 0.03] 1.02
Kim 2018 16-64 years 0.04 [0.04, 0.04] 1.02
Kim 2018 >64 years 0.06 [0.05, 0.07] 1.01
Liao 2015 a All ages 0.03 [0.02, 0.03] 1.01
Lu 2012 All ages 0.16 [0.14, 0.18] 1.02
Owusu 2014 b All ages 0.14 [0.11, 0.17] 1.01
Heterogeneity: τ² = 0.49, I² = 98.96%, H² = 95.86 0.06 [0.04, 0.09]
Test of θi = θj: Q(7) = 420.57, p = 0.00
Mixed or Unclear
Al Ramaiti 2020 Children 0.06 [0.05, 0.06] 1.03
Cabeca 2013 a 16-64 years 0.08 [0.03, 0.22] 0.68
Cabeca 2013 b 16-64 years 0.10 [0.05, 0.20] 0.85
Cabeca 2013 c Children 0.05 [0.03, 0.08] 0.93
Cabeca 2013 d All ages 0.03 [0.01, 0.07] 0.82
Cui 2015 Children 0.14 [0.12, 0.17] 1.02
Fairchok 2020 1-5 years 0.15 [0.09, 0.23] 0.93
Goes 2019 1-5 years 0.09 [0.06, 0.13] 0.96
Goktas 2016 All ages 0.06 [0.05, 0.08] 1.00
Goktas 2016 16-64 years 0.07 [0.05, 0.09] 0.98
Heimdal 2019 a 0-1 years 0.09 [0.08, 0.11] 1.01
Heimdal 2019 a 1-5 years 0.09 [0.08, 0.11] 1.02
Heimdal 2019 a 5-16 years 0.09 [0.06, 0.13] 0.96
Huang 2013 0-1 years 0.08 [0.04, 0.17] 0.81
Huang 2013 1-5 years 0.02 [0.01, 0.07] 0.62
Huang 2013 5-16 years 0.11 [0.03, 0.28] 0.67
Jeon 2018 1-5 years 0.02 [0.00, 0.06] 0.62
Jeon 2018 16-64 years 0.03 [0.02, 0.05] 0.95
Jeon 2018 >64 years 0.02 [0.01, 0.04] 0.88
Jevsnik 2012 1-5 years 0.06 [0.04, 0.08] 0.98
Ju 2014 All ages 0.04 [0.03, 0.05] 0.99
Kenmoe 2016 0-1 years 0.06 [0.03, 0.12] 0.84
Kenmoe 2016 1-5 years 0.05 [0.03, 0.10] 0.86
Kenmoe 2016 5-16 years 0.08 [0.02, 0.24] 0.60
Killerby 2018 All ages 0.07 [0.07, 0.08] 1.03
Lee 2014 1-5 years 0.03 [0.03, 0.03] 1.02
Lee 2015 Children 0.01 [0.00, 0.05] 0.50
Lekana-Douki 2014 1-5 years 0.07 [0.05, 0.09] 1.00
Lekana-Douki 2014 5-16 years 0.01 [0.00, 0.12] 0.28
Lekana-Douki 2014 16-64 years 0.05 [0.02, 0.12] 0.78
Lepiller 2013 All ages 0.11 [0.10, 0.12] 1.02
Leung 2009 Children 0.03 [0.02, 0.03] 0.99
Li 2018- 0-1 years 0.03 [0.01, 0.05] 0.86
Li 2018- 1-5 years 0.02 [0.01, 0.03] 0.82
Li 2018- 5-16 years 0.05 [0.02, 0.10] 0.84
Li 2018- 16-64 years 0.05 [0.04, 0.07] 1.00
Li 2018- >64 years 0.06 [0.04, 0.08] 0.99
Liu 2014 0-1 years 0.06 [0.05, 0.07] 1.01
Liu 2014 1-5 years 0.05 [0.04, 0.06] 1.01
Liu 2014 5-16 years 0.05 [0.04, 0.08] 0.97
Liu 2015 1-5 years 0.03 [0.02, 0.07] 0.84
Liu 2015 5-16 years 0.02 [0.00, 0.08] 0.49
Liu 2015 16-64 years 0.03 [0.01, 0.10] 0.62
Liu 2015 >64 years 0.07 [0.03, 0.13] 0.85
Liu 2019 0-1 years 0.05 [0.02, 0.15] 0.69
Liu 2019 1-5 years 0.01 [0.00, 0.18] 0.28
Liu 2019 5-16 years 0.03 [0.00, 0.13] 0.49
Liu 2019 16-64 years 0.16 [0.10, 0.24] 0.94
Liu 2019 >64 years 0.10 [0.05, 0.19] 0.85
Matoba 2015 Children 0.08 [0.07, 0.08] 1.02
Nickbakhsh 2016 All ages 0.04 [0.04, 0.04] 1.03
Nickbakhsh 2020 All ages 0.04 [0.04, 0.04] 1.03
Paloniemi 2015 Children 0.04 [0.03, 0.07] 0.96
Ren 2011 16-64 years 0.01 [0.01, 0.01] 1.01
Ren 2011 5-16 years 0.01 [0.01, 0.01] 0.97
Ren 2011 >64 years 0.04 [0.02, 0.06] 0.96
Soonnarong 2016 1-5 years 0.01 [0.01, 0.02] 0.97
Soonnarong 2016 5-16 years 0.01 [0.00, 0.01] 0.85
Soonnarong 2016 16-64 years 0.00 [0.00, 0.01] 0.79
Soonnarong 2016 >64 years 0.02 [0.01, 0.04] 0.82
Talbot 2009a 1-5 years 0.02 [0.01, 0.03] 0.95
Tuzuner 2016 Children 0.01 [0.01, 0.01] 0.95
Ye 2017 >64 years 0.02 [0.01, 0.03] 0.95
Yip 2016 1-5 years 0.01 [0.01, 0.01] 0.96
Yip 2016 16-64 years 0.00 [0.00, 0.01] 0.79
Yip 2016 >64 years 0.01 [0.01, 0.01] 0.99
Yu 2012 Children 0.12 [0.09, 0.15] 0.99
Yu 2012 16-64 years 0.13 [0.09, 0.17] 0.98
Yu 2012 >64 years 0.08 [0.03, 0.18] 0.78
Zeng 2018 Children 0.04 [0.04, 0.05] 1.02
Zhang 2018 a 1-5 years 0.01 [0.00, 0.02] 0.70
Zhang 2018 a 5-16 years 0.01 [0.01, 0.02] 0.95
Zhang 2018 a 16-64 years 0.01 [0.01, 0.01] 0.95
Zhang 2018 b 1-5 years 0.03 [0.03, 0.04] 1.02
Zhang 2018 b 5-16 years 0.03 [0.02, 0.04] 1.00
Zhang 2018 b 16-64 years 0.02 [0.02, 0.03] 1.00
Heterogeneity: τ² = 0.76, I² = 98.90%, H² = 91.19 0.04 [0.03, 0.05]
Test of θi = θj: Q(75) = 2191.59, p = 0.00
Overall 0.04 [0.03, 0.04]
Heterogeneity: τ² = 0.71, I² = 98.68%, H² = 75.48
Test of θi = θj: Q(114) = 3445.53, p = 0.00
Test of group differences: Q1(2) = 3.98, p = 0.14
0.00 0.00 0.02 0.12 0.50
Estimates are proportions, not percentages

Figure 21. *Prevalence of HCoV-229E by infection type*

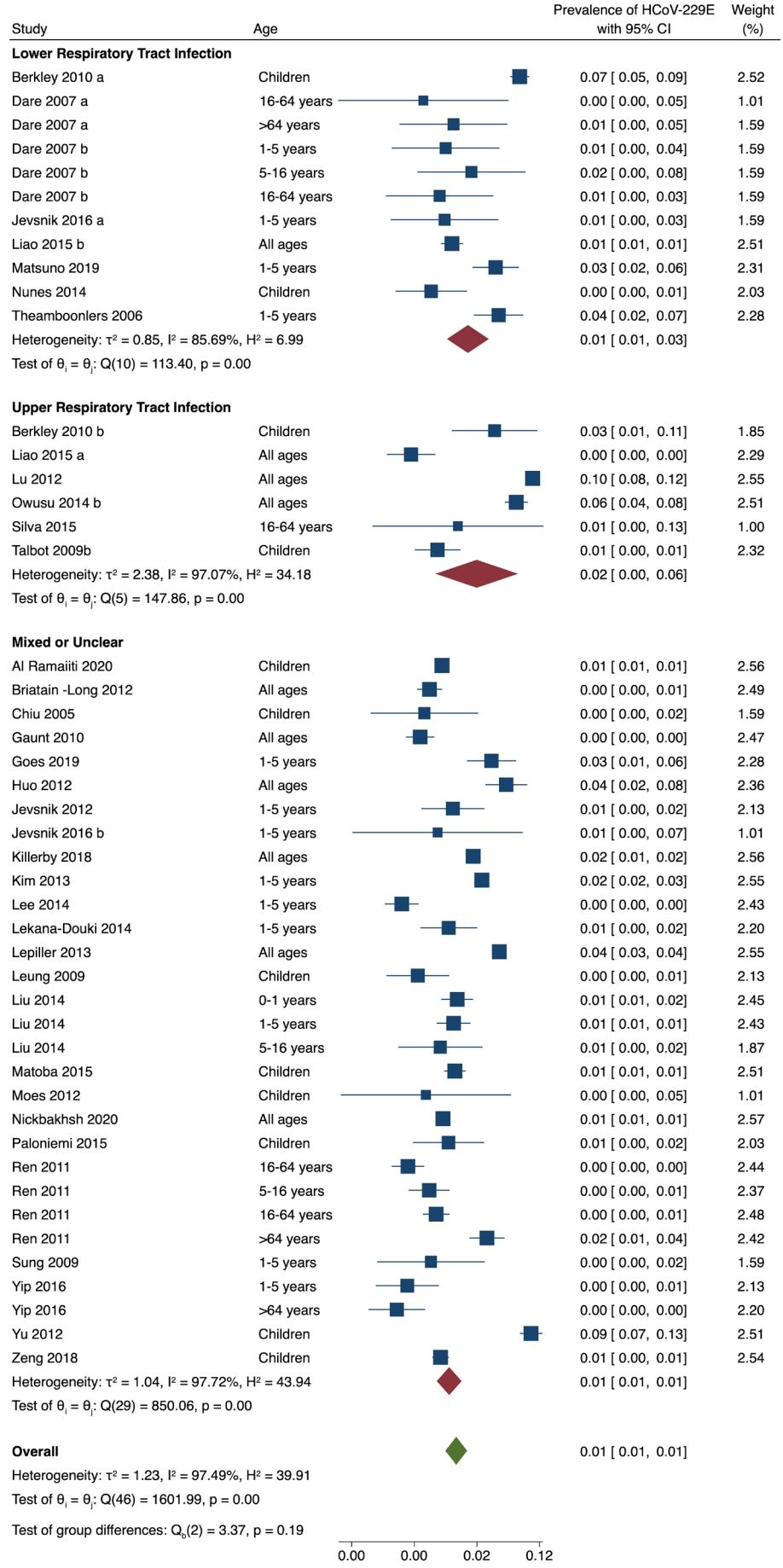


Figure 22. *Prevalence of HCoV-HKU1 by infection type*

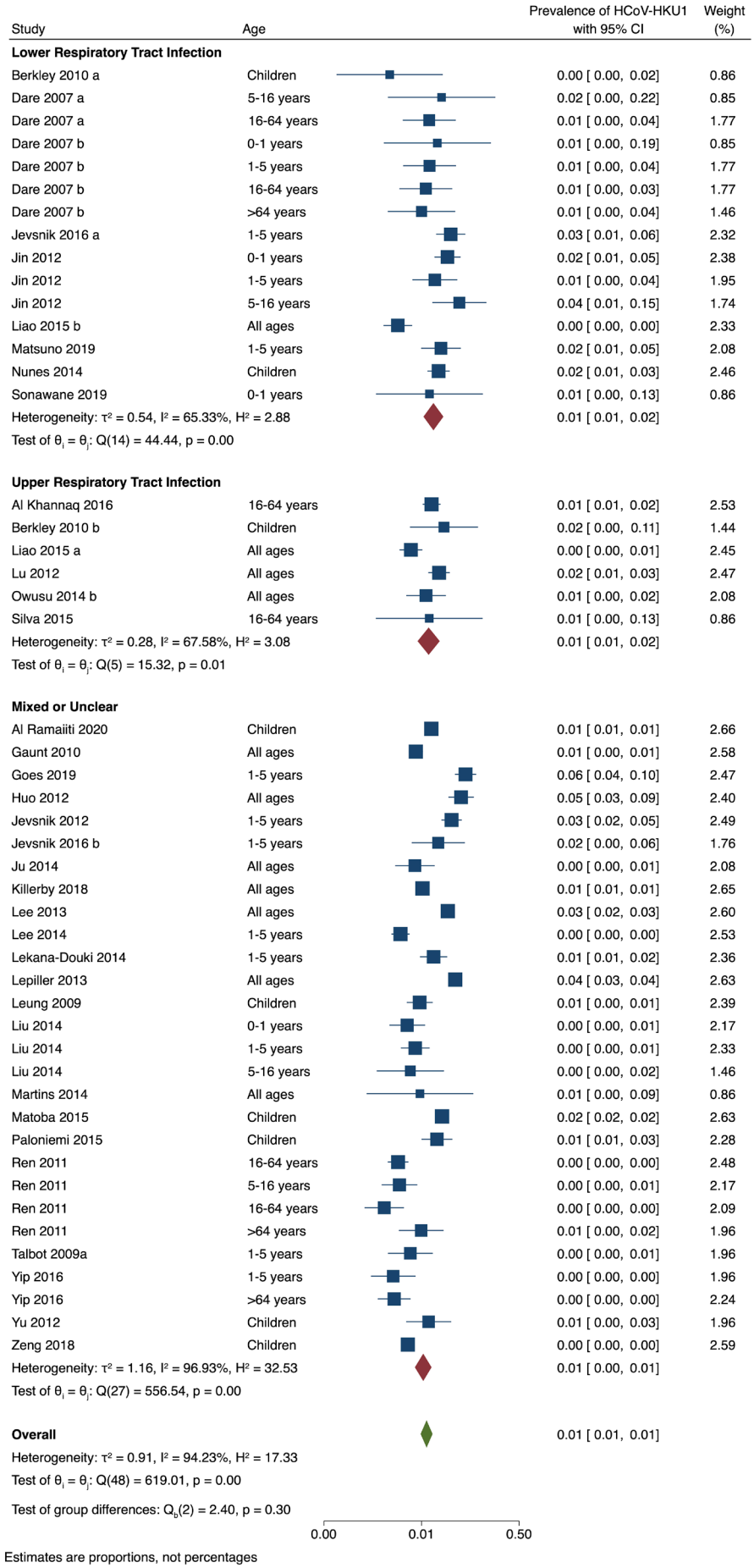


Figure 23. *Prevalence of HCoV-NL63 by infection type*

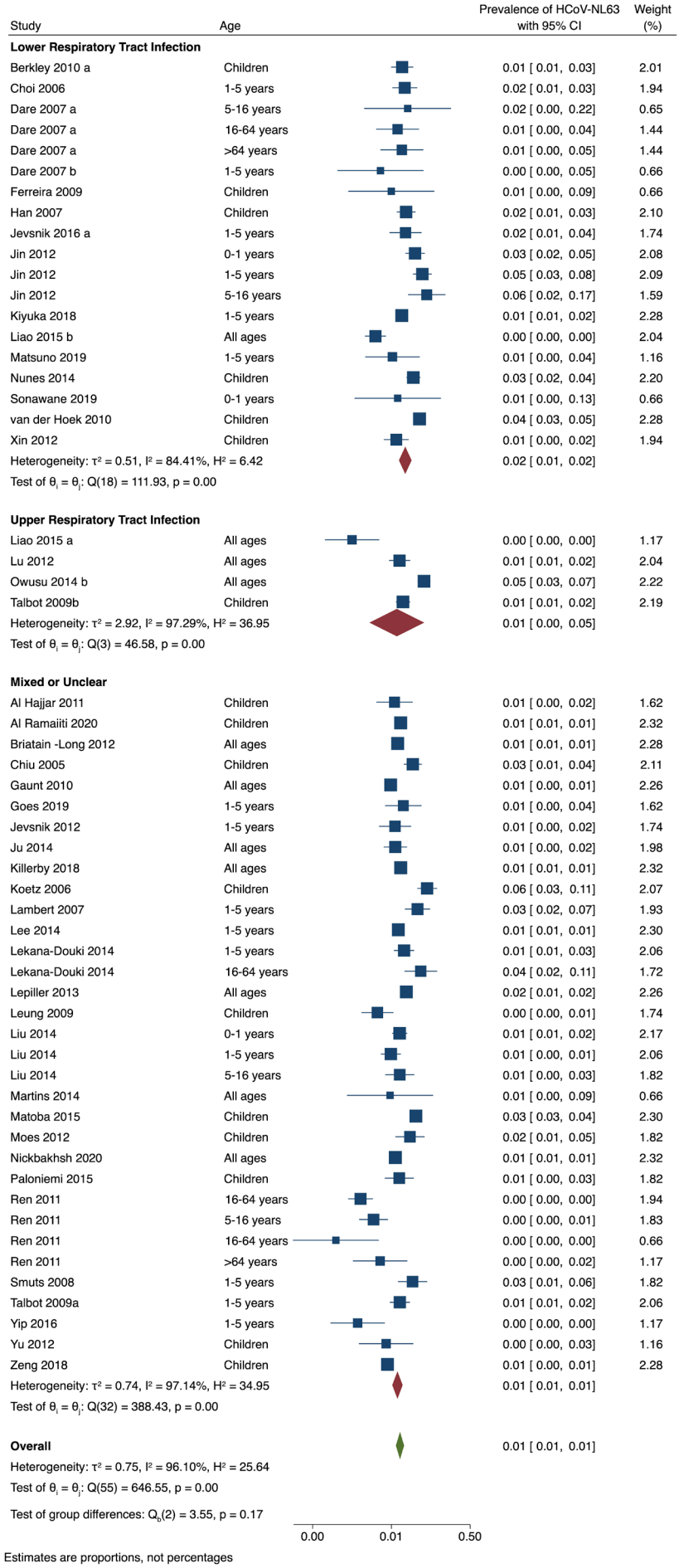
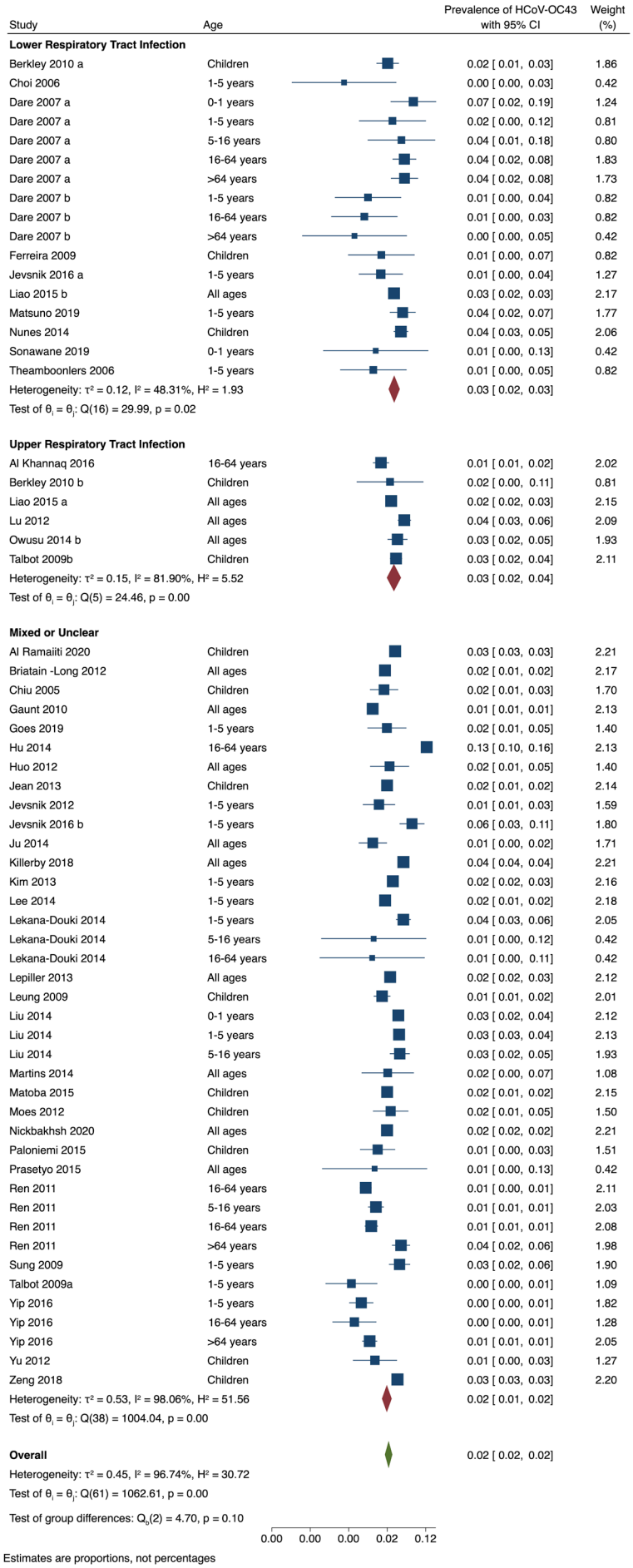


Figure 24. *Prevalence of HCoV-OC43 by infection type*



Prevalence by country income level

The following forest plots show the results for the meta-analyses of prevalence, sub-grouped by country income level.

Figure 25. *Prevalence of HCoV (all) by income level*

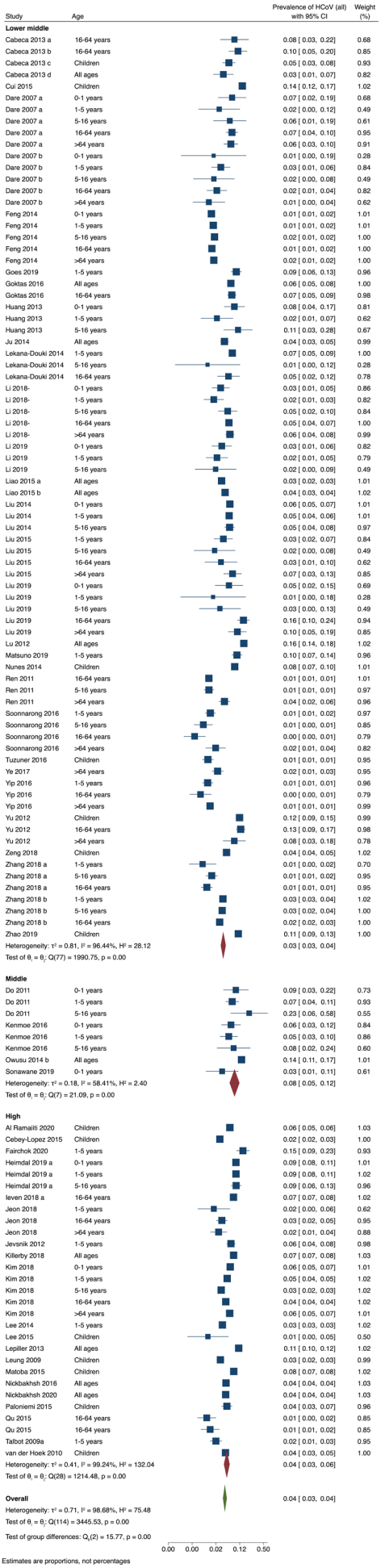
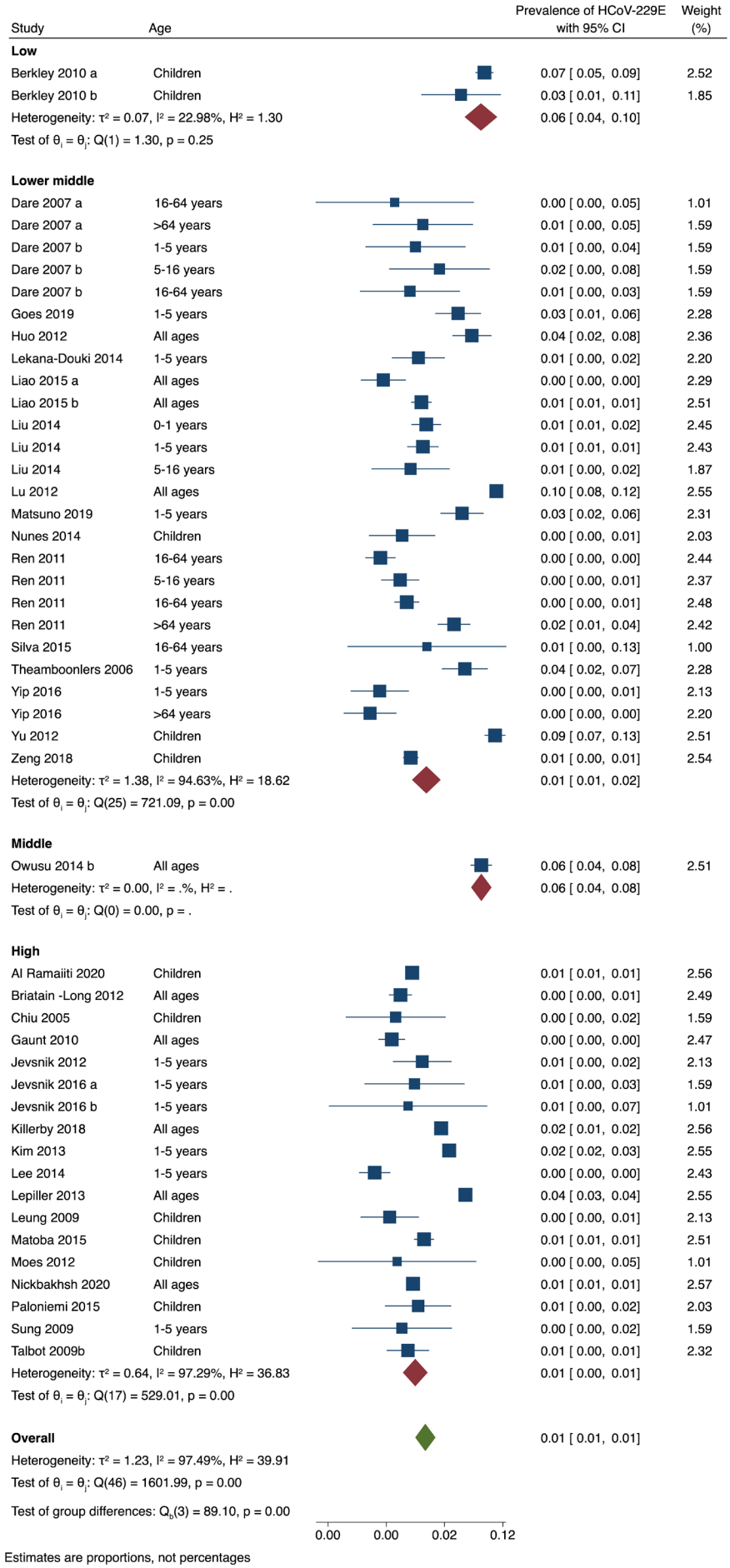

Study
Age
Prevalence of HCoV (all) with 95% CI
Weight (%)
Lower middle
Cabeca 2013 a 16-64 years 0.08 [0.03, 0.22] 0.68
Cabeca 2013 b 16-64 years 0.10 [0.05, 0.20] 0.85
Cabeca 2013 c Children 0.05 [0.03, 0.08] 0.93
Cabeca 2013 d All ages 0.03 [0.01, 0.07] 0.82
Cui 2015 Children 0.14 [0.12, 0.17] 1.02
Dare 2007 a 0-1 years 0.07 [0.02, 0.19] 0.68
Dare 2007 a 1-5 years 0.02 [0.00, 0.12] 0.49
Dare 2007 a 5-16 years 0.06 [0.01, 0.19] 0.61
Dare 2007 a 16-64 years 0.07 [0.04, 0.10] 0.95
Dare 2007 a >64 years 0.06 [0.03, 0.10] 0.91
Dare 2007 b 0-1 years 0.01 [0.00, 0.19] 0.28
Dare 2007 b 1-5 years 0.03 [0.01, 0.06] 0.84
Dare 2007 b 5-16 years 0.02 [0.00, 0.08] 0.49
Dare 2007 b 16-64 years 0.02 [0.01, 0.04] 0.82
Dare 2007 b >64 years 0.01 [0.00, 0.04] 0.62
Feng 2014 0-1 years 0.01 [0.01, 0.02] 1.01
Feng 2014 1-5 years 0.01 [0.01, 0.02] 1.01
Feng 2014 5-16 years 0.02 [0.01, 0.02] 1.00
Feng 2014 16-64 years 0.01 [0.01, 0.02] 1.00
Feng 2014 >64 years 0.02 [0.01, 0.02] 1.00
Goes 2019 1-5 years 0.09 [0.06, 0.13] 0.96
Goktas 2016 All ages 0.06 [0.05, 0.08] 1.00
Goktas 2016 16-64 years 0.07 [0.05, 0.09] 0.98
Huang 2013 0-1 years 0.08 [0.04, 0.17] 0.81
Huang 2013 1-5 years 0.02 [0.01, 0.07] 0.62
Huang 2013 5-16 years 0.11 [0.03, 0.28] 0.67
Ju 2014 All ages 0.04 [0.03, 0.05] 0.99
Lekana-Douki 2014 1-5 years 0.07 [0.05, 0.09] 1.00
Lekana-Douki 2014 5-16 years 0.01 [0.00, 0.12] 0.28
Lekana-Douki 2014 16-64 years 0.05 [0.02, 0.12] 0.78
Li 2018- 0-1 years 0.03 [0.01, 0.05] 0.86
Li 2018- 1-5 years 0.02 [0.01, 0.03] 0.82
Li 2018- 5-16 years 0.05 [0.02, 0.10] 0.84
Li 2018- 16-64 years 0.05 [0.04, 0.07] 1.00
Li 2018- >64 years 0.06 [0.04, 0.08] 0.99
Li 2019 0-1 years 0.03 [0.01, 0.06] 0.82
Li 2019 1-5 years 0.02 [0.01, 0.05] 0.79
Li 2019 5-16 years 0.02 [0.00, 0.09] 0.49
Liao 2015 a All ages 0.03 [0.02, 0.03] 1.01
Liao 2015 b All ages 0.04 [0.03, 0.04] 1.02
Liu 2014 0-1 years 0.06 [0.05, 0.07] 1.01
Liu 2014 1-5 years 0.05 [0.04, 0.06] 1.01
Liu 2014 5-16 years 0.05 [0.04, 0.08] 0.97
Liu 2015 1-5 years 0.03 [0.02, 0.07] 0.84
Liu 2015 5-16 years 0.02 [0.00, 0.08] 0.49
Liu 2015 16-64 years 0.03 [0.01, 0.10] 0.62
Liu 2015 >64 years 0.07 [0.03, 0.13] 0.85
Liu 2019 0-1 years 0.05 [0.02, 0.15] 0.69
Liu 2019 1-5 years 0.01 [0.00, 0.18] 0.28
Liu 2019 5-16 years 0.03 [0.00, 0.13] 0.49
Liu 2019 16-64 years 0.16 [0.10, 0.24] 0.94
Liu 2019 >64 years 0.10 [0.05, 0.19] 0.85
Lu 2012 All ages 0.16 [0.14, 0.18] 1.02
Matsuno 2019 1-5 years 0.10 [0.07, 0.14] 0.96
Nunes 2014 Children 0.08 [0.07, 0.10] 1.01
Ren 2011 16-64 years 0.01 [0.01, 0.01] 1.01
Ren 2011 5-16 years 0.01 [0.01, 0.01] 0.97
Ren 2011 >64 years 0.04 [0.02, 0.06] 0.96
Soonnarong 2016 1-5 years 0.01 [0.01, 0.02] 0.97
Soonnarong 2016 5-16 years 0.01 [0.00, 0.01] 0.85
Soonnarong 2016 16-64 years 0.00 [0.00, 0.01] 0.79
Soonnarong 2016 >64 years 0.02 [0.01, 0.04] 0.82
Tuzuner 2016 Children 0.01 [0.01, 0.01] 0.95
Ye 2017 >64 years 0.02 [0.01, 0.03] 0.95
Yip 2016 1-5 years 0.01 [0.01, 0.01] 0.96
Yip 2016 16-64 years 0.00 [0.00, 0.01] 0.79
Yip 2016 >64 years 0.01 [0.01, 0.01] 0.99
Yu 2012 Children 0.12 [0.09, 0.15] 0.99
Yu 2012 16-64 years 0.13 [0.09, 0.17] 0.98
Yu 2012 >64 years 0.08 [0.03, 0.18] 0.78
Zeng 2018 Children 0.04 [0.04, 0.05] 1.02
Zhang 2018 a 1-5 years 0.01 [0.00, 0.02] 0.70
Zhang 2018 a 5-16 years 0.01 [0.01, 0.02] 0.95
Zhang 2018 a 16-64 years 0.01 [0.01, 0.01] 0.95
Zhang 2018 b 1-5 years 0.03 [0.03, 0.04] 1.02
Zhang 2018 b 5-16 years 0.03 [0.02, 0.04] 1.00
Zhang 2018 b 16-64 years 0.02 [0.02, 0.03] 1.00
Zhao 2019 Children 0.11 [0.09, 0.13] 1.00
Heterogeneity: τ² = 0.81, I² = 96.44%, H² = 28.12 0.03 [0.03, 0.04]
Test of θi = θj: Q(77) = 1990.75, p = 0.00
Middle
Do 2011 0-1 years 0.09 [0.03, 0.22] 0.73
Do 2011 1-5 years 0.07 [0.04, 0.11] 0.93
Do 2011 5-16 years 0.23 [0.06, 0.58] 0.55
Kenmoe 2016 0-1 years 0.06 [0.03, 0.12] 0.84
Kenmoe 2016 1-5 years 0.05 [0.03, 0.10] 0.86
Kenmoe 2016 5-16 years 0.08 [0.02, 0.24] 0.60
Owusu 2014 b All ages 0.14 [0.11, 0.17] 1.01
Sonawane 2019 0-1 years 0.03 [0.01, 0.11] 0.61
Heterogeneity: τ² = 0.18, I² = 58.41%, H² = 2.40 0.08 [0.05, 0.12]
Test of θi = θj: Q(7) = 21.09, p = 0.00
High
Al Ramaiiti 2020 Children 0.06 [0.05, 0.06] 1.03
Cebey-Lopez 2015 Children 0.02 [0.02, 0.03] 1.00
Fairchok 2020 1-5 years 0.15 [0.09, 0.23] 0.93
Heimdal 2019 a 0-1 years 0.09 [0.08, 0.11] 1.01
Heimdal 2019 a 1-5 years 0.09 [0.08, 0.11] 1.02
Heimdal 2019 a 5-16 years 0.09 [0.06, 0.13] 0.96
Ieven 2018 a 16-64 years 0.07 [0.07, 0.08] 1.02
Jeon 2018 1-5 years 0.02 [0.00, 0.06] 0.62
Jeon 2018 16-64 years 0.03 [0.02, 0.05] 0.95
Jeon 2018 >64 years 0.02 [0.01, 0.04] 0.88
Jevsnik 2012 1-5 years 0.06 [0.04, 0.08] 0.98
Killerby 2018 All ages 0.07 [0.07, 0.08] 1.03
Kim 2018 0-1 years 0.06 [0.05, 0.07] 1.01
Kim 2018 1-5 years 0.05 [0.04, 0.05] 1.02
Kim 2018 5-16 years 0.03 [0.02, 0.03] 1.02
Kim 2018 16-64 years 0.04 [0.04, 0.04] 1.02
Kim 2018 >64 years 0.06 [0.05, 0.07] 1.01
Lee 2014 1-5 years 0.03 [0.03, 0.03] 1.02
Lee 2015 Children 0.01 [0.00, 0.05] 0.50
Lepiller 2013 All ages 0.11 [0.10, 0.12] 1.02
Leung 2009 Children 0.03 [0.02, 0.03] 0.99
Matoba 2015 Children 0.08 [0.07, 0.08] 1.02
Nickbakhsh 2016 All ages 0.04 [0.04, 0.04] 1.03
Nickbakhsh 2020 All ages 0.04 [0.04, 0.04] 1.03
Paloniemi 2015 Children 0.04 [0.03, 0.07] 0.96
Qu 2015 16-64 years 0.01 [0.00, 0.02] 0.85
Qu 2015 16-64 years 0.01 [0.01, 0.02] 0.85
Talbot 2009a 1-5 years 0.02 [0.01, 0.03] 0.95
van der Hoek 2010 Children 0.04 [0.03, 0.05] 1.00
Heterogeneity: τ² = 0.41, I² = 99.24%, H² = 132.04 0.04 [0.03, 0.06]
Test of θi = θj: Q(28) = 1214.48, p = 0.00
Overall 0.04 [0.03, 0.04]
Heterogeneity: τ² = 0.71, I² = 98.68%, H² = 75.48
Test of θi = θj: Q(114) = 3445.53, p = 0.00
Test of group differences: Q_b(2) = 15.77, p = 0.00
0.00 0.00 0.02 0.12 0.50
Estimates are proportions, not percentages

Figure 26. *Prevalence of HCoV-229E by income level*



Estimates are proportions, not percentages

Figure 27. *Prevalence of HCoV-HKU1 by income level*

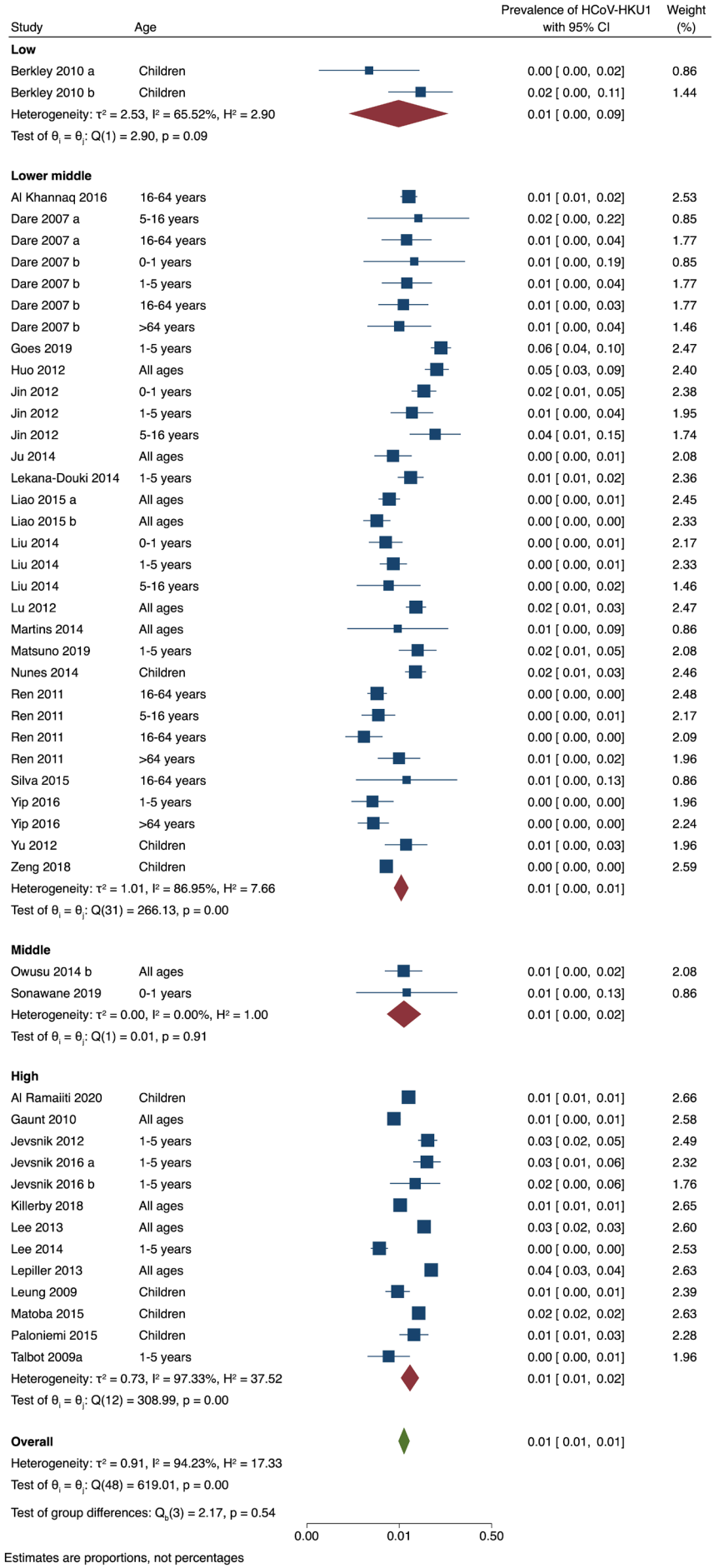


Figure 28. *Prevalence of HCoV-NL63 by income level*

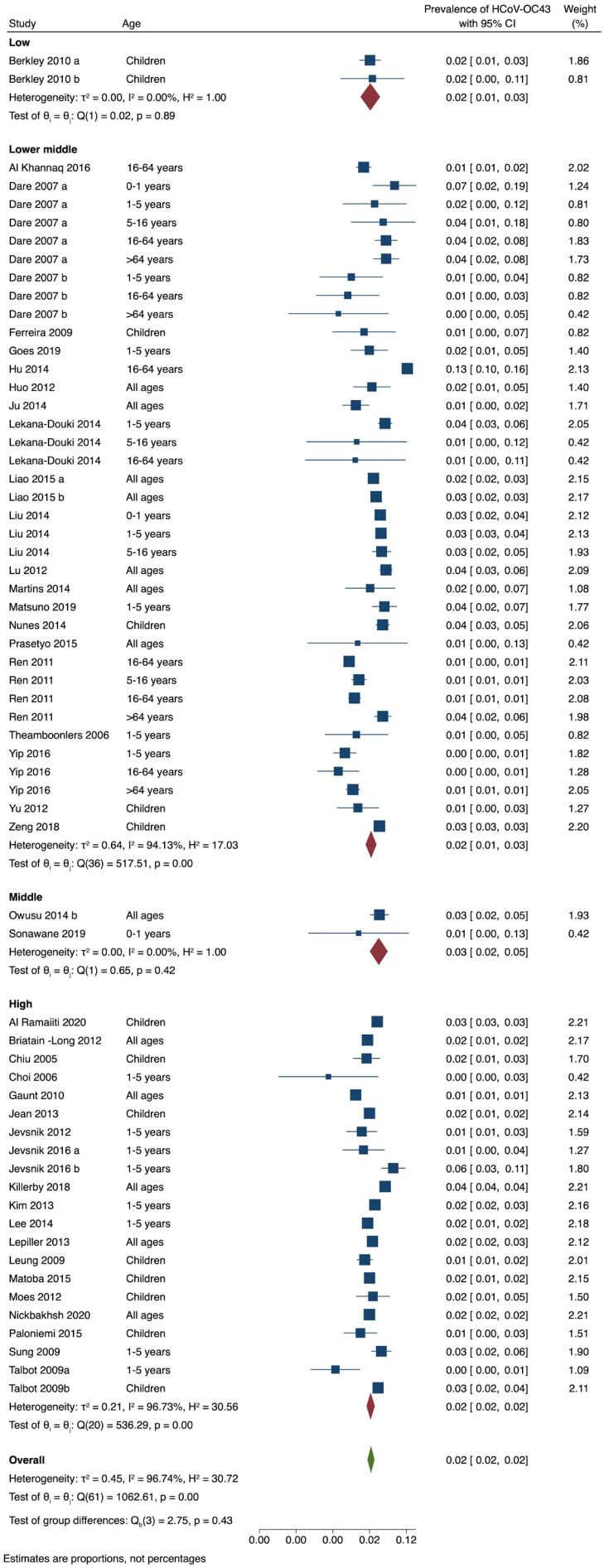
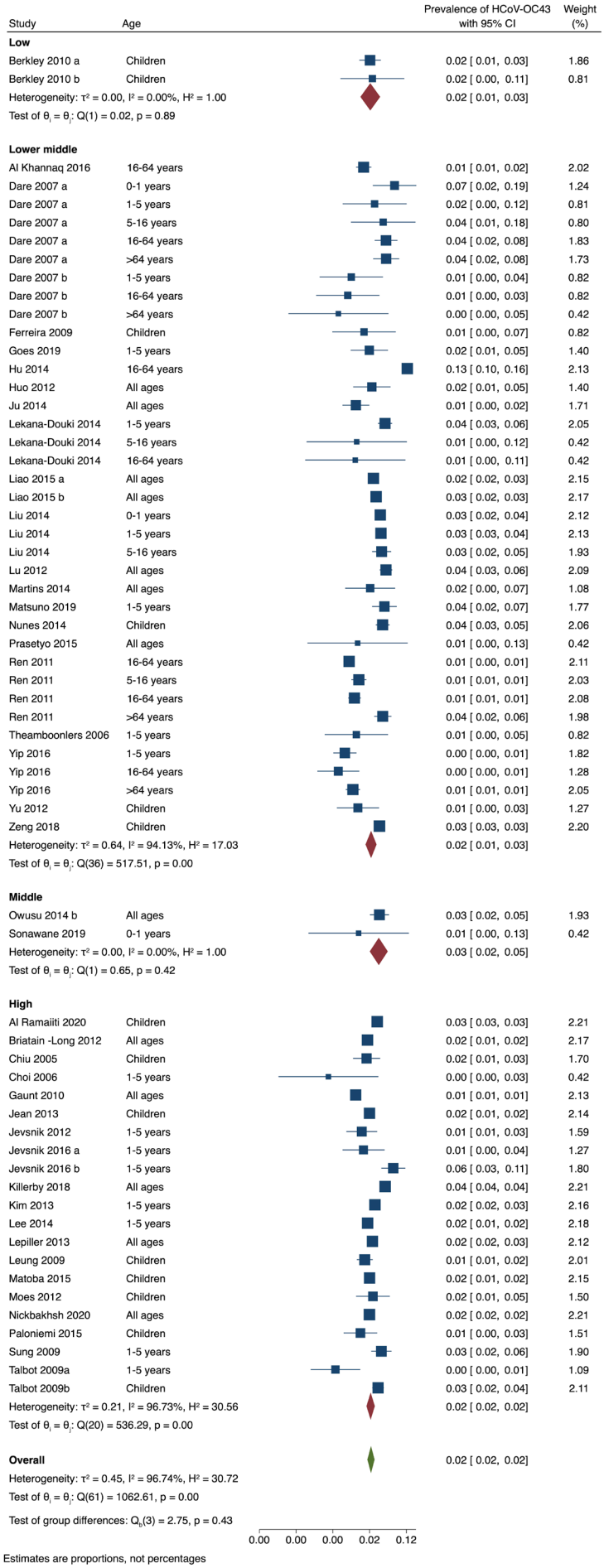


Figure 29. *Prevalence of HCoV-OC43 by income level*



Prevalence by country income level

The following forest plots show estimates of prevalence over time.

Figure 30. *Prevalence of HCoV (all) over time*

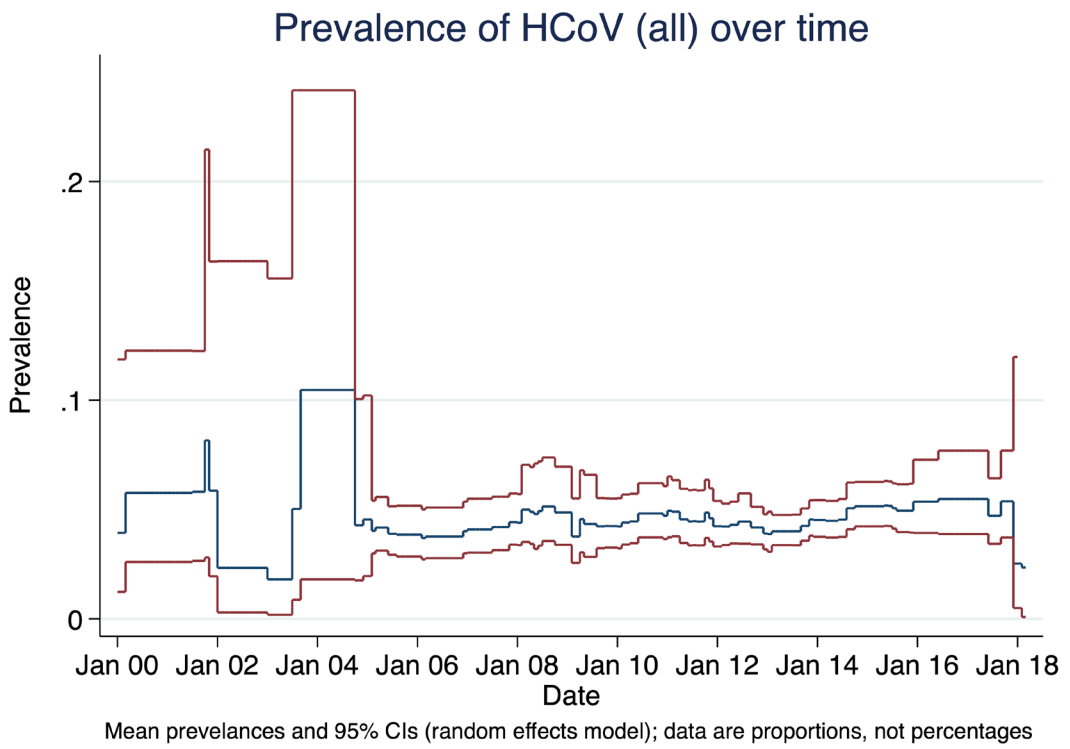


Figure 31. *Prevalence of HCoV-229E over time*

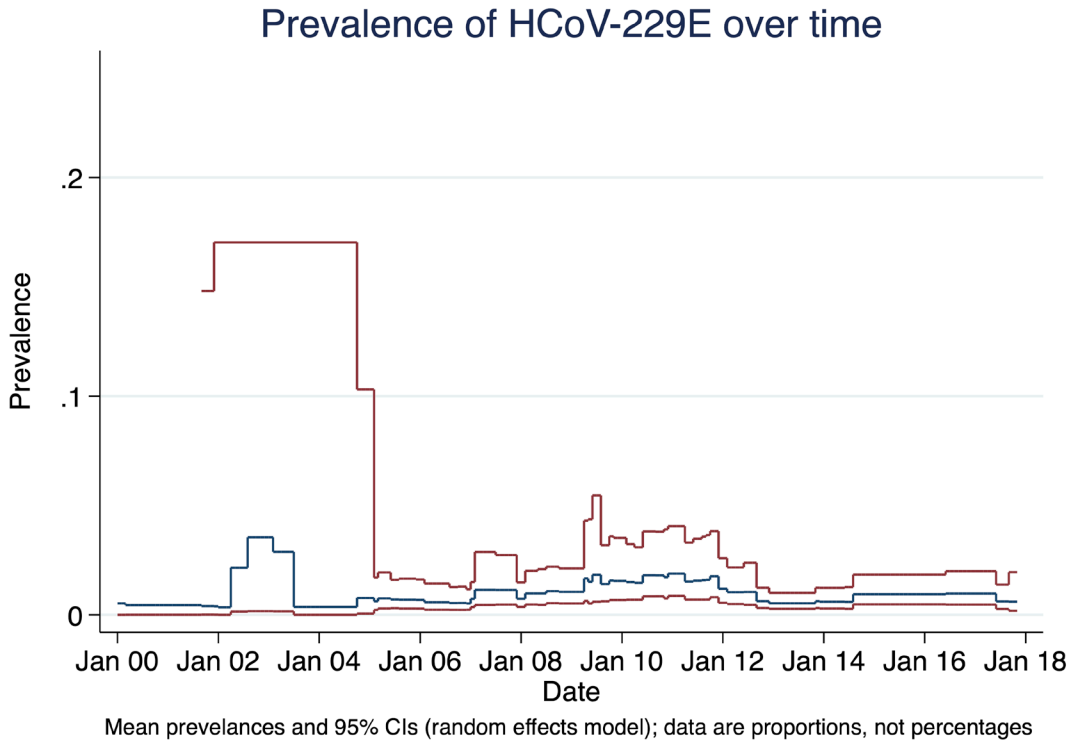


Figure 32. *Prevalence of HCoV-HKU1 over time*

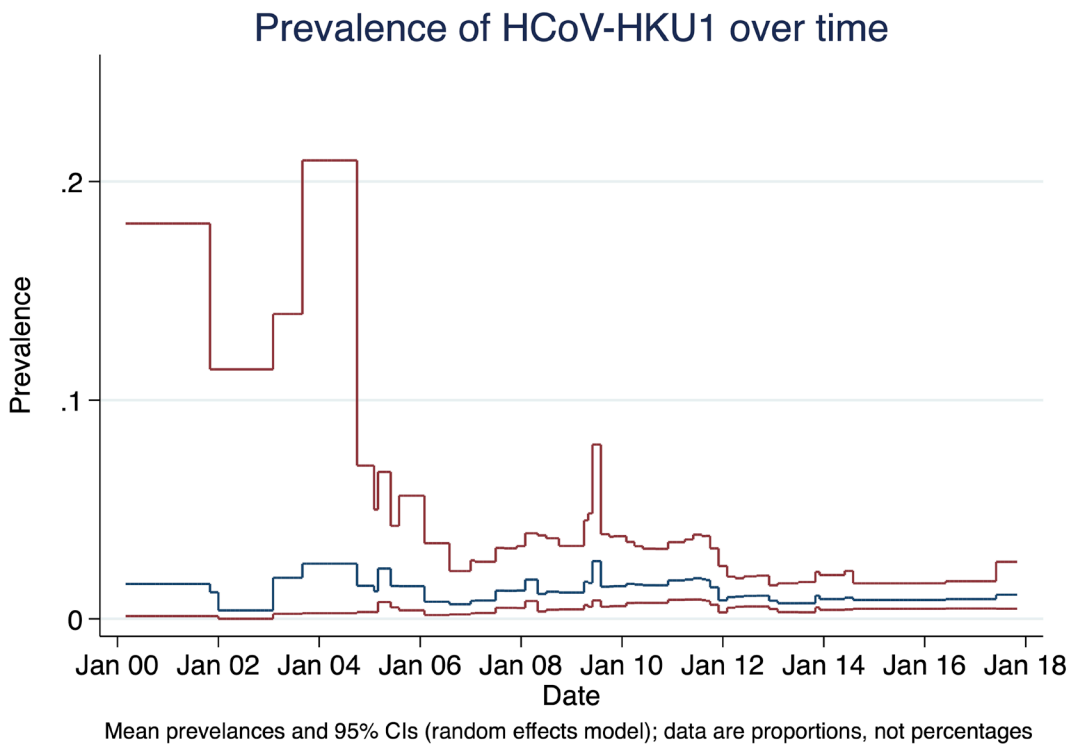


Figure 33. *Prevalence of HCoV-NL63 over time*

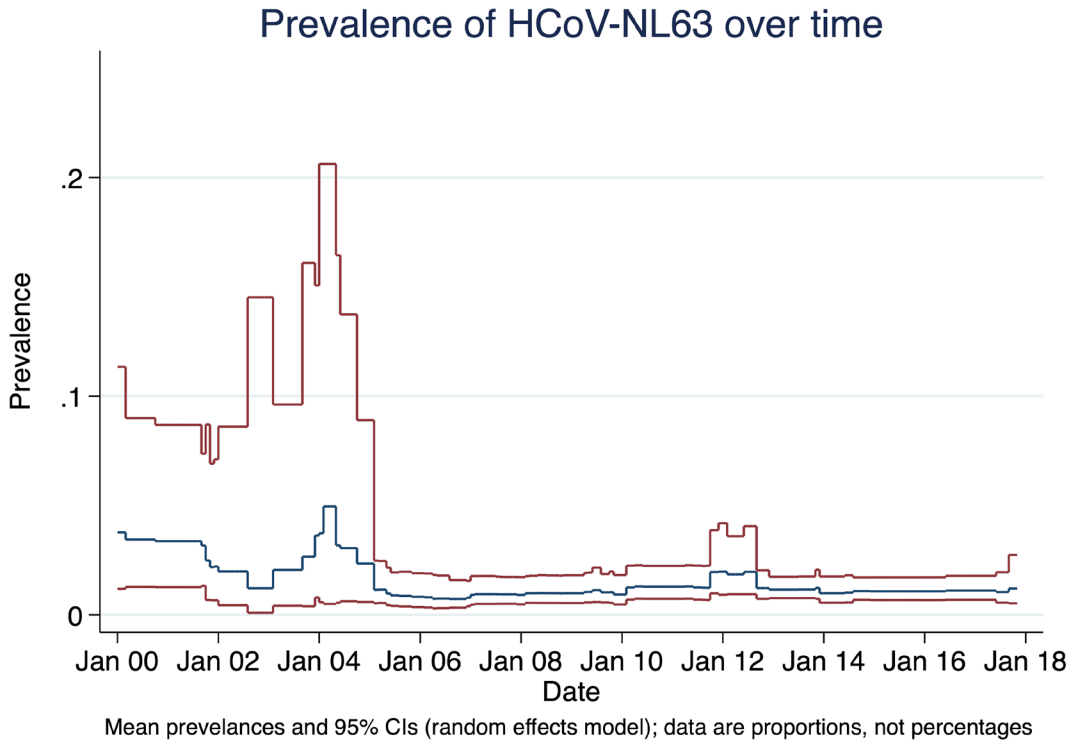
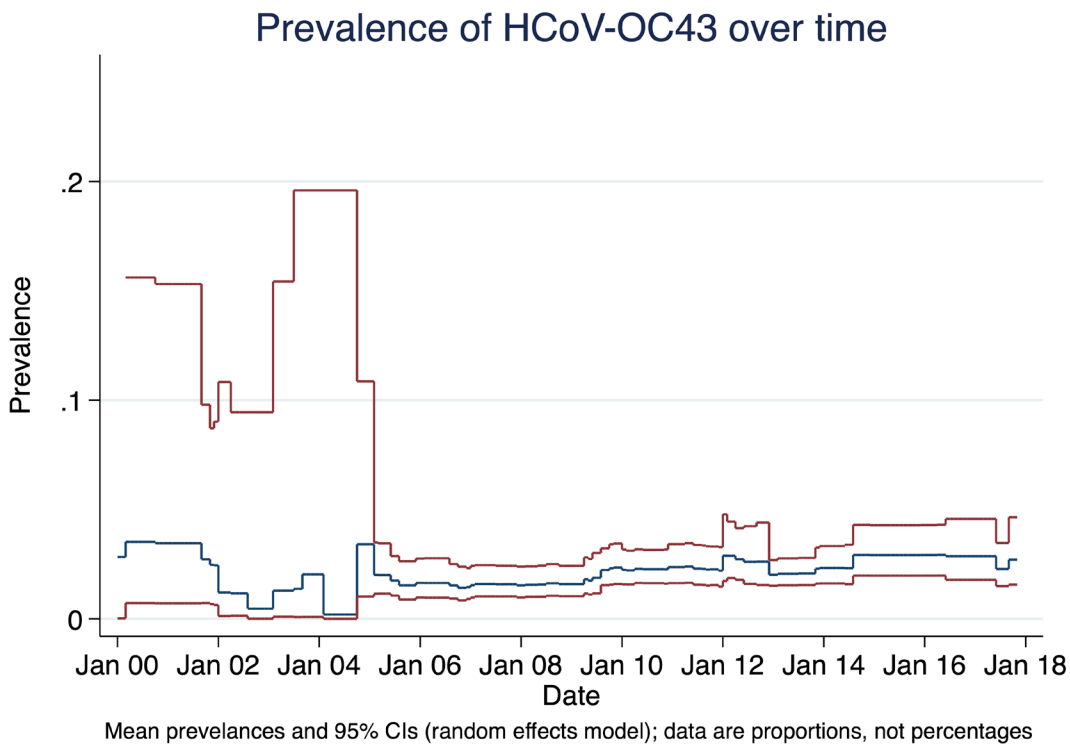


Figure 34. *Prevalence of HCoV-OC43 over time*



Cases versus controls

The following forest plots show estimates of the relative prevalence of each virus, comparison cases to controls.

Figure 35. *Relative prevalence of HCoV (all)*

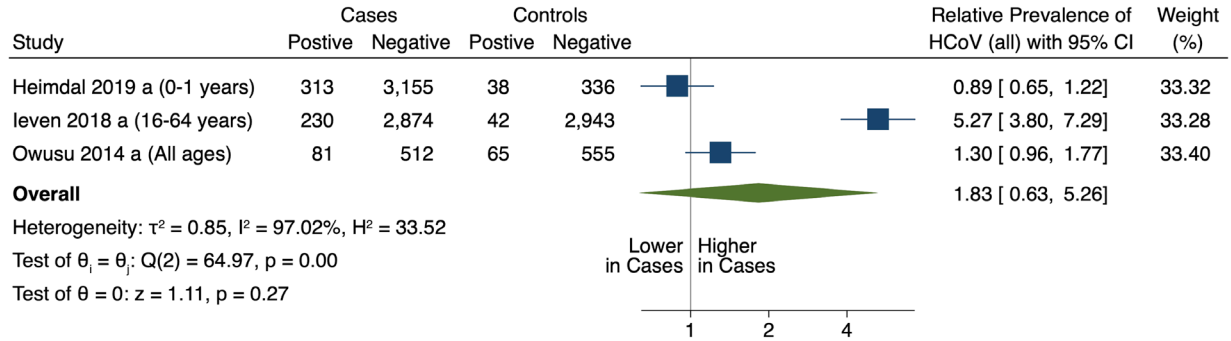


Figure 36. *Relative prevalence of HCoV-229E*

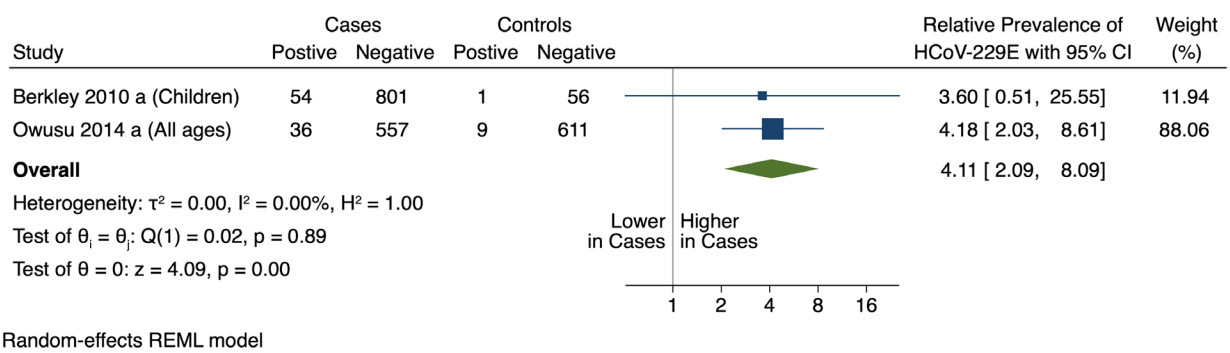


Figure 37. *Relative prevalence of HCoV-HKU1*

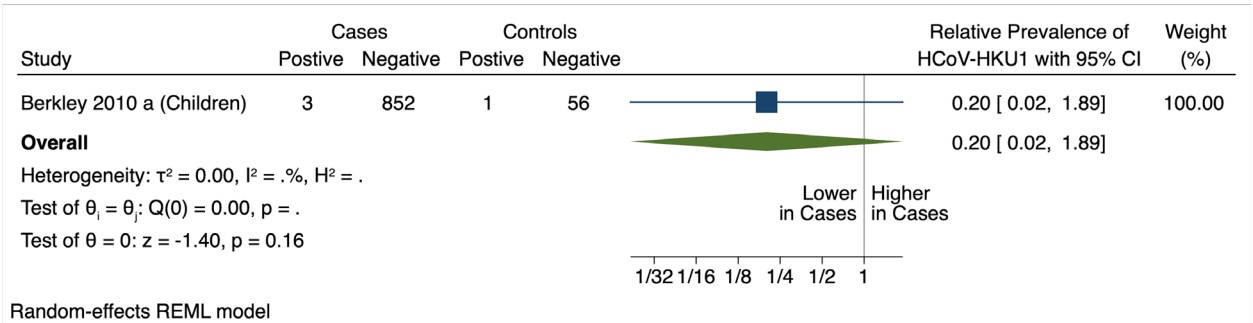


Figure 38. *Relative prevalence of HCoV-NL63*

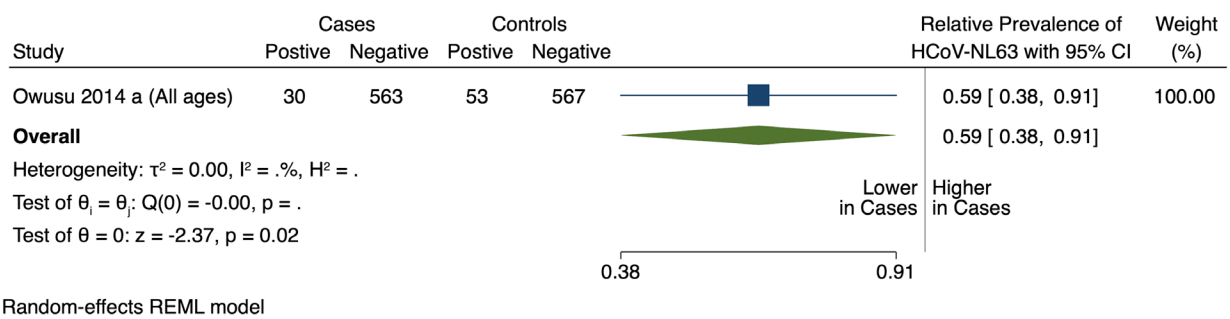
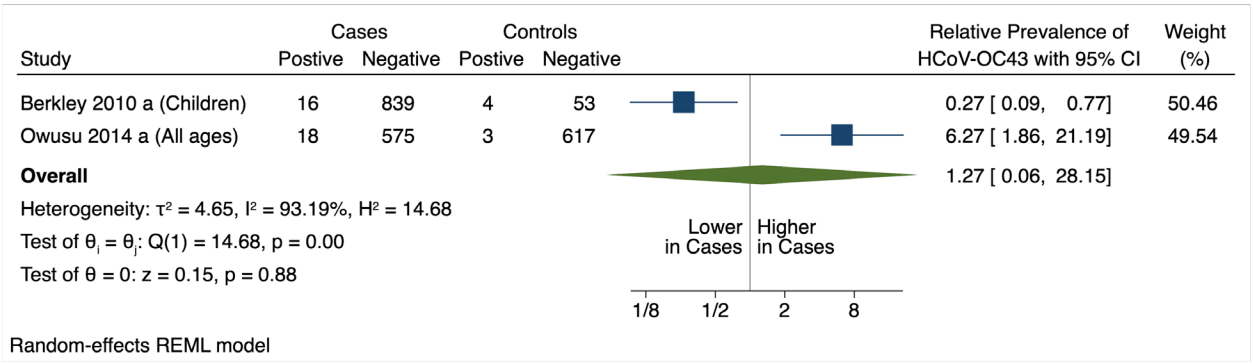


Figure 39. *Relative prevalence of HCoV-OC43*



Appendix 4. Co-infections among HCoV positive cases

Author Year	No samples	No (%) co-infections among all HCoVs detected	No (%) HCoV-229E	No (%) HCoV-NL63	No (%) HCoV-OC43	No (%) HCoV-HKU1	No (%) HCoV-HCoV co-infections of all HCoV infections	HCoV co-infections with one, or more, other viruses
Al Khannaq 2016	2,060	0/48 (**0**)	-	-	0/26	0/22	None.	NA.
Cebey-Lopez 2015	204	4/5 (**80**)	-	-	-	-	NR	HRV: 2; HBoV:1; >1: RSV+HRV:1
Chiu 2005	587	5/26 (**19.2**)	0/2(**0**)	3/15(**20.0**)	2/9(**22.2**)	-	NR	NL63: IFV A: 3; OC43: PIV1:2
Cui 2015	1,074	139/155 (**89.7**)	-	-	-	-	NR	51 double; 62 triple;15 quadruple, 11>4 virus*
Dare 2007	734	25/82 (**30.5**)	5/13 (**38.5**)	9/19 (**47.4**)	7/36 (**19.4**)	4/15 (**26.7**)	NR	*All:* IFV:5; RV: 4; PTV-1-3: 3; RSV: 2; MPV:2; AV 1: HBoV:1; >1 :9: *229E*; MPV: 1; IFV:1; RV: 1; >1: 2; *OC43*: PTV-1-3-:1; MPV:1: IFV:1; HRV: 1; >1:3; *HKU1*: RSV:2; PTV-1-3-:1; IFV:1: >1: 2; *NL63*; PTV-1-3-:1; IFV:2; HRV: 2; AV: 1: BoV:1; >1: 2;
Fairchok 2020	318	34/48 (**77.0**)	-	-	-	-	NR	*
Gaunt 2010	11,661	78/280 (**27.8**)	4/35 (**11.2**)	22/61 (**36.1**)	44/111 (**39.6**)	24/61 (**39.3**)	HCoV-NL63 +OC43: 2 (0.7) None for 229E/HKU1.	*229E*: AdV: 3; HRSV:1 (double); *NL63*: RSV:10; AdV:7; IFV B: 1; PIV-3: ;2 (14 double, 4 triple); *OC43*: RSV:26; AdV:17; IFV A:4; PIV-3:1 (38 double, 6 triple) *HKU1*: RSV:17; AdV:3; PIV-1:2; PIV-3: 2 (22 double,1 triple)
Goktas 2016	845	36/51 (**70.6**)	-	-	-	-	NR	12 double; 22 triple: 2>3 virus; *
Han 2007	872	-	-	2/14 (**14.3**)	-	-	NR	RSV:1; RSV+MPV:1
Heimdal 2019 (cases)	3,458	213/313 (**68.1**)	12/18 (**66.7**)	69/101 (**68.3**)	96/146 (**65.8**)	38/50 (**76.0**)	HCoV-229E +HCoV-NL63: 2 (0.6)	Common co-infection: HRV (24.9%), RSV (23.3%), HEV (16.6%) (41.9% double; 26.2% triple).
Heimdal 2019 (controls)	38	26/38 (**68.4**)	5/6 (**83.3**)	7/12 (**58.3**)	9/14 (**64.2**)	6/7 (**85.7**)	HCoV-229E+HCoV-NL63 :1 (2.6)	15.8% double; 52.6% triple. Common co-infection: HRV (42.1%), HEV (34.2%), PIV 1–4 (21.1%)
Hu 2014	559	-	-	-	25/70 (**36.0**)	-	HCoV-OC43+ HCoV-HKU1: 2 (2.8)	Common co-infections: HRV: 6 (8.6), IFV A:4(5.7), others <5% each.
Huang 2013	279	11/14 (**78.6**)	-	-		-	NR	HCoV-OC43:1; HCoV-NL63: 7;HCoV- HKU1: 2; HCoV-229E: 1 (3 double; 8 >2 virus). *

Jean 2013 (cases)	3,847	-	-	-	22/68 (**32.4**)	-	None.	AdV:12; RV/EV: 6; RSV A/B:2; PIV 1-3:3; IFV:0; hMPV:0
Jean 2013 (controls)	136	-	-	-	62/136 (**45.6**)	-	None.	AdV:7; RV/EV: 30; RSV A/B:15; PIV 1-3:3; IFV:3; hMPV:0
Jesvnik 2012	664	28/40 (**70.0**)	-	-	-	-	NR	Common co-infections: RhV (42.8%), HBoV (32.1%), RSV (28.6%), hMPV (21.4%), AdV (3.6%) (18 dual, 6 triple, 4 quadruple)
Jin 2010	645	9/19 (**47.5**)	-	-	-	-	NR	Double: RSV: 6; HRV:1; Triple: RSV+ IFV A; 1; HRV + AdV:1.
Kenmoe 2016	347	11/20 (**55.0**)	-	-	-	-	NR	AdV:2; RSV:1; RV/EV:1; PIV:1; HBoV:0 (6 double; 4 triple; 1 quadruple)
Killerby 2018	20,806	622/1,538 (**40.4**)	111/325 (**34.1**)	100/253 (**39.5**)	338/836 (**40.4**)	73/151 (**48.3**)	All:28 (1.8): HCoV-OC43+HCoV-NL63: 8; HCoV-OC43+HCoV-229E: 8; HCoV-OC43+HCoV-HKU1:4; HCoV-NL63+HCoV-229E: 3; HCoV-NL63+HCoV-HKU1: 5	Common co-infections: RSV (11%), HRV/EV (6.6%), IFV A (5.7%); 1.7% reported two or more HCoV species,
Kim 2013	5,318	-	39/10 (**38.2**)	-	59 /123 (**48.0**)	-	NR	5 HCoV-OC43, HRSV-A, and HRV co-infections*
Lambert 2007	543	-	-	10/18 (**55.5**)	-	-	NA	PICs: 6; RSV:1; IFV A:1, HMPV:1, HMPV/PICs:1
Lee 2014	9,628	113/205 (**55.1**)	9/17 (**53**)	38/100 (**38.0**);	54/156 (**35.0**);	12/22 (**55**)	NR	HCoV-OC43*: Double:46; >2: 8; HCoV-NL63: Double.38; >2:3; HCoV-HKU1*: Double:10; >2: 2; HCoV-229E: Double: 9; >2: 0.
Lekana-Douki 2014	1,041	33/61 (**54.1**)	4/6 (**67.0**)	6/12 (**50.0**)	15/33 (**45.4**)	8/10 (**80.0**)	NR	HCoV-OC43: AdV:2, HRV:1; P (H1N1):1; PIV3:3; IVF B:1; HCoV-NL63: AdV:1; HCoV-HKU1: AdV:1; EV:1; RSV:1; IFV:1; HCoV-229E: RSV:1; P (H1N1):1, IFV B:2
Lepiller 2013	6,014	141/291(**45.0**)	-	-	-	-	HCoV-229E+HCoV-HKU1: 1 (0.3)	NR
Liao 2015	12,502	313/665 (**47.1**)	-	-	-	-	NR	IFV A: 28%; RSV:20%; EV:10%; MP:8%; IFV B:8%; AdV:6%; the

								rest all <5%: HMPV; HRV; PIV1-4; HBoV and CP
Liu 2014	4,242	135/231 (**58.4**)	21/37 (**56.8**)	27/39 (**69.2**)	76/138 (**55.1**)	11/17 (**64.7**)	All:10 (4.3); HCoV-229E+HCoV-OC43:5; HCoV-229E+HCoV-NL63: 2; HCoV-OC43+HCoV-NL63: 2; HCoV-NL63+HCoV-HKU1:1	HCoV-*229E:* IFV A/B: 5; RSV:8; EV:3; AdV:3; PIV1-4: 2; HCoV-*OC43*: IFV A/B:19; RSV:19; EV:9; AdV:4; PIV1-4: 21; HCoV-*NL63*: IFV A/B:4; RSV:10; EV:5; AdV:5; PIV1-4:2; HCoV-*HKU1*: IFV A/B:3; RSV:1; EV: 0; AdV:1; PIV1-4: 0;
Liu 2015	607	7/22 (**31.8**)	-	-	-	-	NR	*
Liu 2019	445	20/36 (**55.6**)	-	-	-	-	HCoV-OC43+HCoV-HKU1: 5 (13.8)	IFV:6; ADV:2; RV/EV:1; RV/EV+IFV:1
Lu 2012	981	48/157 (**30.6**)	-	-		-	All:4 (2.5); HCoV-OC43+HCoV-229E:3; HCoV-OC43+HCoV-229E+HCoV-NL63:1 HCoV+HCoV+ additional virus: +IFV A:5; +hRSV:1; +RV:2)	All: IFV A:18; IFV B:1; AdV:6; hRSV:1; RV:18; hMPV:1; >30% with hRV and IFV A; HCoV-*229E:* IFV A:10; IFV B: 1; AdV: 2; RV:9; hMPV:1; HCoV-*NL63*: IFV A:1; HCoV-HKU1+IFV A: 1; AdV+RV*:1; HCoV-HKU1+RV:1; HCoV-*HKU1*: IFV A:2; RV:1; HCoV-*OC43*: HCoV-229E+IFVA: 2; HCoV-HKU1+IFV A: 2; AdV:3; HCoV-HKU1+hRSV:1; RV:5; HCoV-NL63+RV:1;
Martins 2014	162	2/8 (**25**)					NR	NL63: RSV A/B:1; OC43:hMPV A/B: 1
Matoba 2015	4,342	81/332 (**24.4**)	11/38 (**28.9**)	38/133 (**28.6**)	16/78 (**20.5**)	16/83 (**19.3**)	NR	All: EV: 14; HPIV: 12; AdV:11, RhV: 10, CMV: 10; hMPV: 9, IFV: 5, RSV, 4, all others only 1 each (Parechovirus; Mumps; HSV; hPIV+RhV; PIV +Parechovirus; HMPV+CMV)
Moes 2005	309			2/7 (**28.6**)			NR	RSV type B:1; AdV +PIV:1. Unclear no of viruses tested.
Nunes 2014	509	57/77 (**74.0**)	3/4 (**75.0**)	19/24 (**79.2**)	26/34 (**76.5**)	9/15 (**60.0**)	All: 2 (2.6); HCoV-NL63+HCoV-HKU1 1; HCoV-OC43+HCoV-NL63:1;	All: hRV:21; RSV:14; WUPyV:13; hBoV: 12; KIPyV: 7; hMPV:10; PIV:4; IFV A:2; AdV:1
Owusu 2014	1.213	4 /150(**2.6**)	-	-	-	-	All: 4 (2.6); HCoV-OC43+HCoV-229E:3; HCoV-	NA.

							NL63+HCoV-229E:1	
Ren 2011	8,396	11/87 (**12.6**)	4/15 (**26.7**)	0/8 (**0**)	5/50 (**10.0**)	2/14 (**14.3**)	NR	HRV:4; PIV3:3; EV:2, IFV A/B:2. No co-infections for HCoV-NL63.
Sipulwa 2016	417	5/35 (**14.2**)	-	-	-	-	NR	HCoV-*HKU1:* RSV:1; IFV A+hAdV:1; HCoV-*OC43*: IFV A:1; IFV B;1; HCoV-*NL63*: IFV A+AdV:1 (3 double and 2 triple)
Soonnarong 2016	5,833	0/46 (0)	-	-	-	-	NA	NA
Talbot 2009	1,055	6 /19 (**32.0**)	-	-	-	-	NR	**RSV:4** (1 HCoV-HKU1; 3 HCoV-NL63); PIV:1 (HCoV-NL63); hMPV:1 (HCoV-NL63)
Theamboonlers 2006	226	1/10 (**10.0**)	-	-	-	-	HCoV-229E+HCoV-OC43:1 (10.0)	NA
Xin 2012	878	5/8 (**62.5**)	-	-	-	-	NR	RSV: 3, hMPV: 2
Ye 2017	967	3/20 (**15.0**)	-	-	-	-	NR	IFV A:1; HMPV:1; HRV:1
Yu 2012	416	14/49 (**28.6**)	15/39 (**38.5**)	0/2 (**0**)	1/4 (**25.0**)	1/4 (**25.0**)	NR	HCoV-*OC43*: AdV:1; HCoV-*229E*: IFV:5: AdV:3; PICs:6; PIV:1, HCoV-*HKU1*: PICs:1
Zeng 2018	11.399	231/489 (**47.2**)	38/65 (**58.4**)	33/60 (**55.0**)	161/346 (**46.5**)	19/38 (**50.0**)	All: 18 (3.6*); HCoV-229E+HCoV-OC43:15; HCoV-229E+HCoV-NL63:2*; HCoV-*OC43*+HCoV-NL63:2; HCoV-OC43+HCoV-HKU1:1; HCoV-NL63+HCoV-HKU1:1	**IFV A:50 (21.6); RSV:50 (21.6), MP:9(16.9);** HPIV:33(14.3); AdV:22 (9.5); EV:20(8.6); HBoV:15(6.5); HMPV: 15 (6.4); HRV:13(5.6); the rest all <5%;.Common co-infections (individual HCoVs): HCoV-*229 E*: RSV (26.3); HCoV-*OC43*: IFV A (23.6); HCoV-*NL63*: RSV (30.3); HCoV-*HKU1*: MP (42.7); IFV A (21.1)
Zhang 2018	13,048	101/294 (**34.7**)	-	-	-	-	HCoV-OC43+HCoV-HKU1: 1(0.3)	**IFV:30 (29.7); RSV:23 (22.8)**: **PIV: 12 (11.9):** HRV:10 (9.9); HMPV: 7 (6.9); AdV: 6 (5.9), All other < 5%+. Double: 91 (90.2); Triple:10 (9.8).

AdV: adenovirus; HBoV: human bocavirus; HCoV: human coronavirus; EV: entero virus; IFV A/B: influenza virus A/B; HMP: human metapneumovirus, MP: add here; NA: not applicable; HRV:human rhinovirus; PICs:picomavirus; PIV: parainfluenza virus; RSV: respiratory syncytial virus. * No information on the co-infecting viruses.

Appendix 5. Results of the quality assessment using the ROB-SPEO tool

Author Year	Risk of selection bias	Justification for rating	Risk of Numerator/ Denominator bias	Justification for rating	Overall risk of bias*
Al Hajjad 2011	Probably low	Prospective study. No definition of the condition and inclusion/exclusion criteria. All children were tested, and all presented with ARI.	Probably low	Unclear no of pts, but number of specimens described. All pts were tested.	Probably low
Al Khannaq 2016	Probably low	Prospective. All pts. presenting with URTI included and screened. URTI not further described/specified.	Probably low	Not explicitly stated the number of specimens tested, but appears to have been one from each pts.	Probably low
Al Romihi 2020	Probably high	Retrospective study, with retrospectively anlysed data. provided a definition of the condition (ILI).	High	The first three years have 100% missing data. Unclear if the number of samples and the number of pts are the same. Datasheets were cleaned or errors and duplicate samples taken within the same fortnight.	High
Berkley 2010	Probably low	Prospective. Diagnosis/inclusion criteria specified. Not all pts (critically ill) were tested.	Probably low	Number of pts the same as number of samples, and exclusions described.	Low
Britain-Long 2012	Probably high	Retrospective. Selection criteria not defined.	High	The number of pts and the number of samples are not the same.	High
Cabeca 2013	High	Retrospective study, that cannot include all eligible pts during a 9 year period. Unclear selection, and exclusions.	High	Unclear if number of pts and number of samples are the same, but there must be pts missing during the 9 year period.	High
Cebey-Lopez 2015	Probably low	Prospective. All but one patient included (missing data). Inclusion criteria (but not exclusion criteria provided).	Low	One sample per patient. Low.	Probably low
Chiu 2005	Probably low	Prospective. All children with signs and symptoms of respiratory infection presenting on Mondays, and later on Monday and Tues-	Probably low	Not explicitly stated that the number of samples were the same as the number of pts, but probably they were as this is a prospective study.	Probably low

		days. No definition of condition (signs and symptoms), or exclusion criteria.			
Choi 2006	Probably high	Retrospective Samples selected for analysis by random number sampling. Inclusion and exclusion criteria, and definition of condition under study provided.	Probably high	Samples selected did not differ from samples not selected. Unclear if the number of samples and the number of pts were the same.	Probably high
Cui 2015	Probably low	Prospective study. Inclusion criteria and WHO standard for ARI. No exclusion criteria.	Proabably high	Unclear if the number of pts and samples are the same.	Probably high
Dare 2007	Probably high.	Retrospective.	Probably high	Unclear if the number of pts and samples are the same.	Probably high
Do 2011	Probably low.	Prospective. Provides inclusion and exclusion criteria.	Probably low.	Unclear if the number of pts and samples are the same. Not so likely that the same patient would come back with LRTI.	Probably low
Fairchok 2020	Probably high.	Prospective cohort study. many of the children had repeat infections.	Probably high	Not the same number of patient s as number of samples.	Probably high.
Feng 2014	Probably low.	Prospective. 81 of 108 initially included hospitals were included in the analysis due to little data provided.	Probably high.	Unclear if number of pts and number of samples are the same, Various types of specimens used for the analysis.	Probably high.
Ferreira 2009	Probably low.	Prospective. Inclusion and exclusion criteria provided.	Probably low	Not stated whether the number of pts and the number of samples are the same, but it is likely they are.	Probably low.
Gaunt 2010	Probably high.	Retrospective. Includes also groups of people with comorbidities (unclear how many). Many different types of specimens collected. Not a well-defined group. In-pts- and out-pts (no common diagnosis)?	High	The number of pts and the number of samples were not the same.	High
Goes 2019	Proabably low	Prospective. Inclusion criteria (but no exclusion criteria) provided. No of children with different no of symptoms reported (but no definition of ARI).	Proabably low	Appear that the number of children and number of samples are the same.	Probably low
Goktas 2016	Proabably high	Retrospective. The total sample from which the study population (people with ARTI) is drawn is not described. Neither is the criteria for inclusion of ARTI	Probably low	The number of pts and the number of samples appear to be the same. But this is not explicitly stated.	Probably high.

		pts. Unclear if pts are in- or outpts or both.			
Han 2007	Probably high.	Unclear if prospective. Unclear recruitment process. The total sample from which the study sample is drawn is mentioned, but exclusions are not described.	Probably low	The number of samples and the number of pts are not the same, but the difference is only 5 %.	Probably high.
Heimdal 2019	Probably low.	Prospective. Provides both inclusion and exclusion criteria.	Probably high.	The number of samples and the number of pts are not the same. The same child could be included more than once.	Proably high
Hu 2014	Probably low.	Prospective. Provide inclusion criteria (definition of condition) but little information on the population from which the sample is drawn. No exclusions described/or exclusion criteria.	Probably low	Unclear if the number of samples are the same as the number of pts, but the study is prospective.	Probably low
Huang 2013	Probably low	Prospective study. Inclusion criteria provided, and a definition of the condition	Low	The number of pts and the number of samples were the same.	Probably low
Huo 2012	Probably low.	Prospective. Description of inclusion criteria (and condition) provided. No exclusion criteria.	Probably low.	No information on number of pts, only on number of analysed samples. But prospective study so most likely one per patient.	Probably low.
Ieven 2018 a	Probably low.	Prospective. Definition of condition, inclusion /exclusion criteria.	Probably kow	Unclear if the number of samples are the same as the number of pts, but the study is prospective.	Probably low.
Jean 2013	Probably high	Retrospective.	Probably high	Unclear if number of samples are the same as number of pts.	Probably high
Jeon 2018	Probably high.	Prospective. Doctors were encouraged to sample ARI suspected cases, but unclear if they included all eligible subjects.	Probably high	Number of pts and number of samples are the same, but unclear if all eligible cases were included.	Probably high
Jevsnik 2012	Probably low.		Probably low	Not the same number of samples as number of children. But they had excluded samples from the same episode.	Proababl y low
Jevsnik 2016	Probably low.	Prospective. Describes the population from which the sample is drawn. Exclusions, and definition of condition.	Probably low.	Not the same number of samples as number of children. But they have excluded samples from the same episodes.	Probably low

Jin 2010	Probably low.	Appear to be prospective. Definition of condition, and inclusion (not exclusion) criteria provided.	Probably low	Number of pts and number of samples appear to be the same.	Probably low.
Jin 2012	Probably low.	Appear to be prospective. Definition of condition, and inclusion (not exclusion) criteria provided.	Probably low	Number of pts and number of samples appear to be the same.	Probably low.
Ju 2014	Proababl y high	Unclear if prospective. Unclear if all eligible pts were tested.	Probably high	Unclear if number of samples and number of pts are the same.	Ptobably high
Kenmoe 2016	Probably low	Prospective, and data collected at hospital. Diagnosis /inclusion criteria specified.	Probably low	Number of pts and number of samples analysed appear to be the same.	Probably low
Khadadah 2010	Probably low	Prospective, and data collected at hospital. Inclusion criteria WHO LRTI and American Thoracic association for adults.	Probably high	Not explicitly stated that the number of samples were the same as the number of pts.	Probably high
Killerby 2018	Probably high	Retrospective. No inclusion and inclusion criteria specified. Register study. Selection bias with certain laboratories or regions being overrepresented at certain times.	Probably high	The number pts and samples are not the same. and aggregated data reported might include multiple specimens from the same patient	Probably high
Kim 2013	Probably high	Retrospective. Unclear inclusion and exclusion criteria. Register study. Possible selection bias of participants and systematic differences in the study sample	Probably high	Not explicitly stated that the number of samples were the same as the number of pts, but probably they were as this is a retrospective study.	Probably high
Kim 2018	Probably high	Retrospective and total number of HCoV tests. Vague diagosis/inclusion criteria specified.	Probably low	Not explicitly stated that the number of samples were the same as the number of pts, but probably they were as this is a retrospective study.	Probably low
Kiyuka 2018	Probably low	Prosepective, and inclusion and reporting of selected cases	Probably low	Unclear if the number of pts and the number of samples are the same.	Probably low
Koetz 2006	High	Retrospective, and data collected at hospital. No diagnosis/inclusion criteria specified.	High	Unclear if the number of pts and the number of samples are the same. No information about duplicate sample from the individual or missing sample.	High
Lambert 2007	Probably high	Retrospective and data collected of parents. Possible selection bias. Inclusion de-	Probably high	Unclear if the number of pts and the number of samples are the same. Small sample size.	Probably high

		scribed, but possible selection bias according to samples and pts enrolled.			
Lee 2013	High	Retrospective, and data collected at hospital. Inclusion defined unclear, more symptom.	High	Unclear if the number of pts and the number of samples are the same. Small sample size.	High
Lee 2014	Probably high	Prospective, and data collected at hospital. Inclusion defined, and condition, vague inclusion criteria	Probably high	Unclear if the number of pts and the number of samples are the same.	Probably high
Lee 2015	Probably high	Prospective, and data collected at hospital. Inclusion defined, but selection bias, sampling, and short study period.	Probably high	Unclear if the number of pts and the number of samples are the same. No information about duplicate sample from the individual or missing sample.	Probably high
Lekana-Douki 2014	Probably low	Prospective, but good description of diagnosis/inclusion criteria specified. Selection age.	Probably low	Number of pts and number of samples appear to be the same.	Probably low
Lepiller 2013	Probably high	Retrospective. Unclear inclusion and exclusion criteria. Register study. Possible selection bias of participants and systematic differences in the study sample	Probably high	The number of samples tested and the number of participants are not the same (i.e. there may be more than one analysed (duplicate) sample from the same individual, or samples may be missing).	Probably high
Leung 2009	Probably high	Retrospective and prospective. No inclusion and exclusion criteria.	Probably high	Unclear if the number of pts and the number of samples are the same.	Probably high
Li 2018	Proably low	Prospective, and description of diagnosis/inclusion criteria specified. Selection bias, tested for HCov not reported	Probably low	Number of pts and number of samples analysed appear to be the same.	Probably low
Li 2019	Probably low	Prospective, and description of diagnosis/inclusion criteria specified.	Probably low	Number of pts and number of samples analysed appear to be the same.	Probably low
Liao 2015 a	Probably low	Prospective, and description of diagnosis/inclusion criteria specified.	Probably low	Number of pts and number of samples analysed appear to be the same.	Probably low
Liao 2015 b	Probably low	Prospective, and description of diagnosis/inclusion criteria specified.	Probably low	Number of pts and number of samples analysed appear to be the same.	Probably low
Liu 2014	Probably low	Prospective, and data collected at hospital. Inclusion specified and no exclusion.	Probably low	Number of pts and number of samples analysed appear to be the same.	Probably low
Liu 2015	Probably high	Prospective, and data collected at hospital. Inclusion specified and no exclusion.	Probably high	Unclear if the number of pts and the number of samples are the same.	Probably high

		Small sample size and selection in age groups			
Liu 2019	Probably high	Prospective, and data collected at hospital. Inclusion specified and no exclusion.	Probably high	Unclear if the number of pts and the number of samples are the same.	Probably high
Lu 2012	Probably low	Prospective, and data collected at hospital. Inclusion specified and no exclusion.	Probably low	Number of pts and number of samples analysed appear to be the same.	Probably low
Martins 2014	Probably high	Probably prospective, and data collected at hospital. Inclusion specified. Small sample size and possible selection bias	Probably high	Unclear if the number of pts and the number of samples are the same.	Probably high
Matoba 2015	Probably high	Prospective, and data collected at hospital. Inclusion unclear and no exclusion. Big sample size and selective reporting	Probably high	The number of samples tested and the number of pts are not the same (i.e. there may be more than one analysed (duplicate) sample from the same individual, or samples may be missing).	Probably high
Matsuno 2019	Probably low	Prospective, and data collected at hospital. Inclusion and exclusion specified. Small sample size.	Probably low	Number of pts and number of samples analysed appear to be the same.	Probably low
Moes 2012	Probably high	Probably prospective, inclusion and exclusion are not specified. Small sample size and possible selection bias.	Probably high	The number of samples tested and the number of pts is not the same (i.e. there may be more than one analysed sample from the same individual, or samples may be missing).	Probably high
Nickbakhsh 2016	Probably high	Retrospective, inclusion and exclusion are not specified. Large sample size and long study.	Probably high	Unclear if the number of pts and the number of samples are the same. No information about duplicate sample from the individual or missing sample.	Probably high
Nickbakhsh 2020	Probably high	Retrospective, inclusion and exclusion are not specified. Big sample size and long study.	Probably high	Number of pts and number of samples analysed appear to be the same.	Probably high
Nunes 2014	Low	Prospective, and data collected at hospital. Inclusion specified and exclusion. Control group, HIV, selection, comparable	Low	Number of pts and number of samples analysed are the same.	Low
Owusu 2014	Probably low	Prospective, recruitment bias seasons, inclusion criteria and exclusion specified	Probably low	Number of pts and number of samples analysed are the same.	Probably low

Owusu 2014 b	Probably low	Prospective, recruitment bias seasons, inclusion criteria and exclusion specified	Probably low	Number of pts and number of samples analysed are the same.	Probably low
Paloniemi 2015	Probably low	Prospective, and data collected at hospital. Inclusion specified and no exclusion.	Probably low	Number of pts and number of samples analysed appear to be the same.	Probably low
Prasetyo 2015	Probably low	Prospective, and data collected at hospital. Inclusion specified. Small sample size and possible selection bias	Probably low	Unclear if the number of pts and the number of samples are the same. No information about duplicate sample from the individual or missing sample.	Probably low.
Qu 2015	Probably low	Prospective, and data collected at hospital. Inclusion criteria and exclusion specified	Probably low	Number of pts and number of samples analysed are the same.	Probably low
Ren 2011	Probably high	Retrospective, and data collected in outpatient clinic. Inclusion criteria and exclusion specified	Probably high	Number of pts and number of samples analysed appear to be almost the same.	Probably high
Silva 2015	Probably high	Unclear if prospective. Unclear if all eligible pts are included.	Probably high	The number of samples and pts are not the same.	Probably high
Sipulwa 2019	Probably high	Retrospective.	Probably high	Unclear number of pts, and unclear if only one test per person.	Probably high
Smuts 2008	Probably low.	Prospective. Describes the population, consecutive pts included.	Probably low.	Number of pts and number of samples about the same.	Probably low.
Sonawane 2019	Probably low.	Prospective. Definition of condition.	Probably low	Unclear if number of samples and number of pts are the same, but prospective study.	Probably low
Soonnarong 2016	Probably high	Unclear if prospective.	Probably high	Unclear if number of samples and number of pts are the same.	Probably high
Talbot 2009a	Probably low	Retrospective analysis from prospective study1055 of 1123 re-analysed	Probably low	Number of pts and number of samples analysed appear to be the same.	Probably low
Talbot 2009b	High	Retrospective study. Many specimens were missing for various reasons	High	Unclear if number of samples and number of pts are the same.	Probably high
Theamboonlers 2006	Probably high	Prospective, but not stated how many that were eligible, only that 226 were analysed	Probably low	Number of pts and number of samples analysed appear to be the same.	Probably high
Tuzuner 2016	Probably high	Retrospective, unclear selection process	Probably low	Number of pts and number of samples analysed appear to be the same.	Probably high

van der Hoek 2010	Probably low	Randomized selection of subsample. Checked that the subsamples were representative on several variables	Probably low	Number of pts and number of samples are the same.	Probably low
Xin 2012	Probably low	Prospective, all children with ALTRI enrolled. Unclear whether some pts declined	Probably low	Number of pts and number of samples analysed appear to be the same.	Probably low
Ye 2017	Probably high	Prospective, but with convenience sampling	Probably low	Number of pts and number of samples analysed appear to be the same.	Probably low
Yip 2016	Probably high	Probably prospective, but enrollment procedures unclear	Probably low	Number of pts and number of samples analysed appear to be the same.	Probably low
Yu 2012	Probably low	Prospective, unclear selection	Probably low	Number of pts and number of samples analysed appear to be the same.	Probably low
Zeng 2018	Probably high	Unclear whether prospective or retrospective, and unclear selection process	Probably low	Number of pts and number of samples analysed appear to be almost the same.	Probably low
Zhang 2018	Probably low	Prospective study, but patient flow not described in detail	Probably low	Number of pts and number of samples analysed appear to be almost the same.	Probably low
Zhao 2019	Probably low	Prospective study, but patient flow not described in detail	Probably low	Number of pts and number of samples analysed appear to be almost the same.	Probably low

***** Two probably low, gives overall rating of 'probably low'. Two probably high gives an overall rating of 'high'. One probably high and one probably low gives an overall rating of high.

Published by the Norwegian Institute of Public Health
Juli 2022
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The report can be downloaded as pdf
at www.fhi.no/en/publ/