BMJ Open Effectiveness of contact tracing apps for SARS-CoV-2: a rapid systematic review

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ABSTRACT

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Objective To systematically review evidence on effectiveness of contact tracing apps (CTAs) for SARS-CoV-2 on epidemiological and clinical outcomes. Design Rapid systematic review.

Data sources EMBASE (OVID), MEDLINE (PubMed), BioRxiv and MedRxiv were searched up to 28 October 2020.

Study selection Studies, both empirical and modelbased, assessing effect of CTAs for SARS-CoV-2 on reproduction number (R), total number of infections, hospitalisation rate, mortality rate, and other epidemiologically and clinically relevant outcomes, were eliaible for inclusion.

Data extraction Empirical and model-based studies were critically appraised using separate checklists. Data on type of study (ie, empirical or model-based), sample size, (simulated) time horizon, study population, CTA type (and associated interventions), comparator and outcomes assessed, were extracted. The most important findings were extracted and narratively summarised. Specifically for model-based studies, characteristics and values of important model parameters were collected.

Results 2140 studies were identified, of which 17 studies (2 empirical, 15 model-based studies) were eligible and included in this review. Both empirical studies were observational (non-randomised) studies and at high risk of bias, most importantly due to risk of confounding. Risk of bias of model-based studies was considered low for 12 out of 15 studies. Most studies demonstrated beneficial effects of CTAs on R, total number of infections and mortality rate. No studies assessed effect on hospitalisation. Effect size was dependent on model parameters values used, but in general, a beneficial effect was observed at CTA adoption rates of 20% or higher.

Conclusions CTAs have the potential to be effective in reducing SARS-CoV-2 related epidemiological and clinical outcomes, though effect size depends on other model parameters (eg, proportion of asymptomatic individuals. or testing delays), and interventions after CTA notification. Methodologically sound comparative empirical studies on effectiveness of CTAs are required to confirm findings from model-based studies.

INTRODUCTION

The SARS-CoV-2 outbreak has dominated worldwide news and scientific research throughout 2020. Since its emergence in

Strengths and limitations of this study

- This is the first paper to provide a comprehensive overview and critical appraisal of studies assessing the effectiveness of contact tracings apps for SARS-CoV-2 on clinical and epidemiological outcomes.
- Studies were retrieved using a large repository that is developed by a specific search string dedicated to identify studies on SARS-CoV-2 published in various underlying databases.
- Critical appraisal was performed by reviewers from diverse backgrounds (ie, mathematical modelling, epidemiology, medicine, systematic reviews) using predefined customised templates for both empirical and model-based effectiveness studies.
- Given the rapid execution and (preprint) publication of studies on effectiveness of contact tracing apps (CTAs) for SARS-CoV-2, this review is unlikely to include the most recent studies published after the search date.
- Due to high heterogeneity across studies, it was not feasible to provide a pooled meta-analysis estimate of the effectiveness of CTAs for SARS-CoV-2 on the clinical and epidemiological outcomes.

Wuhan (People's Republic of China) in early December 2019, reducing transmission of SARS-CoV-2 has been a worldwide priority. Digital technology could be applied for efficient contact tracing. Contact tracing applications (CTAs) are able to identify individuals who have recently been in close contact with infected individuals (and may have acquired infection as a consequence). After identification, the contact person can be instructed to go in self-quarantine, preventing further transmission and spread of the virus.

A substantial amount of research on CTAs for SARS-CoV-2 has been performed since the start of the pandemic. Summarising all evidence, including results from research that has not yet undergone, or is currently undergoing peer-review, is warranted to provide an overview of what is known regarding CTA effectiveness. Research that has not yet undergone peer-review is often published by

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authors through so-called preprint databases. However, identifying these articles, extracting data and drawing conclusions can be a challenge, as this requires knowledge on epidemiology, mathematical modelling, systematically appraising evidence and summarising that evidence.

A few overviews of evidence on effectiveness of CTAs have been published in recent time. Anglemyer *et al* provided an overview of study characteristics and quality appraisal of studies on effectiveness of CTAs and other digital contact tracing technologies.¹ However, their data are based on both SARS-CoV-2 infections and other infections (eg, Ebola), and lack a quantitative effectiveness measure of CTAs on clinically relevant outcomes. Other systematic reviews focused only on user experience in using a CTA for SARS-CoV-2 detection,² or only studied manual, as opposed to digital, contact tracing.³ One systematic review did look into studies on automated and semi-automated CTAs for SARS-CoV-2, but lacked reporting on CTA effectiveness on total number of infections, and hospitalisation or mortality rates.⁴

In this rapid systematic review, we aim to evaluate all (empirical and model based) studies addressing effectiveness of CTAs for SARS-CoV-2 on relevant epidemiological and clinical outcomes. We will provide descriptive characteristics, critical appraisal and a narrative summary of evidence of included studies.

METHODS

Search strategy

The *Bern COVID-19 Open Access Project (COAP)* database was used for identification of relevant research. The COAP database is comprised research from EMBASE (OVID), MEDLINE (PubMed), BioRxiv en MedRxiv databases, specifically focused on SARS-CoV-2. On 28 October 2020 the COAP database was searched for scientific literature evaluating the effectiveness of CTAs for SARS-CoV-2 on epidemiological and clinical outcomes. The complete search strategy, as well as background information on the COAP database provided by Bern University, are provided in online supplemental file 1.

Eligibility criteria

Empirical (both observational and experimental) and model-based studies evaluating effectiveness of CTAs for SARS-CoV-2 were eligible for inclusion. Peer-reviewed publications as well as preprint papers were considered.

CTAs were considered when they provided feedback about potential recent exposure to an infected individual, based on proximity measurements (eg, Bluetooth or GPS). Feedback should be provided directly to the individual through a CTA, although other feedback mechanisms, such as personal devices (eg, a smartwatch), were also considered. National emergency warning systems using SMS were also included, provided they used proximity data to inform individuals.

All epidemiologically or clinically relevant outcomes quantifying the impact of CTAs were considered, which include but are not limited to: the reproduction number (R), total number of infections, hospitalisation rate and mortality rate related to SARS-CoV-2. Studies investigating other relevant outcomes, such as prevention of outbreaks or a second infection wave of SARS-CoV-2, were also included. Studies solely assessing (determinants affecting) adoption rate of CTAs (ie, the proportion of citizens using, and following recommendations provided by, the CTA), temporal change in incidence SARS-CoV-2, or other non-epidemiological or clinical outcomes were excluded.

Study selection

Studies identified in the search were first screened independently on title and abstract by two reviewers. Relevant studies were included for full-text screening, and further selection of articles was performed by two independent reviewers. Any discrepancies were discussed and resolved. When consensus was not reached, a third reviewer was consulted to provide the final judgement.

Critical appraisal

Risk of bias was systematically assessed by two researchers using separate checklists for empirical and model-based studies. Discrepancies between researchers were discussed, and a final verdict was provided by a third reviewer if consensus was not reached. Empirical studies were appraised using a formal scoring method based on the Critical Appraisal Skills Programme and Cochrane's Effective Practice and Organisation of Care checklists^{5 6} (online supplemental file 2). Risk of bias in model-based research was evaluated by assessing use of empirical input data for the model, number of scenarios analysed and transparency of model reporting (online supplemental file 3).

Data extraction

Data extraction was performed by one reviewer, and checked by a second reviewer. Descriptive characteristics on type of research, that is, empirical or model-based, sample size, (simulated) time horizon, study population, CTA properties and intervention, comparator, and epidemiological and clinical outcomes studied, were extracted from all included studies.

Specifically for model-based research, model characteristics (ie, type of model and distributions used) and values used for important model parameters were collected. Furthermore, CTA-specific properties were extracted, such as the method of contact tracing used by these apps. Forward tracing CTAs can only detect the 'offspring', that is, individuals the index case has infected. Bidirectional tracing CTAs also detect the 'parents', that is, the individual that infected the index case. Models were considered to use bidirectional (as opposed to forward) tracing when, after the index case is detected and registered, all contacts within a period of at least the incubation time are identified, such that the parent of the index case could be found.

Another CTA-specific property included the use of 1-step-tracing or sequential tracing. When a CTA-identified

Table 1 Descr	iptive chara	acteristics of	f included studie	Se						
Study	Country (of first author)	Study type	Sample size/ simulations (n)	Time horizon	Population	Specific setting(s)	Intervention	Comparison	Outcome(s)	Main findings
Bradshaw 2020 (peer-reviewed)	Germany	Modelling	500 or 1000 simulations	52 weeks or 10000 cases	General population	1	Contact tracing app (Bluetooth) with quarantine	 Manual contact tracing. Current practice. 	 R. Outbreak control. 	 Bidirectional tracing will enable more effective control of COVID-19. Switching from forward to bidirectional tracing can reduce R by 0.3 if the tracing time window is sufficiently wide. High adoption of bidirectional manual and digital contact tracing is 3x more effective at outbreak control compared with current practice.
Bulchandani 2020 (preprint) ⁷	NSA	Modelling	4000 simulations	N/R	Susceptible population (ie, no immunity)	1	Contact tracing app (not specified) with quarantine	1	 R. Outbreak control. 	 Outbreak control is possible regardless of proportion of asymptomatic transmission. Outbreak control requires a contact tracing app adoption of 75%-95%.
(preprint) ⁸	Italy	Modelling	20 simulations	50 days	General population	University campus P High school. Workplace.	Contact tracing app (Bluetooth) with quarantine	1	 R. Outbreak control. 	 Reduction of R and outbreak control is dependent on contact tracing efficiency, isolation efficiency and R₀. Outbreak control can be achieved through tracing and isolation, provided that hygiene and social distancing measures limit R₀ to 1.5. Outbreak control not feasible if contact tracing app adoption is insufficient or if R₀ is >2.
Chen 2020 (peer-reviewed) ²³	Taiwan	Empirical	3000 individuals	40 days	General population (Taiwan)	1	Public Warning System SMS (GPS) with quarantine and symptom monitoring	Current practice	 Respiratory syndrome. Pneumonia. 	 Contact tracing and SMS feedback resulted in less cases of respiratory syndrome (16.87 vs 19.23 per 1000) and pneumonia (2.36 vs 3.81 per 1000) compared with the general population. Resource requirements for manual contact tracing could be reduced by using contract tracing apps combined with big data analytics.
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Table 1 Contil	hued									
Study	Country (of first author)	Study type	Sample size/ simulations (n)	Time horizon	Population	Specific setting(s)	Intervention	Comparison	Outcome(s)	Main findings
Currie 2020 (peer-reviewed) ¹⁷	Australia	Modelling	Not reported	12 months	General population (Australia)	1	contact tracing app (Bluetooth) with quarantine	No contact tracing app	 Outbreak control. Cumulative incidence SARS-CoV-2. 	 Outbreak control by a contact tracing app can be achieved when adoption is sufficient, and is combined with testing and social distancing. Cumulative incidence of SARS-CoV-2 can within 8 months (depending social distancing and testing intensity) be reduced to: 13%-24% at an app adoption of 27%. 13%-59% at an app adoption of 40%. 36%-59% at an app adoption of 61%. 47%-76% at an app adoption of 80%.
(peer-reviewed)	Italy	Modelling	5500 simulations (per scenario)	50 days 300 days 400 days	General population (Italy)	1	Contact tracing app (not specified) with quarantine and symptom monitoring	1	 P. R. control. Cumulative indence sinclence sinclence (symptomatic). Mortality. 	 Reduction of R below 1.0 can be achieved when contact tracing apps have sufficient adoption, efficacy of case identification and compliance to quarantine. Outbreak control can be achieved using contact tracing apps combined with voluntary self-quarantine and fransportation density and transportation. Outbreak control was achieved with 75% app adoption rate. Cutbreaks will be sustained by districts with high population density. Montality was reduced by: 10% at 55% app adoption rate. 25% at 50% app adoption rate. 25% at 50% app adoption rate. 25% at 50% app adoption rate.
Ferretti 2020 (peer-reviewed) ¹⁶	China	Modelling	40 simulations (pairs)	12 days 20 days	General population (China)	 Home. Train. Work. 	Contact tracing app (Bluetooth) with quarantine	Manual contact tracing	œ	 Manual contact tracing is not able to stop outbreaks due to delays (~3 days), whereas contact tracing apps are able to prevent outbreaks. Reduction of R below 1.0 is feasible using instantaneous (red. without delays) contact tracing apps.
										Continued

Table 1 Conti	panu									
Study	Country (of first author)	Study type	Sample size/ simulations (n)	Time horizon	Population	Specific setting(s)	Intervention	Comparison	Outcome(s)	Main findings
Grimm 2020 (preprint) [°]	Germany	Modelling	N/R	500 days	General population (Germany)	 High risk of severe course of infection. Low risk of severe course of infection. 	Contact tracing app (not specified) with quarantine	 No intervention. Uniform social distancing. Group- specific social distancing. 	 Cumulative incidence SARS-CoV-2. Number of days ICU capacity exceeded. Mortality. 	 ICU capacity and mortality can be kept low by using contract tracing apps combined with tailored social distancing and personal protection measures. ICU capacity was not exceeded at any point with a contact tracing app adoption of 20% or more. Mortality was reduced by 85% when a high (80%) adoption rate of the contact tracing app was achieved.
Guttal 2020 (preprint) ¹⁰	R	Modelling	N.N.	150-200 days	General population	1	Contact tracing app (Bluetooth) with quarantine	1	Cumulative incidence SARS- CoV-2	 Peak cumulative incidence can be flattened significantly even when a small fraction of cases are identified using contact tracing apps, tested and isolated. Peak cumulative incidence can strongly be reduced even if contact tracing app testing is only performed in the most probable individuals (p>0.8).
Kendall 2020 (peer-reviewed) ²⁴	сĸ	Empirical	Population-size Isle of Wight Population-size UK (except Wales)	<2 months	General population (Isle of Wight and UK (except Wales))	1	NHS contact tracing app (V.1) (Bluetooth) with social distancing	1	 ▼ R. Cumulative incidence SARS-CoV-2. 	 Reduction of R from 1.3 to 0.5 was achieved after implementation of a contact tracing app. Cumulative incidence of SARS- CoV-2 reduced by 87% in 2-3 weeks after implementation of a contact tracing app.
Kretzschmar 2020 (peer-reviewed) ¹⁵	Netherlands	Modelling	1000 simulations	КŽ	population	 Close contacts. Casual contacts. 	Contact tracing app (Bluetooth) with quarantine	Social distancing without contact tracing app	œ	 Contact tracing apps, with short delays and high coverage for testing and tracing, could substantially reduce the R, alleviating more stringent control measures. Reduction of the R from 1.2 with social distancing alone to 0.8 (95% CI 0.7 to 1.0) by adding a contact tracing app with an adoption of 80%. Reduction of the R through contact tracing apps is more effective compared with manual contact tracing, with nespectively 17.6% and 2.5% reduction of R compared with no contact tracing. Reduction of R compared with no contact tracing apps is more effective contact tracing. Reduction in transmission rate delay: 41.8% with 7-day testing delay.
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Table 1 Conti	nued									
Study	Country (of first author)	Study type	Sample size/ simulations (n)	Time horizon	Population	Specific setting(s)	Intervention	Comparison	Outcome(s)	Main findings
Kucharski 2020 (peer-reviewed) ¹⁴	ž	Modelling	25 000 simulations	N/R	General population (UK)	 ➡ Household. ➡ Work. ■ School. Other. 	Contact tracing app (Bluetooth) with quarantine	1	R. Outbreak control.	 Combining contact tracing app with quarantine and reduce transmission more than mass testing or self-isolation alone. Reduction in transmission rate (reflective of R) was 47% when contact tracing app was used at 53% adoption rate. Maintaining an R<1.0 requires a combination of self-isolation, contact tracing and physical distancing. Outbreak control in a scenario where incidence is high requires a considerable number of individuals to be quarantined after contact tracing.
Kurita 2020 (peer-reviewed)	Japan	Modelling	RX	5 months	General population (Japan)	1	COCOA contact tracing app (Bluetooth) with quarantine	1	œ	 Reduction of R<1.3 using a contact tracing app is not feasible if there are no voluntary restrictions. Reduction of R<1.01s feasible if contact tracing app adoption is 10% combined with 15% compliance for voluntary restrictions against going out.
Nuzzo 2020 (peer-reviewed) ²⁰	NSA	Modelling	R	400 days 150 days	Susceptible individuals	1	Contact tracing app (GPS, WiFi and/or Bluetooth) with quarantine	Shelter in place	Cumulative incidence SARS-CoV-2. Mortality.	 Contact tracing apps can mitigate infection spread similar to universal shelter-in-place, but with considerably fewer individuals isolated. Cumulative peak incidence can be reduced by 49% at 20% app adoption rate. Cumulative peak incidence can be reduced by 90% at 50% app adoption rate (similar to 40% compliance to shelter in place). Mortality can be reduced by 23% at 20% app adoption rate.
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 Recursive tracing by contact tracing apps is more efficient than 1-step-tracing. T-step-tracing. Contact tracing apps alone cannot bring R below 1.0, unless 100% adoption is approached, and app notifications are strictly followed by quarantining and testing. Reducing an R_o of >3.0, in which 40% example and the string. Reducing an R_o of >3.0, in which 40% example and the string. Reducing an R_o of >3.0, in which 40% example and the string. Reducing an R_o of >3.0, in which 40% example and the string. Reducing an R_o of >3.0, in which 40% example and the string. Reducing an R_o of >3.0, in which 40% example and the string. Reducing and the string application tract tracing application the string. Reducing R significantly requires a contact tracing application tracting application tracting application. 	 Impact of policy changes on cumulative incidence can take >2 months to become apparent. Opening pubs/bars was identified as the greatest risk for increasing incidence of SARS-coV-2. This could be mitigated by either of these masures. 30% app adoption rate is anovide a particulation of the masures. 30% app adoption rate is was reduced by >40% through physical distancing policies. Manual contact tracing was used that enabled >60% of contacts to be traced. Cumulative incidence is unlikely to be significantly impacted when app adoption rates are low-moderate. 	Continued
R. Outbreak control. Cumulative incidence SARS-CoV-2.	Cumulative incidence SARS- CoV-2	
Contact tracing app (Bluetooth) with quarantine	COVIDSafe - contact tracing app (Bluetooth) with quarantine	
I E	ble Various*	
General populatic	Suscepti populatic (Victoria, Australia,	
500 days	3.5 months	
100 simulations	RN	
Modelling	Modelling	
Germany	Australia	
Pollmann 2020 (preprint) ¹²	Scott 2020 (peer-reviewed)	

Main findings

Outcome(s) Ъ. Б. Б.

Comparison

Intervention

Specific setting(s)

Population General

Time horizon 500 days

Sample size/ simulations (n) 100 simulations

> Study type Modelling

Country (of first author)

Continued

Table 1

Study

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individual could only notify their contacts after testing positive themselves, this was considered 1-step-contact tracing. When notified contacts could subsequently also notify their own contacts, creating a cascade, even before that individual has shown symptoms or received a positive test result for SARS-CoV-2, this was considered sequential tracing.

The most important findings regarding effectiveness of CTAs for SARS-CoV-2 on epidemiological and clinical outcomes were extracted, synthesised and reported narratively. These outcomes were pooled quantitatively whenever it was feasible to do so.

RESULTS

Study selection

A total of 2140 potential studies were identified by the search. After selection based on title and abstract, 2059 articles were excluded. Full texts of the 81 remaining studies were assessed, after which 17 articles were included for critical appraisal and data extraction (online supplemental file 4). The 64 excluded studies with their reasons for exclusion are summarised in online supplemental file 5.

Characteristics of included studies

Seventeen primary studies were included, of which two were empirical observational (non-randomised) studies, and 15 were model-based studies (table 1).

Six of the 17 studies were published preprints, meaning they had not (yet) gone through the peer-review process at the time of submitting this paper.^{7–12} Included studies focused predominantly on the general population, although some analysed the effectiveness of CTAs for specific populations such as hospital personnel, or school children.^{8 9 11 13–16} Especially in model-based studies, results were often presented graphically. Consequently, the effectiveness of CTAs on epidemiological and clinical outcomes was only partly, or not at all, reported in key numerical figures.

The model-based studies typically assessed the effectiveness of CTAs by simulating one or more scenarios based on certain baseline or input values (eg, proportion of asymptomatic infections). Table 2 provides an overview of characteristics and the most important input parameters used in models of the 15 included articles. Nine of the 15 model-based studies evaluated forward tracing CTAs,^{8 9 11 13–18} four studies analysed bidirectional tracing CTAs^{7 10 12 19} and one used an alternative method.²⁰ Four studies used a CTA that used sequential tracing.^{7 10 12 19} All of these also used bidirectional CTAs, which are more effective than forward tracing CTAs in reducing R, but require quarantining many more contact persons. This is especially the case when a significant number of infections come from asymptomatic individuals (ie, transmission from a case who does not (yet) have symptoms), who are unaware they have SARS-CoV-2.¹⁹

Table 2 Pro	perties of model- Model-related prope	based studies erties	Contact- and tra	tcing app relate	ed properties	Disease-rela	ted properties			Modifyable pr	roperties	
Study	Model type	Input parameter properties	Tracing direction	Sequential generations (n)	Adoption rate app (%)	ш	Incubation	Infectious period	Probability of disease transmission	Delay symptom onset and testing	Delay testing and feedback app	Quarantine effectiveness
Bradshaw 2020 (peer-reviewed)	Branching-process model	Distributions	Bidirectional	Infinite generations	53; 80	2.5	5.5 days	Fitted to curve, value not specified	Fitted to curve, value not specified	1 days	0 days	%06
Bulchandani 2020 (preprint) ⁷	Branching-process model	Based on exponential distributions	Bidirectional	3-infinite generations	0-100	3.0	N/A*	N/A	N/R	N/A†	0 days	100%
Cencetti 2020 (preprint) ⁸	Continuous weighted temporal network	Distributions	Forward	1 generation	60; 80; 100	1.2; 1.5; 2.0	Fitted to curve, value not specified	Fitted to curve, value not specified	Fitted to curve, value not specified	2 days	0 days	0%100%
Currie 2020 (peer- reviewed) ¹⁷	ODE compartmental model	Based on exponential distributions	Forward	1 generation	0; 27; 40; 61; 80	2.5	2.0 days	11 days	N/R	3 days	N/R	%06
Ferrari 2020 (peer-reviewed)	ODE compartmental model	Based on exponential distributions	Forward	1 generation	0; 25; 50; 75	1.5	5.1 days	10 days	10%	2 days	N/R	%06
Ferretti 2020 (peer- reviewed) ¹⁶	PDE compartmental model	Distributions	Forward	1 generation	0-100	2.0	5.5 days	12 days	Fitted to curve, value not specified	1.6 days	0 days	0%100%
Grimm 2020 (preprint) ⁹	ODE compartmental model	Based on exponential distributions	Forward	1 generation	20-80	2.2; 3.0	5.0 days	10;12.5;14;20 days	N/R	N/R	N/R	100%‡
Guttal 2020 (preprint) ¹⁰	Individual-based network model	Based on exponential distributions	Bidirectional	>1 generation	100	3.0; 4.0	N/A	20 days	0.2%	N/R	N/R	100%
Kretzschmar 2020 (peer- reviewed) ¹⁵	Branching-process model	Distributions	Forward	1 generation	20; 40; 60; 80; 100	2.5	6.4 days	10 days	2%-12%	0 days	0 days	0%; 20%; 40%; 60%; 80%; 100%
Kucharski 2020 (peer- reviewed) ¹⁴	Individual-based network model	Distributions	Forward	1 generation	53	2.6	5.0 days	5 days	20% within HH 6% outside HH 50% less for asymptomatic	0 days	0 days	%06
Kurita 2020 (peer-reviewed)	ODE compartmental model	Based on exponential distributions	N/R	1 generation	0; 10; 20; 30; 40; 50; 60; 70; 80; 90; 100	1.5	6.6 days	N/R	N/R	2 days	0 days	R/R
Nuzzo 2020 (peer- reviewed) ²⁰	ODE compartmental model	Based on exponential distributions	N/A§	N/A§	0; 10; 20; 30; 40; 50; 60; 70; 80; 90	3.02	5.1 days	N/R	Fitted to curve, value not specified	N/R	N/R	100%
Pollmann 2020 (preprint) ¹²	ODE compartmental model	Based on exponential distributions and distributions	Bidirectional	>1 generation	60; 75; 90; 100	2.0-3.0-4.0	4.0; 7.4 days	10 days	L%2	0; 2; 4; 6 days	N/R	100%
												Continued

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Table 2 Co	ntinued											
	Model-related prope	sties	Contact- and tr	acing app relate	ed properties	Disease-rela	ated propertie	s		Modifyable p	roperties	
Study	Model type	Input parameter properties	Tracing direction	Sequential generations (n)	Adoption rate app (%)	н	Incubation time	Infectious period	Probability of disease transmission	Delay symptom onset and testing	Delay testing and feedback app	Quarantine effectiveness
Scott 2020 (peer-reviewed)	Agent-based model	Distributions	Forward	1 generation	0-50	Fitted to curve, value not specified	4.6 days	8-14 days	Fitted to curve, value not specified	1 day	1 day	0% in HH 80%–100% in other settings
Shamil 2020 (preprint) ¹¹	Agent-based model	Distributions	Forward	1 generation	60; 75	Fitted to curve, value not specified	6.0 days	10 days	N/R	0 days	0 days	100%
Model-specific ch *Fraction of infecti fisolation based c thonging app co \$No true tracing, f fTime-dependent, HH, household: M	aracteristics of model-basi ions before symptoms are in positive notification, not verage covers imperfect is ixed proportion cases will s. maximum vulue reported A. not applicable: N/R. not	ed studies looking at . relevant. a positive test. solation. self-isolate. in table. trenorted: ODE. ordin	effectiveness of con	tact and tracing a	pps for SARS-Co	V-2: Dashes (-) tions: R. reproc	indicate a contir duction number.	nuous range betw	een numbers, semicolons	s indicate separa	ate distinct values	

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The percentage of CTA adoption was varied in almost all studies, allowing for assessment of the impact of CTAs on epidemiological and clinical outcomes. Average incubation time, that is, the mean time between infection and symptom onset of SARS-CoV-2, was estimated to be 5–6 days for SARS-CoV-2.^{9 11–21} The proportion of asymptomatic SARS-CoV-2 infections, used as input parameter in model-based studies, was estimated at 20%-50% based on empirical data,⁸⁹¹⁶¹⁸ but could vary between 18% and 86%.⁹ The baseline R value chosen in the model-based studies varied between 1.2 and 4.0.7-10 12 14-21

Furthermore, so-called superspreaders (ie, individuals that infect numerous other individuals, and consequently have a high individual R) were discussed in context of the SARS-CoV-2 pandemic. Tracing these superspreaders is key in containing outbreaks. Hence, it is warranted to use bidirectional CTAs to trace these superspreaders, and advise them to immediately enter guarantine on identification.14 22

Critical appraisal

Risk of bias in the two empirical studies was judged to be high (table 3).^{23 24} Confounding variables (such as smoking, work status and income) were insufficiently taken into account given the explanatory and observational nature of these empirical studies. It was also unclear how missing (outcome) data were dealt with.

Most model-based research was judged to have a low risk of bias (table 4). Three of the 15 studies had a high risk of bias due to the lack of use of empirical distributions for variables, the limited number of scenarios analysed and insufficient transparency regarding reporting of the model.^{11 20 21}

Synthesis of results

not reported; ODE, ordinary differential equations; PDE, partial differential equations; R, reproduction number

hold; N/A, not applicable; N/R,

househ

Evidence from empirical studies

Two empirical comparative observational studies assessed the effectiveness of CTAs compared with a control group that did not use CTAs (table 1).^{23 24} One study looked at effectiveness of a text warning system used in 627 386 individuals who came in contact with a SARS-CoV-2 exposed population, and compared it to the general population of Taiwan who did not use such a warning system.¹⁷ They showed a reduction in incidence of respiratory syndrome from 19.23 to 16.87 per 1000 individuals. They also showed a reduction in pneumonia incidence from 3.81 to 2.36 per 1000 individuals.¹⁷ The second observational study investigated the introduction and adoption of a 'Test and Trace' app by 34000 individuals living on the Isle of Wight (UK), and compared the estimated value of R in that region to that in the general UK population.²⁴ The CTA marked individuals as positive based on selfreporting of symptoms. Individuals that came in contact with an individual marked as positive were provided with social distancing advice. The study found that R was reduced from 1.3 to 0.5 after implementation of the CTA. Within 2-3 weeks after implementation, incidence of SARS-CoV-2 diagnoses declined by around 90%.²⁴

Table 5 Citical	appraisar or er	inplineal studies					
Study	Confounding?	Selection bias: participants?	Selection bias: missing data?	Information bias: intervention misclassification/non- compliance?	Information bias: misclassification of the outcome?	Other concerns?	Overall risk of bias
Chen 2020 (peer- reviewed) ²³	Yes*	No	Unclear	No	Unclear	None	High
Kendall 2020 (peer- reviewed) ²⁴	Yes	No	Unclear	No	No	Competing interests and funding not reported	High

Critical appraisal empirical epidemiological studies looking at effectiveness of contact and tracing apps for SARS-CoV-2. *Only adjusted for age.

Evidence from model-based studies *Effect on R*

Effectiveness of a 1-step-contact tracing in reducing R can be approached using the following formula:

$$\mathbf{R}_{c} = \mathbf{R} \times (1 - \mathbf{p}^{2} \times \mathbf{f})$$

Here, R_c is the reproduction number when a CTA is used, R is the reproduction number without the use of a CTA, p is the proportion of the population using the CTA and f is the combination of other factors that affect effectiveness of notification by the CTA. Such factors include, but are not limited to: delay between CTA notification and testing, delay between testing and test result, delay between reception of test result and entry of that result in the CTA, compliance to interventions (eg, self-quarantine), and the proportion of infections that occur presymptomatically or asymptomatically. Note that p occurs as a quadratic term, which reflects the fact that both infector and infectee have to use the CTA for the transmission to get traced.

Nine of the 15 model-based studies assessed the effect of CTAs on reduction of R.^{8 11} ^{14–16} ^{18 19 21} CTAs were able to control an ongoing outbreak or epidemic through

Table 4 Critical appraisal	of model-based studi	es			
Study	Were empirical distributions used for a varying infectiousness since time of infection?	Were various different scenarios evaluated for important model assumptions and parameter values?	Were models reported transparently? (ie, no black box)	Other concerns?	Overall study validity
Bradshaw 2020 (peer-reviewed)	Yes	Yes	Yes	External funding*	High
Bulchandani 2020 (preprint) ⁷	No	Yes	Yes	Competing interests and funding not reported	High
Cencetti 2020 (preprint) ⁸	Yes	Yes	Yes	No	High
Currie 2020 (peer-reviewed) ¹⁷	Yes	Yes	Yes	No	High
Ferrari 2020 (peer-reviewed)	No	Yes	Yes	Competing interests†	High
Ferretti 2020 (peer-reviewed) ¹⁶	Yes	Yes	Yes	No	High
Grimm 2020 (preprint) ⁹	No	Yes	Yes	No	High
Guttal 2020 (preprint) ¹⁰	Yes	Yes	Yes	Competing interests and funding not reported	High
Kretzschmar 2020 (peer- reviewed) ¹⁵	Yes	Yes	Yes	No	High
Kucharski 2020 (peer-reviewed) ¹⁴	Yes	Yes	Yes	Funding‡, though no influence of funder on study results	High
Kurita 2020 (peer-reviewed)	No	No§	Unclear	Type of model used unclear	Low
Nuzzo 2020 (peer-reviewed) ²⁰	No	No§	Yes	Potential competing interests¶	Low
Pollmann 2020 (preprint) ¹²	Yes	Yes	Yes	Competing interests and funding not reported	High
Scott 2020 (peer-reviewed)	Yes	Yes	Yes	Funding**	High
Shamil 2020 (preprint) ¹¹	No	Yes	Unclear	No	Low

Critical appraisal model-based studies looking at effectiveness of contact and tracing apps for SARS-CoV-2.

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+ES works for Bayer, is collaborating to COVID-19 Safe Paths app, by MIT, and advising LEMONADE tracing app, by Nuland. ASC works for Roche Pharma. MTF is a consultant for Ely Lilly.

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§Scenarios were limited only to variation in rate of adoption of the contact and tracing app and voluntary quarantine.
¶Dr Raskar is the founder of a non-profit to facilitate digital contact tracing. The other authors report no potential competing interests.

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quicker and more efficient feedback of a positive test result, and by notifying close contacts of a positively tested individual.^{15 16 19} This speed and efficiency were not feasible using traditional manual contact tracing.¹⁶ New outbreaks could be controlled (ie, R <1.0) by CTAs, by combining them with quarantine or self-isolation interventions, provided that hygiene and social distancing measures are maintained.⁸¹⁴¹⁸²¹ CTAs were able to reduce R by 0.3 more than traditional manual contact tracing, provided that feedback about contact with a positively tested individual is given to all contacts of the index case of the preceding 7 days.¹⁹ Another model-based study demonstrated that a CTA with 20% adoption rate reduces R by 17.6% compared with no contact tracing, whereas traditional manual contact tracing reduced R by 2.5% compared with no contact tracing.¹⁵ This study also demonstrated that a CTA is able to reduce the R further, even when social distancing has already reduced R to 1.2. In this situation, R can be reduced further by 30%-0.8 when CTA adoption rate is 80%.¹⁵ Another model-based study determined that 60% adoption rate of a CTA could result in an R below 1.0.¹¹ In one study, adoption rate of 53% resulted in a 47% reduction in R when the complete household of an individual with a positive test result is advised to be guarantined.¹⁴ The last study looking at effect of CTA on R showed that only at 60% adoption rate of the app a significant beneficial effect on R would become apparent.¹² When R is high (eg, 3.0), and a considerable proportion of individuals is asymptomatic (eg, 40% of all infections), CTAs need to be combined with other interventions (such as social distancing and random testing) to be able to lower the R below 1.0^{12} Potential for CTAs to reduce R is not only dependent on the adoption rate of the app, but also on (effectiveness of) various other measures that are provided after a positive notification, the delay between positive notification and opportunity for testing, and delay between receiving a positive test result and sharing that result through the CTA.⁵⁶¹⁰ One study found that the percentage of preventable infections by one individual strongly depends on the time delay between CTA notification and the ability to be tested.¹⁵ When there was no delay (ie, 0 days) 79.9% of infections could be prevented, compared with 41.8% and 4.9% for 3 and 7 days delay, respectively.

Effect on total number of infections

Eight of the 15 model-based studies assessed the effect of CTAs on reducing the total number of infections.^{8–11 13 17 18 20} Two studies indicated that the success of CTAs in reducing the total number of infections could only be ensured with a high adoption rate of that app.^{8 13} Another study showed that with a high CTA adoption rate of 75%, there would be no more new infections occurring within 3 months after implementation.¹¹ It was found that adequate hygiene and social distancing measures are needed to enable CTAs to reduce the total number of infections.^{8 9 17 18} Especially in areas where there is low compliance to social distancing, a sufficiently high

adoption rate of a CTA is essential to maintain control of an outbreak. 9

The height of the peak number of new infections can, according to one study, be reduced by half with a 50% adoption rate of a CTA,¹⁸ whereas another study showed that this could be achieved with an adoption rate as low as 20%.²⁰ Another study demonstrated that at 27% CTA adoption rate, a quarter of all new infections can be prevented.¹⁷ However, according to another study that used a similar adoption rate, the number of infections would stabilise, but the epidemic would be maintained by core groups in densely populated areas.¹⁸ There may be a period of time of more than 2 months between implementation of interventions (such as CTAs) and the effect of that implementation on the total number of SARS-CoV-2 infections.¹³

Effect on number of hospitalisations

None of the 15 model-based studies assessed the effect of CTAs on the number of hospitalisations due to SARS-CoV-2 infection, possibly because the number of hospitalisations is expected to be proportional to the number of infections, only with a time-delay. A German study did look into the effect of a CTA on the number of days that intensive care unit (ICU) capacity was exceeded.⁹ They found in their simulations that—based on the German population, and assuming an ICU capacity of 24 000 beds—a CTA adoption rate of 20% would prevent exceedance of ICU capacity at any point in time. In contrast, if no contact tracing (either manual or digital) would be used, ICU capacity would be exceeded on a quarter of days.

Effect on mortality rate

Three of the 15 model-based studies assessed the effect of CTAs on mortality rate.^{9 18 20} One study demonstrated that a high adoption rate (80%) of a CTA would result in an 85% reduction in mortality rate, over a period of 500 days.⁹ Another study found that a low CTA adoption rate (25%) is associated with a 10% decrease in mortality rate, an average adoption rate (50%) with 25% decrease, and a high adoption rate (75%) with 40%–60% decrease.¹⁸ A third study showed that at 40% adoption rate, during the peak of an outbreak, a reduction in number of deaths by 97% could be achieved.²⁰

DISCUSSION

Empirical evidence regarding the effectiveness of using CTAs for detection of SARS-CoV-2 is still limited. Currently, no randomised studies have been performed, and only two observational comparative studies were identified in this systematic review. Although some benefits of using CTAs for detection of SARS-CoV-2 were observed, both studies were deemed to be of low methodological quality. However, the results of these studies were in accordance with the 15 included, higher quality, model-based studies assessing effectiveness of CTAs. These studies showed that CTAs can be effective and a valuable addition to manual

contact tracing. CTA use resulted in a lower R, lower total number of infections, and lower mortality rate. These reductions were already observed at relatively low adoption rates (eg, 20%), though higher adoption rates of CTAs resulted in greater reductions. Shortening delays between CTA notification and diagnostic testing may increase its effectiveness.

Strengths and limitations

This rapid systematic review assesses key features, quality, and main clinical and epidemiological outcomes of a set of studies, both empirical and model-based, on effectiveness of CTAs for SARS-CoV-2. To our knowledge, no such systematic review has been published, assessing these specific properties. Methodological quality of empirical studies was assessed using standardised tools. No such tool was available in literature for model-based studies, and as such a set of key features used in other systematic reviews on this topic was used. This set was validated by experts in mathematical modelling.

To fully appreciate the findings from this systematic review, some considerations should be taken into account. First, the set of studies identified in the literature search may not be comprehensive. Studies on SARS-CoV-2 are published at a rapid, almost daily, basis in various online repositories. Although we cannot ensure that all studies on the effectiveness of CTAs for SARS-CoV-2 have been identified, we believe that the set of included studies that we have identified is a representative sample.

Furthermore, effectiveness of CTAs for SARS-CoV-2 described in model-based studies is complex. Numerous input variables used in the models interact with one another, and consequently affect effectiveness of, for example, adoption rate of CTAs on clinical or epidemiological outcomes. Summarising these findings into a general effectiveness is difficult, and will always suffer from simplification of a system of complex interactions. Though we feel that providing some (conditional) findings from these studies will help provide some general insight in the impact CTAs can have on clinical and epidemiological outcomes for SARS-CoV-2.

CONCLUSION AND IMPLICATIONS FOR FURTHER RESEARCH

Current evidence on the effectiveness of CTAs for SARS-CoV-2 is predominantly based on modelling studies, which indicate that there is potential in beneficially affecting key clinical and epidemiological outcomes. High-quality empirical evidence, either from experimental or methodologically sound observational studies, is needed in order to be able to draw more robust conclusions regarding effectiveness of CTAs for SARS-CoV-2.

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Supplementary file 1. Search strategy

Search strategy

On October 28th 2020 the comprehensive set of studies included in the COAP database (available on <u>https://ispmbern.github.io/covid-19/living-review/collectingdata.html</u>) was loaded in Endnote X9.

The dataset consisted of 82,401 references related to research on COVID-19. The following search was performed within this dataset:

(contact OR tracing OR track OR tracking OR warn OR warning) AND (smartphone OR app OR smartwatch OR device OR mobile OR smart phone OR bluetooth OR wearable OR iphone OR cell phone)

Background COAP database

The COAP database is a repository provided by Bern University, in which studies related to COVID-19 are incorporated. (available on <u>https://ispmbern.github.io/covid-19/living-review/collectingdata.html</u>)

Studies included in this repository are extracted on a daily basis from <u>EMBASE</u> (OVID), MEDLINE (PubMed), BioRxiv, and MedRxiv. References that are not yet available in the repository are added based on the date of publication provided by the aforementioned databases. The date on which the reference is added to the COAP database is included under the heading 'strategydate'.

Search strategies used for the COAP database are updated on a regular basis. An overview of these updates can be found below.

Initial search: 01.01.2020

MEDLINE

("Wuhan coronavirus" [Supplementary Concept] OR "COVID-19" OR "2019 ncov"[tiab] OR (("novel coronavirus"[tiab] OR "new coronavirus"[tiab]) AND (wuhan[tiab] OR 2019[tiab])) OR 2019-nCoV[All Fields] OR (wuhan[tiab] AND coronavirus[tiab])))))

EMBASE ncov OR (wuhan AND corona) OR COVID

<u>BioRxiv/MedRxiv</u> ncov or corona or wuhan or COVID

Update #1: 26.03.2020

MEDLINE

("Wuhan coronavirus" [Supplementary Concept] OR "COVID-19" OR SARS-CoV-2 OR "2019 ncov"[tiab] OR (("novel coronavirus"[tiab] OR "new coronavirus"[tiab]) AND (wuhan[tiab] OR 2019[tiab])) OR 2019-nCoV[All Fields] OR (wuhan[tiab] AND coronavirus[tiab]))

<u>EMBASE</u>

(nCoV or 2019-nCoV or ((new or novel or wuhan) adj3 coronavirus) or covid19 or covid-19 or SARS-CoV-2).mp.

BioRxiv/MedRxiv

ncov or corona or wuhan or COVID or SARS-CoV-2 With the kind support of the <u>Public Health & Primary Care Library PHC</u>, and following guidance of the <u>Medical Library Association</u>

Update #2: 01.04.2020

From 01.04.2020, we retrieve the currate BioRxiv/MedRxiv dataset Link

Update #3: 29.04.2020

MEDLINE

("coronavirus"[MH] OR "coronavirus infections"[MH] OR "coronavirus"[TW] OR "corona virus"[TW] OR "HCoV"[TW] OR "nCov"[TW] OR "covid"[TW] OR "covid19"[TW] OR "Severe Acute Respiratory Syndrome Coronavirus 2"[TW] OR "SARS-CoV2"[TW] OR "SARS-CoV 2"[TW] OR "SARS Coronavirus 2"[TW] OR "MERS-CoV"[TW]) AND (2019/1/1:3000[PDAT])

Update #4: 01.05.2020

<u>EMBASE</u>

(SARS coronavirus/ or middle east respiratory syndrome/ or severe acute respiratory syndrome/ or (coronavirus* or corona virus* or HCoV* or ncov* or covid or covid19 or sars-cov* or sarscov* or Sars-coronavirus* or Severe Acute Respiratory Syndrome Coronavirus*).mp.) and 20191201:20301231.(dc).

Update #5: 30.10.2020

<u>EMBASE</u>

(exp SARS-related coronavirus/ or severe acute respiratory syndrome/ or coronavirus disease 2019/ or (coronavir* or corona virus* or HCoV* or ncov* or 2019 cov or covid or covid19 or sars-cov* or sarscov* or sars-coronavirus* or Severe Acute Respiratory Syndrome Coronavirus* or nCoV).mp.) and 20191101:20301231.(dc).

<u>MEDLINE</u>

("severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "COVID-19" [Supplementary Concept] OR "coronavirus" OR "corona virus" OR "HCoV" OR "nCoV" OR "2019 CoV" OR "covid" OR "covid19" OR "Severe Acute Respiratory Syndrome Coronavirus 2" OR "SARS-CoV2" OR "SARS-CoV 2" OR "SARS Coronavirus 2") AND (2019/11/01:3000/12/31[PDAT])

Supplementary file 2. Method for critical appraisal of empirical studies

Method used for critical appraisal of empirical epidemiologic studies

Confounding
Have the authors identified all important confounding factors? Yes / No / Unclear
Were the identified confounding factors <u>adjusted</u> for in the design and/or analysis? Yes / No
/ Unclear
- Model-based adjustment of confounders
- Stratification
- Matching
- No adjustment required (randomization)
Selection bias
Was patient exposure / intervention status <u>at inclusion</u> likely to result in bias? Yes / No /
Unclear
- Non-randomized study
- Randomized study with issues regarding allocation concealment or non-random sequencing
- Stringent exclusion criteria
Was missing data or loss to follow-up during the study likely to result in bias? Yes / No /
Unclear
- Missingness likely not completely at random (i.e. not MCAR or % of missingness different between
groups)
- No methods described for handling missingness (i.e. imputation)
- Other methods explored to prevent missingness (i.e. cross checking data sources)
Informationbias
Was measurement of exposure / administration of the intervention likely to result in bias? Yes
/ No / Unclear
- Blinding
- Standardization
- Objective
- Non-compliance
- Breaking protocol
Was measurement of outcome likely to result in bias? Yes / No / Unclear
- Blinding
- Standardization
- Objective (note: if this is the case item should be scored 'No')
Other concerns? FREE TEXT
Items to consider (but not limited to)
- Reporting bias
- Conflict of interest

Supplementary file 3. Method for critical appraisal of model-based studies

Method used for critical appraisal of model based studies

Were empirical distributions used for a varying infectiousness since time of infection? Yes / No / Unclear

Keywords indicating distributions were used

- Weibull
- Log-normal
- Exponential distribution

Were various different scenarios evaluated for important model assumptions and parameter values? Yes / No / Unclear

Keywords indicating uncertainty was taken into account

- Sensitivity analysis
- Scenario analysis

Were models reported transparently? (i.e. no black box) Yes / No / Unclear

Key elements indicating that model can be reproduced

- (differential) Equation specified
- Behavior of agents specified
- Graphic representation of model
- All variables and distributions specified

Other concerns? FREE TEXT

Items to consider (but not limited to)

- Reporting bias
- Conflict of interest
- Illogical properties of the model not captured by the criteria above

Supplementary file 4. Flowchart study selection

Flowchart regarding selection of studies looking at effectiveness of contact- and tracing apps for SARS-CoV-2



Supplementary file 5. Excluded studies

Studies not meeting inclusion criteria after full text screening, and excluded from analyses (n=64)

Reference	Reason for exclusion
Aleta 2020	No app or individual feedback
Aleta 2020	No app or individual feedback
Ayres 2020	Wrong outcome
Bian 2020	Wrong article type
Bianconi 2020	Full text not accessible
Braithwaite 2020	Wrong article type
Braithwaite 2020	Duplicate
Braun 2020	Full text not accessible
Brooks-Pollock 2020	No app or individual feedback
Chan 2020	Wrong article type
Chen 2020	No app or individual feedback
Di Domenico 2020	No app or individual feedback
Drake 2020	Wrong article type
Drew 2020	App without tracking
Fateh-Moghadam 2020	App without tracking
Fenton 2020	Wrong outcome
Firth 2020	No app or individual feedback
Gozzi 2020	App without tracking
Grantz 2020	Wrong outcome
Güemes 2020	App without tracking
Haller 2020	Wrong article type
Huang 2020	Wrong outcome
Hussein 2020	No app or individual feedback
Jian 2020	Wrong outcome
Kassaye 2020	App without tracking
Kendall 2020	Duplicate
Khataee 2020	Wrong article type
Kogan 2020	Wrong outcome
Kretzschmar 2020	Duplicate
Lambert 2020	Wrong article type
Leith 2020	Wrong article type
Liu 2020	No app or individual feedback
Maghdid 2020	Wrong article type
Marín-García 2020	Wrong article type
Menni 2020	App without tracking
Menni 2020	App without tracking
Milenkovic 2020	No app or individual feedback
Mishra 2020	App without tracking
Morley 2020	No app or individual feedback

Nagarajan 2020	No app or individual feedback
Ni Lochlainn 2020	App without tracking
Pépin 2020	Wrong outcome
Petrellis 2020	Wrong article type
Ranjan 2020	App without tracking
Ruediger 2020	No app or individual feedback
Salathe 2020	Wrong outcome
Sattler 2020	Wrong article type
Serafino 2020	App without tracking
Sun 2020	App without tracking
Sun 2020	No app or individual feedback
Szocska 2020	No app or individual feedback
Unwin 2020	No app or individual feedback
Vannoni 2020	No app or individual feedback
Varsavsky 2020	No app or individual feedback
Vinceti 2020	App without tracking
Wallentin 2020	Wrong article type
Whaiduzzaman 2020	Wrong article type
Wilson 2020	Wrong article type
Wong 2020	Wrong article type
Yabe 2020	No app or individual feedback
Yap 2020	Wrong outcome
Yasaka 2020	Wrong article type
Zens 2020	App without tracking
Zhan 2020	No app or individual feedback