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1 **Antibiotic prescribing for acute infections in synchronous telehealth**
2 **consultations: a systematic review and meta-analysis**

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1 **Abstract**

2 Background

3 Antibiotic prescribing is a major concern that contributes to the problem of antibiotic resistance.

4

5 Aim

6 To assess the effect on antibiotic prescribing in primary care of telehealth (TH) consultations
7 compared to face-to-face (F2F).

8 Design and setting

9 Systematic review and meta-analysis of adult or paediatric patients with a history of a community
10 acquired acute infection (respiratory, urinary, or skin and soft tissue). We included studies that
11 compared synchronous TH consultations (phone or video based) to F2F consultations in primary
12 care.

13 Methods

14 We searched PubMed, Embase, Cochrane CENTRAL (inception-2021), clinical trial registries and
15 citing-cited references of included studies. Two review authors independently screened the studies
16 and extracted the data.

17 Results

18 We identified 13 studies. The one small randomized controlled trial found a non-significant 25%
19 relative increase in antibiotic prescribing in the TH group. The remaining 10 were observational
20 studies but did not control well for confounding, and therefore at high risk of bias. When pooled by
21 specific infections, there was no consistent pattern. The six studies of sinusitis – including one
22 before-after study - showed significantly less prescribing for acute rhinosinusitis in TH consultations,
23 whereas the two studies of acute otitis media showed a significant increase. Pharyngitis,
24 conjunctivitis, and urinary tract infections showed not-significant higher prescribing in the TH group.
25 Bronchitis showed no change.

26 Conclusions

27 The impact of telehealth on prescribing appears to vary between conditions with more increases
28 than reductions. However, there is insufficient evidence to draw strong conclusions, and higher
29 quality research is urgently needed.

30

31 **Keywords:** Anti-Bacterial Agents, Respiratory Tract Infections, Urinary Tract Infections,
32 Telemedicine, primary health care

33

1 **How this fits in**

2 Acute infections are commonly treated with antibiotics adding to the problem of antibiotic
3 resistance. Due to the coronavirus pandemic (COVID-19), there was a shift towards remote
4 consultations to decrease the risk of infection and transmission. However, it is not clear if telehealth
5 consultations are contributing to antibiotic overuse or not. This study assessed the effect on
6 antibiotic prescribing in primary care of telehealth (TH) consultations compared to face-to-face (F2F)
7 for acute infections. The impact of telehealth on prescribing appears to vary between conditions
8 with more increases than reductions. However, there is insufficient evidence to draw strong
9 conclusions, and higher quality research is urgently needed.

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1 **Introduction**

2

3 Antibiotic prescribing is a major concern that contributes to the problem of antibiotic resistance.¹ In
4 Australia, more than 41% of the population received at least one antibiotic in 2017,² and 80% of
5 antibiotic prescriptions occurred in primary care.³

6 In primary care antibiotics are frequently prescribed for self-limiting acute respiratory infections
7 (ARIs) such as; middle ear infections, acute bronchitis, and sore throat,⁴ where antibiotics have little
8 benefits⁵⁻⁸ and may cause harms (such as vomiting, diarrhoea and rash).

9 Before the coronavirus pandemic in 2019 (COVID-19), several strategies (such as delayed
10 prescribing) and campaigns (such as the Choosing Wisely campaigns) aimed to reduce antibiotic
11 prescribing. In Australia antibiotics are usually prescribed in a face-to-face consultation with general
12 practitioners. However, in the era of COVID-19, remuneration for telehealth was introduced and
13 many clinicians have shifted to deliver patient care remotely to decrease the risk of transmission.
14 This change in mode of delivery may influence prescribing.

15 A recent systematic review concluded that there is insufficient evidence for an impact of telehealth
16 consultations on antibiotic prescribing.⁹ This review has several limitations, mainly related to the
17 search strategy, including studies for both synchronous and asynchronous telehealth consultations,
18 and the method of analysis of the included studies, hindering the interpretation of the impact of
19 telehealth on antibiotic prescribing. Our systematic review focuses only on synchronous telehealth
20 consultations- better comparable to face-to-face consultations, our search strategy included broader
21 keywords and mesh terms to find any relevant studies, and with a more detailed analysis sub-
22 grouped by the different conditions.

23 In this systematic review we aimed to identify and synthesize studies that have assessed the effect
24 of synchronous telehealth consultations on antibiotic prescribing compared to face-to-face clinical
25 encounters.

26 **Methods**

27

28 This systematic review is reported following the Preferred Reporting Items for Systematic Reviews
29 and Meta-Analyses (PRISMA) statement¹⁰. The protocol was developed prospectively and registered
30 on the International prospective register of systematic reviews (PROSPERO) Registration number
31 CRD42021239164. We followed the "2-week systematic review" (2weekSR) processes.¹¹

32

33 Eligibility criteria

34 *Participants*

35 We included studies of adult or paediatric patients with a history of a community acquired acute
36 infection (respiratory, urinary, or skin and soft tissue). We excluded studies of patients with chronic
37 infections, or hospitalized patients.

38 *Interventions*

39 We included studies of any type of synchronous telehealth consultations (phone or video-based).
40 Studies that reported the use of asynchronous telehealth consultations (text-based or web-based
41 with automated feedback) were excluded. Studies with telehealth consultations combined with an
42 education component were excluded unless it was given to both groups.

43 *Comparators*

44 We included studies that compared telehealth consultations to the usual face-to-face consultations.

1 *Outcomes (primary, secondary)*
2 The primary outcome was the number of antibiotic prescriptions in each type of consultation.
3 The secondary outcomes were follow-up visit rates, testing rates or number of samples sent to the
4 laboratory, any reported adverse events, hospitalization, and associated costs.
5
6 *Study design*
7 We included randomized controlled trials of any design (e.g., parallel, cluster, crossover), and any
8 type of observational studies. Reviews of primary studies (e.g., systematic reviews, literature
9 reviews, etc.) were excluded.

10 *Search strategies*
11 *Database search*
12 We searched PubMed, Embase, Cochrane CENTRAL from inception until 23 February 2021. We
13 designed the search string in PubMed, then translated it for use in the other databases using the
14 Polyglot Search Translator.¹² The complete search strings for all databases are provided in
15 **Supplementary Box 1**.
16
17 Clinical trial registries were searched on 2 March 2021 via Cochrane CENTRAL, which includes the
18 WHO International Clinical Trials Registry Platform (ICTRP) and clinicaltrials.gov. We also searched
19 for preprint articles through the Europe PMC database.
20 On 1 March 2021, we conducted a backwards (cited) and forwards (citing) citation analysis in Scopus
21 on the included studies identified by the database searches. These were screened against the
22 inclusion criteria.

23 No restrictions by language or publication date were imposed. We included publications that were
24 published in full. Publications available as abstract only (e.g., conference abstract) were included if
25 they had a clinical trial registry record, or other public report, with the additional information
26 required for inclusion. We excluded publications available as abstract only (e.g., conference abstract)
27 unless additional information available.

28 *Study selection and screening*
29 Two review authors (MB and EB or NK) independently screened the titles and abstracts for inclusion
30 against the inclusion criteria. One author (JC) retrieved full-text, and two authors (EB and NK)
31 screened the full-texts for inclusion. Any disagreements were resolved by discussion, or reference to
32 a third author (MB, MVD, CDM). The selection process was recorded in sufficient detail to complete
33 a PRISMA flow diagram (see Figure 1) and a list of excluded (full text) studies with reasons for
34 exclusions (**Supplementary Table 1**).

35 *Data extraction*
36 We used a data extraction form for study characteristics and outcome data, which was piloted on 2
37 studies in the review. Two authors extracted the following data from included studies:
38

- **Methods:** study authors, location, study design, duration of follow-up
- **Participants:** N, age (mean/median, range/SD), conditions, recent antibiotic use.
- **Interventions:** Type of telehealth consultation (video, phone, mixed, online), duration, who provided it, training, previous experience.
- **Primary and secondary outcomes:** indication for antibiotics, antibiotic prescribing rate, adverse events, number of follow-up visits, number of tests requested, or samples sent to the laboratory, hospitalization, antibiotic resistance (if measured in a follow-up visit).

45

1 Assessment of risk of bias

2 Two authors (MB and EB or NK) independently assessed the risk of bias for RCTs using the Cochrane
3 Risk of Bias Tool¹³ and for observational studies using ROBINS-I.¹⁴ We did not use the Newcastle-
4 Ottawa Scale as initially reported in our protocol, due to the lack of comprehensive manuals,
5 which meant that the tool instructions could be interpreted differently by different assessors. All
6 disagreements were resolved by discussion.

7
8 Measurement of effect and data synthesis

9 *Review Manager 5.4* was used to calculate the treatment effect¹⁵. We used odds ratios for
10 dichotomous outcomes reporting the number of patients with an event (e.g., antibiotic prescribing).
11 We undertook meta-analyses only when meaningful (when ≥ 2 studies or comparisons reported the
12 same outcome); anticipating considerable heterogeneity, we used a random effects model.

13
14 We separated analysis for RCTs, and observational studies (e.g., cross-sectional studies). We split our
15 analysis by reported conditions (e.g., sinusitis, bronchitis). No studies reported the severity of the
16 condition and thus we did not perform this subgroup analysis.

17
18 The individual was used as the unit of analysis, where possible. However, the data on the number of
19 individuals with primary and secondary outcomes of interest was not available. We extracted the
20 information as it was presented, e.g., the number of antibiotic prescriptions for all encounters/visits
21 in each group.

22
23 We contacted the authors of all included cross-sectional studies to obtain data of antibiotic
24 prescribing in previous years to control for any trend of change in antibiotic prescribing. However,
25 the responding authors stated they were unable to provide this for a variety of reasons.

26
27 We used the I^2 statistic to measure heterogeneity. As we only included one trial, we did not create a
28 funnel plot.

29 **Results**

30 Search results

31
32 The searches across 3 databases yielded 650 records. A backwards (cited) and forwards (citing)
33 citation analysis yielded an additional 433 records. The clinical registry search returned 19 records,
34 and the preprint search via Europe PMC returned an additional 150, resulting in a total of 1067
35 records to screen after deduplication. We excluded 1011 records after title and abstract screening
36 and obtained 56 records for full-text screening. We included 13 studies in the qualitative synthesis
37 and the meta-analysis (**Figure 1**). See **Supplementary Table 1** for a full list of excluded Studies with
38 reasons for exclusion.

39 **[Figure 1]**

40 Study characteristics

41
42 Of the 13 included studies (**Supplementary Table 2**¹⁶⁻²⁸), all except two, were conducted in the
43 United States of America (USA); they comprised 11 cross-sectional studies,^{16-18 21-28} one retrospective
44 before-after study²⁰ and just one RCT.¹⁹ Nine studies reported antibiotic prescribing for a respiratory
45 infection only, two studies provided data for all acute infections (respiratory, urinary, and skin and
46 soft tissue infections), one for both urinary and respiratory infections, and one for urinary infections

1 only. We did not find any studies that reported on antibiotic prescribing in telehealth versus face-to-
2 face consultations for skin and soft tissue infections. The type of telehealth consultations varied; five
3 studies reported the use of mixed phone and video consultation, four phone-only consultations, two
4 video consultations, and the mode was not clearly reported in two studies.

5 Risk of bias assessment

6
7 For the only RCT identified, we used the Cochrane risk of bias tool-1 to assess the risk of bias.¹⁹ The
8 overall risk of bias was generally unclear. Blinding of the patients and health care providers was not
9 possible. Random sequence generation, allocation concealment, blinding of outcome assessment
10 and the conflict-of-interest statement were all unclear due to inadequate reporting in the trial. We
11 found no evidence of incomplete outcome data or selective reporting of outcomes. The study
12 funding was reported.

13 For the remaining 12 studies, using the ROBINS-I tool to assess the risk of bias,^{16-18 20-28} found the
14 studies were mostly of moderate or serious risk of bias (**Table 1**). Due to the study designs, most
15 studies were considered at serious risk of confounding, unless the study authors reported an
16 appropriate analysis method used to adjust for important baseline confounding factors such as: age,
17 severity of infection, and any reported co-morbidities. Most studies had serious bias for the
18 selection of participants, as patients with less severe infections may differentially choose a mode of
19 consultations (telehealth rather than face-to-face). No information was available for the reporting of
20 missing data or selection of the reported results (no available protocols). The included studies had
21 moderate or serious risk of bias in classification of interventions and reported deviations from
22 intended interventions. Measurement of outcomes was rated 'moderate' for all studies.

23 **[Table 1]**

24 Primary outcome: Antibiotic prescribing

25

26 Randomized controlled trials (n=1)

27 Only one small trial investigated the difference of antibiotic prescribing between patients requesting
28 same-day appointments managed by face-to-face consultation (n=187) compared with telephone
29 consultation (n=180).¹⁹ There was more, but not significant, antibiotic prescribing in the telehealth
30 group compared to F2F consultations (Odds ratio (OR) 1.25, 95% CI 0.73 to 2.15) (**Figure 2**).

31 Before-After study (n=1)

32 One study examined antibiotic prescribing patterns after the transition to telehealth visits, due to
33 COVID-19 pandemic, and compared it to the previous F2F visits for acute rhinosinusitis.²⁰ There was
34 significantly less antibiotic prescribing in telehealth consultations (OR 0.78, 95% CI 0.69 to 0.89)
35 (**Figure 2**).

36 Cross-sectional studies (n=11)

37 Comparison of telehealth consultations with face-to-face in cross-sectional studies was sub-grouped
38 into the type of reported condition, to reduce confounding of type of consultation by condition
39 (**Figure 2**).

1 *Acute sinusitis (n=6)*

2 There was higher, but not significant, antibiotic prescribing in the F2F group (OR 0.83, 95% CI 0.68 to
3 1.0). Heterogeneity was high (78%).

4 *Pharyngitis (n=4)*

5 There was higher, but not significant, antibiotic prescribing in the telehealth group (OR 1.4, 95% CI
6 0.95 to 2.1). Heterogeneity was high (81%)

7 *Bronchitis (n=3)*

8 There was no significant difference in antibiotic prescribing for patients with bronchitis (OR 0.98,
9 95% CI 0.6 to 1.6). Heterogeneity was high (90%)

10 *Acute otitis media (n=2)*

11 There was significantly more antibiotic prescribing for patients with acute otitis media in telehealth
12 consultations (OR 1.3, 95% CI 1.11 to 1.5), with no heterogeneity.

13 *Conjunctivitis (n=2)*

14 There was higher, but not significant, antibiotic prescribing in the telehealth group (OR 1.8, 95% CI
15 0.7 to 4.5). Heterogeneity was high (91%).

16 *Urinary tract infections (n=2)*

17 There was higher, but not significant, antibiotic prescribing in the telehealth group (OR 1.4, 95% CI
18 0.7 to 2.9). Heterogeneity was high (79%).

19 **[Figure 2]**

20 Secondary outcomes

21 Diagnostic tests performed

22

23 **Table 2** shows the reported diagnostic tests performed after each type of consultation from six
24 studies. Generally, there are fewer diagnostic tests performed with telehealth consultations
25 compared to F2F.

26 **[Table 2]**

27 One study reported the percentage of adults who were diagnosed with pharyngitis and received an
28 appropriate Group A Streptococcus (strep) test to confirm the diagnosis.²⁸ The F2F group (n=2297,
29 49.5%) performed better than the telehealth group (n=4, 3.4%) on appropriate testing for
30 pharyngitis.

31

32 Follow-up visits

33

34 Seven studies provided results of follow-up visits (See **Table 3**). In general, patients who were
35 initially evaluated through phone contact were more likely to receive follow-up. The studies show

1 different follow-up time points.

2

3

[Table 3]

4 Adverse events (AE)

5

6 One study reported no statistically significant difference in the reported adverse events as evaluated
7 by diagnosis of pyelonephritis within 30-day follow-up duration for patients with urinary tract
8 infections.²¹ The study reported no hospitalization or sepsis in any patients for both F2F and
9 telehealth encounters (**Supplementary Table 3**).

10

11 **Discussion**

12 ***Summary of findings***

13 Our review identified only one RCT that assessed the impact of telehealth compared with face-to-
14 face consultations on antibiotic prescribing: finding a non-significant 25% relative increase. Most
15 studies were observational, did not control well for confounding, and therefore were prone to bias.
16 Pooling observational studies does not show a consistent pattern when analysed for specific
17 infections. For instance, antibiotic prescribing for acute sinusitis may be higher in a F2F consultation
18 and for pharyngitis higher in telehealth. However, many effect estimates do not reach statistical
19 significance and with significant heterogeneity suggesting, other than clinical differences,
20 methodological issues within the included studies.

21 ***Comparison with existing literature***

22 Our general finding is broadly consistent with the systematic review by Han et al⁹ who concluded
23 there was insufficient evidence that telehealth consulting has a significant impact on antibiotic
24 prescribing in primary care. However, in our review we pooled the observational studies and
25 explored the impact in consultations concerning specific infections. These results show a more
26 diverse picture that can make clinical sense. The two cross-sectional studies that assessed
27 prescribing for acute otitis media^{25,26} consistently find that antibiotics are more likely to be
28 prescribed in TH consultations. Perhaps the inability to examine the ear allows clinicians to be more
29 lenient with prescribing, especially under parental pressure.²⁹

30 ***Strengths and weaknesses***

31 This review's main strength is its rigor of methods and analysis: the extensive search is unlikely to
32 missed important studies; and the detailed synthesis of the results by study design and by condition
33 has made best use of the available published research. However, there are also several weaknesses:
34 the paucity of studies with adequate control of confounding; the wide heterogeneity (both of clinical
35 conditions and results); and imprecision of the results, means that there is no single reliable message
36 to take away from this research.

37 ***Implications for research and clinical practice***

38 It is important to note there are different modalities of telehealth, with or without visual that may
39 impact the inclination to prescribe. Also, the link with clinical outcomes and patient satisfaction

1 deserves further exploration.³⁰ In situations like the current COVID-19 pandemic, synchronous
2 telehealth consultations have ensured patients' access to primary care services and have changed
3 the landscape of service delivery for good.³¹ Therefore, better understanding how prescribing adapts
4 is critical for antimicrobial stewardship.

5 While there is insufficient evidence about the rate of antibiotic prescribing in teleconferences
6 compared to the usual face-to-face ones to draw strong conclusions, there are some concerns. The
7 impact appears to vary between conditions, but more suggest increases in antibiotic than
8 reductions. For example, if patients with acute respiratory infections all chose to consult via
9 telehealth, then the antibiotic prescriptions for telehealth would be greater than face-to-face (and
10 the reverse of those patients selectively chose face-to-face consultation). Furthermore, telehealth
11 may change the diagnostic process because of the limitations on physical examination. Given the
12 importance of any increased antibiotic use to the development of antibiotic resistance,³² this clearly
13 this suggests more studies need to be undertaken with better design — either as randomized trials,
14 or at least controlled before-after studies. To study prescribing change at population level, the ideal
15 study process would be to compare the change in antibiotics when a blend of telehealth and face-to-
16 face consultations are introduced with the change of face-to-face is retained. In the situation when
17 randomisation of practices is not possible, then we might adjust for confounding by using the pre-
18 change level of antibiotic prescribing, and ideally for any trends using a series of times prior to the
19 change. If the suggestions that in some diagnoses more antibiotics are prescribed in F2F
20 consultations, then further research to understand ameliorate will become urgent.

21

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28 **Ethical approval:** None required

29 **Competing interests:** None

30

31

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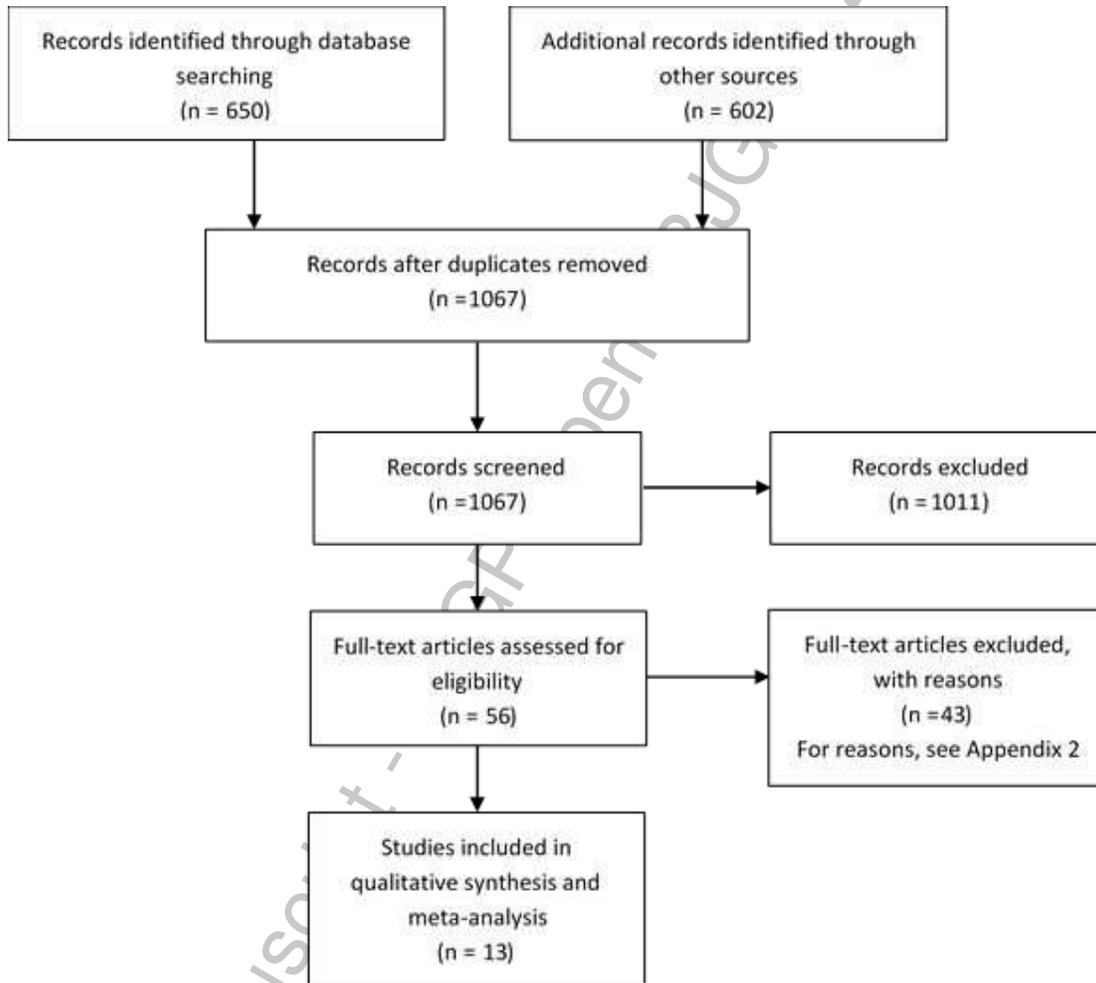
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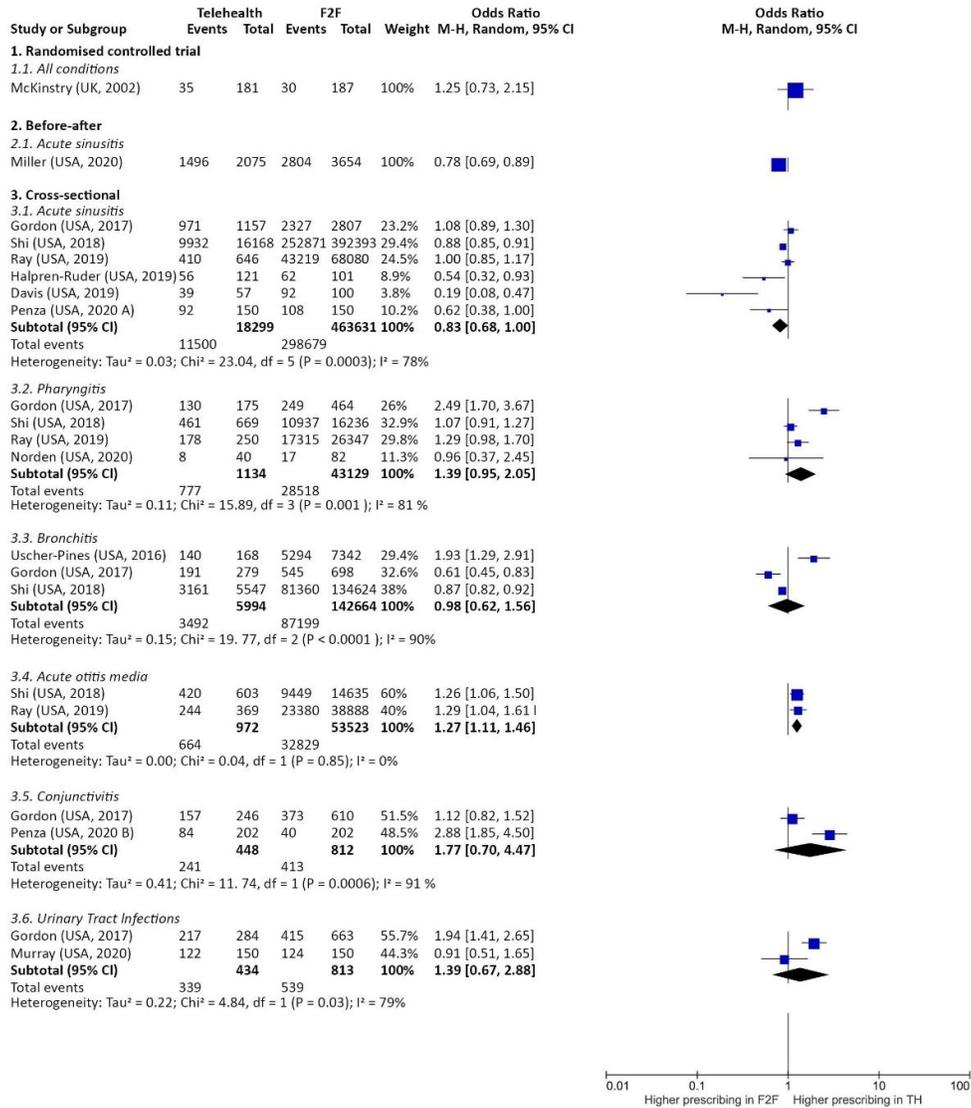
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Figure 1. PRISMA Flow Diagram¹⁰



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Figure 2. Antibiotic prescribing in synchronous telehealth compared to face-to-face (F2F) consultations

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Table 1. Risk of bias of included observational studies using ROBINS-I

Reference	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported results	Overall risk of bias
Uscher-Pines (USA, 2016) ²⁸	Serious	Moderate	Moderate	Serious	No available information	Moderate	No available information	Moderate
Gordon (USA, 2017) ¹⁷	Serious	Moderate	Moderate	Moderate	No available information	Moderate	No available information	Moderate
Shi (USA, 2018) ²⁶	Moderate	Serious	Moderate	Moderate	No available information	Moderate	No available information	Moderate
Davis (USA, 2019) ¹⁶	Serious	Moderate	Moderate	Serious	No available information	Moderate	No available information	Serious
Halpren-Ruder (USA, 2019) ¹⁸	Serious	Serious	Moderate	Moderate	No available information	Moderate	No available information	Moderate
Ray (USA, 2019) ²⁵	Moderate	Serious	Moderate	Moderate	No available information	Moderate	No available information	Moderate
Miller (USA, 2020) ²⁰	Serious	Moderate	Moderate	Serious	No available information	Moderate	No available information	Moderate
Murray (USA, 2020) ²¹	Serious	Serious	Moderate	Serious	No available information	Moderate	No available information	Serious
Penza (USA, 2020 A) ²³	Serious	Serious	Serious	Serious	No available information	Moderate	No available information	Serious
Penza (USA, 2020 B) ²⁴	Serious	Serious	Serious	Serious	No available information	Moderate	No available information	Serious
Stenehjem (USA, 2020) ²⁷	Serious	Serious	Moderate	Serious	Moderate	Moderate	No available information	Moderate
Norden (USA, 2020) ²²	Serious	Serious	Serious	Serious	No available information	Moderate	No available information	Serious

Table 2. Diagnostic test performed

Study ID	Diagnostic tests requested	Condition	Telehealth group N (%)	Face-to-face group N (%)	Reported P value ^a
Randomized controlled trial					
McKinstry (UK, 2002)¹⁹	Not specified blood test	All conditions	8 (4%)	10 (5%)	Not reported
	Not specified urine test		6 (3%)	8 (4%)	
	X-ray		1 (0.6%)	5 (3%)	
Cross-sectional studies					
Gordon (USA, 2017)^{17 b}	Not specified lab tests	UTI	85 (20.6%)	1095 (88.4%)	<0.001
		Pharyngitis	45 (15.8%)	627 (73.5%)	<0.001
		Sinusitis	185 (11%)	1302 (25.7%)	<0.001
		Bronchitis	40 (10.1%)	308 (25.8%)	<0.001
	Not specified Imaging	Cough	18 (11.4)	111 (23.5)	0.001
		Bronchitis	34 (8.6%)	212 (17.8%)	<0.001
		UTI	34 (8.2%)	227 (18.3%)	<0.001
		URI	69 (8.1%)	236 (9.3%)	0.31
Murray (USA, 2020)^{21 c}	Urinalysis/dip stick	UTI	8 (5%)	140 (93%)	<0.0001
	Urine culture		11 (7%)	31 (21%)	<0.001
Norden (USA, 2020)^{22 d}	Not specified lab tests	Pharyngitis	0.125	0.207	0.55
		URI excluding pharyngitis	0.023	0.129	0.096
		Otitis media	0.250	0.107	0.60
Ray (USA, 2019)²⁵	Strep test	Streptococcal Pharyngitis	7 (1%)	10878 (67%)	Not reported
Shi (USA, 2018)²⁶	Strep test	Streptococcal Pharyngitis	9 (4%)	17818 (68%)	Not reported
UTI: Urinary tract infections, URI: Upper respiratory tract infections					
^a Chi-square test					
^b Tests were conducted within 21 days of index visit for all conditions					
^c Tests were conducted at initial encounter					
^d Average numbers of labs ordered					

