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Telemedicine based management of Uncomplicated Urinary Tract Infections – a Scoping Review

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Literature review

Title: Telemedicine based management of uncomplicated urinary tract infections – a scoping review

Running title: Telemedicine and cystitis

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Abstract

Background: Uncomplicated urinary tract infections (uUTI) are very common bacterial infections affecting more than half of all women and constituting a substantial proportion of antibiotic indications. Diagnosis and treatment is primarily based on patient history without the need for laboratory testing. Telemedicine (TM) has been applied for management of uUTI for many years. As this practice rapidly grows, a contemporary review of existing literature and knowledge gaps is beneficial. The purpose of this review was to explore existing literature on the use TM for uUTI and identify possible effects on healthcare resources, patient safety and the use of antibiotics.

Method: A scoping review was conducted consisting of a comprehensive search strategy on two electronic databases, PubMed and Scopus. Studies included for this review were with relevance to primary care and entailed uUTI, adult patients and written in English or Scandinavian.

Results: Search results in Pubmed gave 368 articles and in Scopus 489 articles. After revision, 14 articles were included and synthesized. Several articles demonstrated a reduced use of healthcare resources, through reduced revisits and laboratory analysis. Safety was maintained provided TM was practiced on low-risk patients, primarily due to the low incidence of adverse outcomes. Whilst only one study found a lower proportion of antibiotic prescription in the use of TM, two studies presented results of increased adherence to guideline antibiotics.

Conclusion: TM has shown to be an effective, safe and convenient practice for uUTI. More research is needed to evaluate and clearly identify the optimal patient population suitable for inclusion and the potential risk of antibiotic overuse.

KEYWORDS: Cystitis; Telemedicine; UTI

Background

Urinary tract infections

Urinary tract infections (UTI) are common bacterial infections, ranging from uncomplicated cystitis to complicated UTI requiring hospitalization. Women are more likely to develop UTI than men, mainly because of anatomical differences. More than half of all women will be affected at least once during their lifetime and recurrence rates are high (1).

UTI are defined by anatomic location (upper or lower UTI) and complicating risk factors (complicated or uncomplicated UTI) (1, 2). Uncomplicated cystitis (uUTI) is the most common form of UTI that occur in the lower urinary system in otherwise healthy non-pregnant women (1). In primary healthcare settings, it accounts for approximately 95% of all urinary tract infections (3) and are diagnosed in over one in four of all Swedish women within a 20 year time period (4). The term "uncomplicated" assumes absence of underlying medical conditions, such as urological diseases or anomalies, immunosuppressive conditions or medication, or other health problems that could complicate treatment or management of the UTI (1). If the infection involves the upper urinary tract system, e.g. the kidneys, it is considered a pyelonephritis UTI, which also can be either complicated or uncomplicated (1, 2) but is about 20 times less common than cystitis (5).

Cystitis is characterized by symptoms such as pain or burning sensation during urination (dysuria), frequent urination (pollakiuria), and/or a strong urge to urinate (urgency). While uncomplicated cystitis is generally non-life-threatening or cause serious health problems, they can cause significant discomfort and pain, disturbing an otherwise well-functioning individuals daily life (6). One study presented an average of six symptom days, 2-4 days of restricted activity and 1.2 days of work lost per UTI (7).

The traditional approach to uUTI involves physical visits to healthcare providers for diagnosis and prescription of antibiotics, although research has shown that evaluation and treatment varies among physicians (8). Treatment for uUTI usually involves antibiotics, based on local/regional guidelines. It is one of the most common indications for antibiotics in primary care, however inappropriate prescribing has been demonstrated (9). Although antibiotics reduce symptomatic days, an estimated 30% of cases of uUTI are self-limiting within a week (10). However, a recent Swedish study found that about one percent of all women who succumb to uUTI risks a pyelonephritis within 30 days, but the risk is reduced by antibiotics (11). Absence of treatment

rarely lead to serious disease such as pyelonephritis, and no long term effects on renal function or increased mortality (12).

Telemedicine

Telemedicine (TM) refers to the use of telecommunication and information technologies to provide medical services from a distance. Telemedicine-based treatment may include the use of digital platforms, such mobile apps or online consultations as well as basic telephone calls, to allow patients to communicate with healthcare providers from the comfort of their own homes. During circumstances such as the recent pandemic, TM could reduce the risk of exposure to infectious agents for both patients and healthcare providers. Whilst during ordinary times, TM could reduce the burden on healthcare systems and provide increased potential benefits for the public health. Telemedicine has gained popularity in recent years. It is applied increasingly for the management of various medical conditions, including UTI. TM treatment for uUTI involves patients using remote communication tools to consult with healthcare providers, who diagnose and prescribe treatment (13, 14).

Uncomplicated UTI is very suitable for TM based treatment as diagnosis is based principally on patient history, as recommended by European guidelines (15). Classic UTI symptoms, in the absence of symptoms of other common differential diagnoses, can increase probability of diagnosis to 90%, while laboratory testing supplements minimal value other than in uncertain cases (16).

Overviews of previous research on the use of TM management of uUTI are limited. As modern times change rapidly and the use of TM increases, an updated comprehensive review of existing literature in this field therefore seems warranted, to evaluate efficacy and safety of TM based treatment of uUTI.

Purpose

The purpose of this scoping review is to examine the existing literature on the use TM regarding uUTI and identify possible effects on physician availability, safety, healthcare resources and antibiotic use.

Method

Design

A scoping review was conducted using a comprehensive search strategy on the electronic databases PubMed and Scopus. A scoping review is an appropriate method to provide a broad and current overview of research on this topic, as well as to identify gaps in the knowledge for the focus of further research (17).

Selection

Inclusion criteria:

- Primary care
- Uncomplicated UTI
- Adults
- English or Scandinavian language.

Exclusion criteria:

- Secondary or tertiary care
- Complicated UTI
- Children
- Urological, nephrological or otherwise consequential comorbidities.

A modified PICO to serve the purpose of this scoping review would include a population of healthy adult females, i.e. uncomplicated UTI, treated by TM compared to traditional physical visits. The outcomes of interest are safety, effects on healthcare resources and antibiotic use.

Data charting and analysis

A first unstructured trial search of PubMed using “telemedicine” and “UTI” found six relevant articles, which led to more relevant search words that were used for the structured search.

A structured PubMed search was conducted on 230228 using the following search words:

(telephone-based OR telemedicine OR telephone) AND (UTI OR uUTI OR cystitis OR "urinary tract infection" OR Urinary tract infection[MeSH Terms]) AND (antibiotics OR therapy OR treatment)

Articles revised after the primary search led to new search terms to broaden the scope. A new search in PubMed was conducted 230314 using the following search words:

(telephone-based OR telemedicine OR telephone) AND (UTI OR uUTI OR AUC OR acute uncomplicated cystitis OR cystitis OR "urinary tract infection" OR Urinary tract infection[MeSH Terms]) AND (antibiotics OR therapy OR treatment)

Similarly, a primary search was conducted in Scopus on 230228 using the following search words:

(TITLE-ABS-KEY (telephone-based OR telemedicine OR telephone) AND TITLE-ABS-KEY (uti OR uuti OR cystitis OR "urinary tract infection") AND TITLE-ABS-KEY (antibiotics OR therapy OR treatment)

After the same process as described above, a second search was conducted 230328 using:

(TITLE-ABS-KEY ((telephone-based OR telemedicine OR telephone)) AND TITLE-ABS-KEY ((uti OR uuti OR cystitis OR "urinary tract infection" OR auc OR "acute uncomplicated cystitis")) AND TITLE-ABS-KEY ((antibiotics OR therapy OR treatment)))

The articles found in Scopus and PubMed were systematically processed in the same way, initially by title and if available by abstract. Articles not available in full text (not found or subject to cost) were excluded.

Ethics

As a scoping review, ethical approval was not relevant or needed as no sensitive or patient related information was processed. For the articles included, ethical considerations were explicit but not needed in one (6) and approved for five studies (18, 19, 20, 21, 22).

Results

A structured search performed in PubMed resulted in 368 articles and in Scopus 489 articles. After comprehensive processing, articles were excluded after review of titles, abstracts and availability in full text, based on inclusion and exclusion criteria. The result was 14 studies which were included in this scoping review. See figure 1 and table 1.

Fig. 1 – Flowchart of selection process

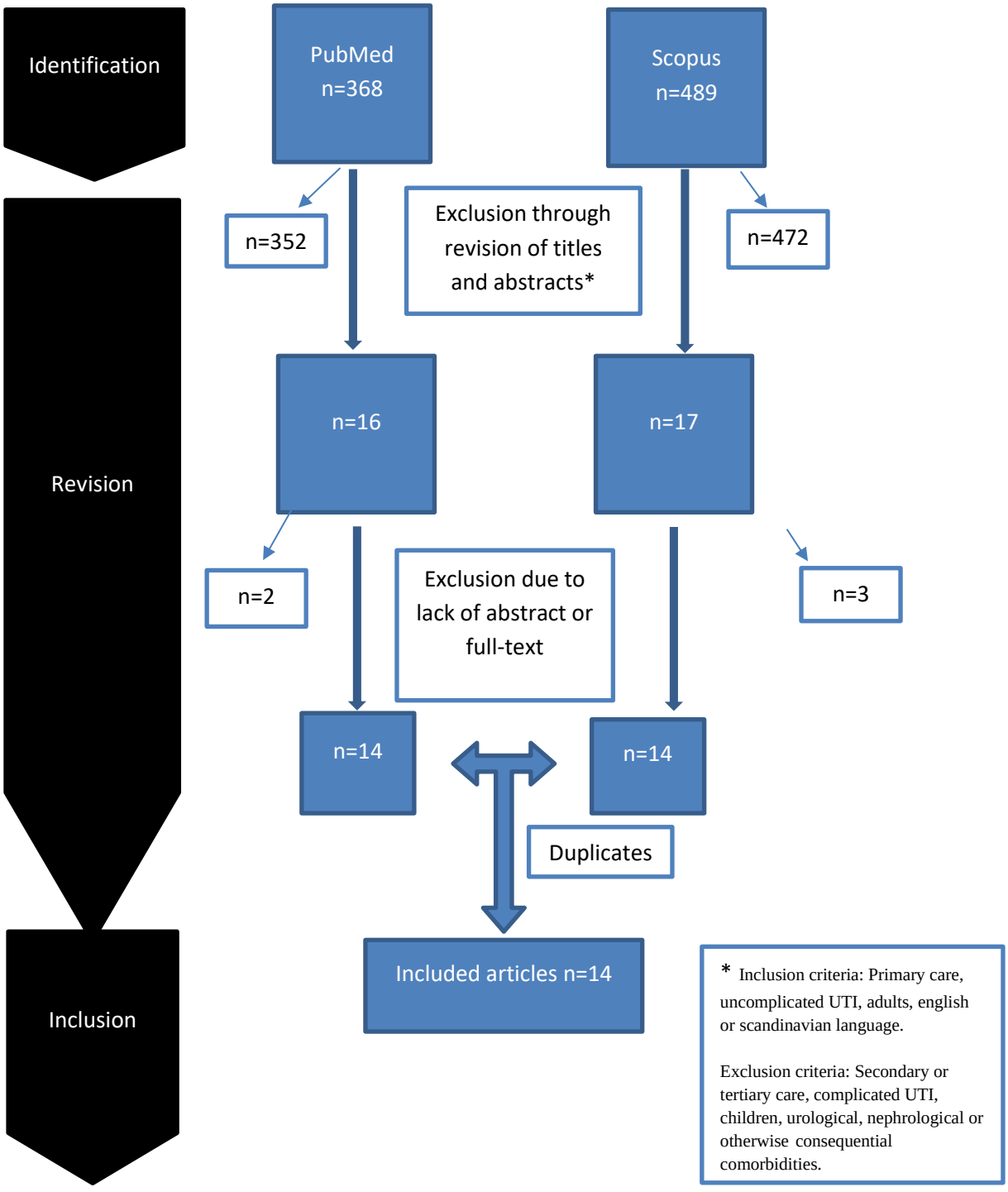

Table 1. Characteristics of included studies

Authors, origin	Year	Study design	Population	Summary points
Saint et al. (23), USA	1999	Population-based, before-and-after study, concurrent control groups	3889 women, age 18-55	TM led to; Decreased proportion of urinalysis. Increased guideline antibiotics. No increase in adverse outcomes.
Campbell et al. (24), USA	1999	Review, survey	100 women surveyed, ages not presented	98 women preferred telephone management over physical visit.
Flottorp et al. (25), Norway	2000	Systematic review, 14 studies (1 RCT)	67-3108 patients	Low risk of adverse outcome. High chance of uUTI based on history without urinalysis.
Vinson et al. (26), USA	2004	Retrospective cohort	4177 women, age 16-97	Reduced physical visits, higher proportion use of guide-line antibiotics. <1% pyelonephritis. No hospitalization, sepsis or deaths.
Schauberger et al. (27), USA	2007	Retrospective chart review	273 women, age 17-85	75% treated without urinalysis. Over 60 days, 17% recurrence, 2% pyelonephritis.
Blozik et al. (20), Switzerland	2011	Observational, prospective	499 women, age 18-65	78% complete recovery, 14% symptom reduction, 3% no effect, 4% worse.
Bollestad et al. (18), Norway	2015	RCT	441 women, age 16-55	No significant differences in days until symptomatic resolution. No cases of adverse outcomes.
Ewen et al. (21), USA	2015	Retrospective cohort	114.610 patients, all ages.	12.4% of all antibiotics prescribed via telephone, UTI most common indication.
Rastogi et al. (22), USA	2019	Observational, Cross-sectional	20,600 patients, 96% female, age 18+	94% of UTI patients received antibiotics through TM. 63% reported otherwise seeking urgent care, 4% emergency care and 26% doctors office.
Novara et al. (28), Italy	2020	Systematic review (no RCT´s)	6 studies, 99-20600 patients.	Data indicative of safe and effective treatment of uUTI through TM.
Johnson et al. (29), USA	2021	Retrospectiv cohort	350 women, age 18-65	TM management more likely to receive guideline-concordant treatment, less likely urinalysis and revisits within 7 days.
Al-Saadi et al. (19), Sweden	2021	Observational, Cross-sectional	307 women, age 16-50	Superior documentation in TM compared to physical visits. Less likely to prescribe antibiotics with TM.
Grigoryan et al. (6), USA and Germany	2022	Qualitative, interview-based	65 women, 40 (USA) 25 (Germany), age ≥18	Wide range of negative emotions due to uUTI symptoms, interference with ADL, relationships and sleep. Delay and frustration with seeking medical help.
Hernández-Hernández et al. (30), Spain	2022	Review, narrative	Not specified	uUTI safe to treat by TM, risk of antibiotic overprescription

Designs

The 14 studies included consisted only of two experimental studies, one RCT (18) and one controlled before-and-after study (23). Four reviews were included, of which two were systematic review (25, 28), one narrative (30) and one which performed a survey (24). One qualitative interview-based study was included (6). The rest were observational studies, consisting of three retrospective cohorts (21, 26, 29), one retrospective chart review (27), one prospective with three day follow-up (20) and two cross-sectional (19, 22).

Populations

The included studies were published between 1999 and 2022. Eight came from USA, of which one was conjointly performed in Germany, two from Norway and one each from Sweden, Switzerland, Italy and Spain. The populations varied somewhat in age, all consisted of adult women, but the lower age limit varied between 16 to 18. The upper age limit varied significantly between 50 to 97. The survey by Campbell et al. (24) didn't specify age of interviewed women and in the large retrospective cohort by Ewen et al. (21), which studied antibiotic prescriptions in a large populations, all ages were included. Although the majority of patient populations consisted of uncomplicated UTI, two studies revealed TM treatment of patients who would be regarded as complicated UTI, including men and pregnant women (22, 26). Vinson et al. included elderly, pregnant women, diabetes and glucocorticoid treatment, which comprised 6% of their cohort. However, they did not see higher incidence of adverse outcomes in this non-low risk population (26).

Interventions/Comparisons

Two studies performed interventions (18, 23):

The RCT by Bollestad et al. randomized women with typical symptoms of uUTI either to a TM group treated by a diagnostic algorithm or for regular physical consultation. The main outcome measured days until symptomatic resolution. No significant difference in days until symptomatic relief was seen by day three. By day four 79% of TM group and 72% of control group were symptom-free. A tendency was noticed that TM provided somewhat shorter symptom days and less likelihood of revisits. No cases of adverse outcomes were seen in either group after two weeks (18).

The study by Saint et al (23) performed a pre- and postintervention, to investigate the use of a telephone-based uUTI algorithm where classic symptoms were treated without laboratory testing and prescribed guideline antibiotics. The preintervention study group included 1,761 patients and the postintervention group 1,883 patients while 245 patients comprised a control group, totaling 3,889 patients in the study. Postintervention, the proportions of laboratory testing and clinic visits decreased substantially whilst the adherence to guideline-recommended antibiotics increased. Adverse effects (sexually transmitted disease (STD), recurrent UTI or pyelonephritis within 60 days) remained without significant difference. Additionally, a patient survey was given 100 women of whom 85% stated that should they acquire another UTI, they would prefer a telephone consultation and prescription rather than a clinic visit. The authors observed a trend in their statistics which could indicate that STD in some women were misdiagnosed as cystitis (23).

Two studies performed comparative studies (19, 29):

The retrospective cohort by Johnson et al. compared antibiotic treatment between physical visits and TM care for treatment of uUTI. The study did not find any difference in antibiotic prescription rate but did see that patients treated through TM were more commonly prescribed guideline-concordant antibiotics and treatment duration. As a secondary outcome it was seen that in the TM group urinalysis was less likely to be taken and the rate of revisit within seven days was lower (29).

The cross-sectional study conducted by Al-Saadi et al compared treatment and documentation between physical and TM based care. Both groups received guideline antibiotics, however the proportion who received antibiotics were significantly higher in the physical group (95%) compared to the TM group (62%). Documentation of two of the core symptoms including correct subsequent antibiotic treatment, whilst negating symptoms of complicated UTI or differential diagnoses, was higher in the TM group. Documentation was therefore assessed as more correct through TM (19).

Outcomes and significant results

Adverse outcomes of uUTI, including serious pyelonephritis, sepsis, hospitalization or death have been shown to be very rare. Several studies demonstrated low incidence or absence of these events and more importantly no increase or difference compared to traditional physical

visits, supporting TM as a safe method of practice (18, 20, 23, 25, 26, 27). The four included reviews concluded that data is indicative of safe and cost-effective treatment of uUTI by TM. (24, 25, 28, 30)

Three studies identified a correlation of lower rates of clinic revisits and therefore less use of healthcare resources in TM groups (18, 26, 29). A lower rate of urinalysis and the lack of necessity was observed by several studies (23, 25, 27, 29). Additionally, in a study by Rastogi et al. (22) 69% of UTI patients were asked what they would have done if telemedicine was not available. 63% reported an urgent care clinic, 26% a regular clinic, 4% emergency department and 7% would have done nothing (22).

Three studies showed results of increased adherence to guideline antibiotics whilst not increasing the amount of antibiotic prescriptions (23, 26, 29) and one study found that the proportion of prescribed antibiotics was lower when treated by TM (19). A large retrospective cohort including 114,610 patients between 2006-2010 showed that 12,4% of all antibiotics were prescribed over the telephone. During a single year, 28% of all telephone prescriptions were for UTI (21).

A large cohort study by Vinson and Quesenberry (26) analyzed a sample of 4177 women who received TM management of presumed uUTI. 18% of the study group was within 6 weeks of telephone management in need of additional one or more medical encounters. Of these, 0.5% were diagnosed with pyelonephritis. 15% were diagnosed with cystitis within 2 weeks. No women required hospital care, acquired sepsis syndrome or died. No increase in hospital admissions, emergency department- or clinic visits was observed. In addition, the study found reduced laboratory and clinic visits and an increased use of guideline-recommended antibiotics, without an increase in total antibiotic prescription (26).

A qualitative study conducted by Grigoryan et al (6) in 2022 investigated the emotional impact UTI. The study presented varied experiences of UTI and the consequent need of medical help. Some sought care as soon as symptoms presented, while others portrayed more resistance. The following barriers were described; “inconvenience or necessity of taking time off work to see a doctor, wanting to avoid the frustration of a doctors´s visit, wanting to solve the problem themselves, hoping the condition would resolve without antibiotics, and a reluctance to take antibiotics unless really needed.” (6).

Ethical considerations were taken for six of the included studies but not mentioned in the rest. Notably the experimental study by Saint et al. (23) did not mention or discuss ethical consideration or implications of their study. The study was published 1999 and conducted a few years previously, indicating perhaps a time and setting where ethics was not discussed as today. Out of the two comparative studies, from the same year 2021, only the Swedish study had ethical considerations and approval to conduct the study.

Discussion

The main findings of this scoping review suggest that under the right circumstances TM is a safe and cost-effective method for the management of uUTI. Presumably, antibiotic use is prescribed more accurately. However, gaps in knowledge exist, as research in this field is limited. Although studies predate more than two decades, very few experimental studies have been performed. Several observational studies exist to support the practice of telemedicine for uUTI. This scoping review presented synthesized results supporting the use of TM for uUTI. Safety was maintained provided that only low-risk patients were included. Adverse outcomes were rare and serious morbidity or mortality was not seen. Healthcare resources are spared principally through fewer laboratory visits and physician consults, also through reduced revisits and averting urgent or emergency care. Antibiotic use matched conventional practice, with indications of higher probability of correct practice.

Previous systematic reviews consistently agree that TM, when including accurate patient populations, is a safe and cost-effective practice. Several studies emphasized the need for further research regarding antibiotic use and optimal patient populations. Nevertheless, all studies presented supporting and favorable conclusions of telemedical practice for uUTI.

Telemedicine seems to follow the general evolution of technology, which is growing exponentially. When applied in healthcare and practiced for management for uUTI some ethical considerations should be taken. More experimental research seems warranted and consideration about inclusion criteria must be taken. As physical visits are prevented, downsides could be the potential risk of overlooking the complexity of diagnosing human beings, where important information is gathered through more than merely verbal communication. As with everything in medicine, benefit does not come without risk to the individual. Fortunately, for research in uUTI, potential risk of serious harm seems low regardless of management method. The potential benefit on both individual and societal levels conceivably outweighs risks. Demographics should be considered in future research as a potential universal safe population may not exist. Additional research could provide a lowest safe standard for further local revision before implementation. The effect of more resources and availability would open further ethical discussion as to where resources then should be focused.

The cost-benefit of TM based care for uUTI seems clear, assuming safety is taken into consideration. Diagnosis of uUTI can reliably be processed based on patient history and therefore by TM, which would result in decreased pressure on physical clinics, both in primary

care as well as secondary/tertiary healthcare (1, 4). A refrain from urinalysis in correct diagnosed uUTI has the potential to save money and both clinic and laboratory resources. As this diagnosis is so common, the scale of potential monetary saving or reallocation of financial resources could provide great benefit to healthcare systems.

Furthermore, research could focus on optimizing cost-effectiveness of TM systems, depending on local or regional settings and populations. The articles included had some variation in sample age and characteristics which affects external validity and increases the possibility to generalize results. Important considerations include population age and socio-economic status, as the risk of significant comorbidities or STD vary based on these factors.

Safety can be viewed through two lenses. Individual safety, where a potential risk of misdiagnosis could lead to serious adverse events and harm an individual. Also, communal safety where antibiotic resistance is a persistent global theme in recent years.

The risk of antibiotic overuse and misuse with the application of TM is discussed in several articles. For example, Vinson and Quesenberry (26) discuss that the presumption of cystitis without laboratory confirmation could result in overdiagnosis and overprescribing of antibiotics. Although discussed by most, none of the reviewed articles could demonstrate or reveal an overprescribing of antibiotics. On the contrary, TM based care has been linked to lesser antibiotic prescription and closer guide-line adherence, as well as correct documentation (19).

Possible reasons may be that in a physical consultation it could be harder to withstand patients requests to treat with antibiotics, as well as the lack of standardized or "closed" questions. When applying an algorithm by TM the chance of managing uUTI in a standardized way increases, as physician variation and bias might abate. However, a risk of overdiagnosing remains, as diagnosis through TM abstains from objective testing. An important aspect is that even in physical consults, modern guidelines recommend against urinalysis for uUTI, as it supplies limited information to diagnosis (15). Studies have shown that in physical consultations as well as TM based management, patients are prescribed antibiotics despite negative laboratory results (26, 31). The effect of this on antimicrobial resistance seems unclear and warrants more research. Further research into possible antibiotic overprescribing of uUTI could be of interest.

The risk of misdiagnosis could lead to prolonged suffering or in some cases a delayed treatment of serious complicated UTI. The studies in this scoping review did not find any serious adverse events or deaths in any sample groups. This apparent rarity of serious outcomes supports the

safety of telephone management. An effective screening algorithm to include adequate low-risk patients and referral of high-risk patients is paramount. A stringent adherence to locally worked out algorithms should apply TM on low-risk patients while maintaining regular practice for the remainder of patients. The safety and effectiveness of TM management of uUTI will rely on how well criteria is applied for inclusion and exclusion of patients. The absence of serious adverse events seems related to the strict exclusion of non-low-risk patients. Regardless of treatment method, but more so to maintain a safe TM practice, it is of vital importance to ensure that patients have a safety-net where follow-up is provided timely if needed. In the studies that observed adverse effects or resulted in a differential diagnosis, a blind spot remains as to whether the non-uUTI diagnoses were present at the time of telephone management or acquired thereafter.

Weaknesses of this scoping review include the limited number of articles and databases searched, due to limitation in time and resources. The lack of experimental studies highlights the need for further research. The articles in this review are relatively heterogenous regarding populations, presenting opportunity for higher generalizability.
Strengths include a broad overview of all existing literature in two large databases and synthesizing of clinically relevant information and data.
The main limitation of TM is the inability to perform a physical examination. Depending on patient history and clinical presentation, a physical exam is essential for diagnosing certain medical conditions, including complicated UTI. Other limitations of TM may also be inadequate technological systems, patients' knowledge of technology or the inability to use it effectively.

Some clinical implications can be extracted from this scoping review, which presents positive results regarding patient safety and saving of healthcare resources. For individual patients, the convenience of TM based care for uUTI could be highly beneficial. As the qualitative study (6) showed, the facilitation of TM could provide great benefit to women who find traditional consults inconvenient and stressful. TM also provides availability for patients, particularly in vast geographic regions where healthcare is not easily or readily accessible. The reduced need for patients to take time off work or arrange transport to a clinic also provides benefits. Based on present research, it is important to be strict in only including low-risk patients, to maintain safety for the individual. In healthcare systems where physical consults are of shortage or implicates a financial cost which certain patients cannot afford, TM could provide considerable

improvement and optimizing of healthcare resources. Finally, on a societal level, the main impact of spared healthcare resources could provide additional physician availability in both primary and specialized care, averting a lack of availability that could lead to the degradation of public health.

The implementation of telemedicine in modern medicine seems inevitable. For certain suitable medical conditions, including uUTI, telemedicine holds several advantages over traditional physical visits.

Conclusions

Applied and practiced correctly TM has demonstrated great promise in the management and treatment for uncomplicated UTI. For this diagnosis, TM has shown to be an effective, safe and cost-efficient practice. The reduced burden of in-person visits on both patients and healthcare providers are highly beneficial. More research is needed to evaluate and clearly identify the optimal patient population for these treatment options and the potential risk of antibiotic overuse.

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