University of Reading

Behavioural Insights into Tackling Antimicrobial Resistance and Urinary Tract Infections during Pregnancy

PhD in Pharmacy Practice

School of Chemistry, Food, and Pharmacy

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July 2021

Abstract

Background

Antimicrobial resistance (AMR) is a global threat linked to excessive antibiotic use. It is concerning in pregnancy because of the limited range of treatment options and transmission of resistant pathogens to the baby during birth. Antibiotics are the most frequently used medication during pregnancy, with urinary tract infections (UTIs) being the most common indication. The aim was to explore how AMR can be tackled in the context of UTIs during pregnancy using behavioural science.

Method

Multiple methods were used for the research collection in this thesis. The first study was a systematic review of measures to prevent UTIs during pregnancy. Second and third studies focused on qualitatively exploring women's perspectives using data from an online forum and semi-structured interviews. The fourth and fifth studies explored professionals' practice through an audit of antibiotic prescribing and qualitative interviews with prescribers.

Results

The systematic review highlighted that preventative behaviours are associated with a reduced incidence of UTIs during pregnancy. The second study showed that women's decision-making is primarily influenced by pre-natal attachment to the baby causing them to favour antibiotics whilst undermining the risks from AMR. The third study adds that they view UTIs through a biomedical model and perceive preventative behaviours as ineffective leading to low self-efficacy in managing personal health and tackling AMR. The audit reveals that prescribers frequently issue empirical broad-spectrum antibiotics and the fifth study indicates that they are highly cautious during pregnancy which might lead to antibiotic overprescribing. Prescribers also view UTIs through the biomedical model and therefore may not emphasise prevention or self-care advice.

Conclusion

Prevention of UTIs through behavioural measures is an effective approach to reducing antibiotics during pregnancy. Interventions targeting women and healthcare professionals require focus on encouraging preventative behaviours which can minimise infections and reduce antibiotic use in response to AMR.

Acknowledgements

I am grateful to have had access to education and therefore my first and most sincere thanks go to my parents, Nasim and Florine, for their hard work and dedication to empower me in this way.

Thank you to my supervisors, Dr. Amelia Hollywood, Prof. Kath Ryan, and Dr. Alexander Edwards for their invaluable insight. Amelia, thank you for being you so encouraging and believing in my ability when I had doubts. To all my colleagues in HN 1.05 and the Pharmacy Practice team, some have also been my teachers - thank you for your help and imparting your knowledge. A special thanks to Prof. Parastou Donyai for her support as my line manager and the University of Reading for the PhD studentship which allowed me to undertake this work.

Thank you to teachers at St. Joseph's Convent School, Karachi, especially Mrs. Benjamin, who told me that she wanted to see my name academically published when I had just failed an aptitude assessment. Those encouraging words at a time of disappointment meant a lot to my ten-year-old self and still motivate me. I also acknowledge Amram Yousaf, for his role in my life, which eventually influenced my decision to pursue this PhD.

I thank my sister, Noelia, for her perpetual support and encouragement. Thank you also to the friends whose presence allowed me to enjoy life when I was frustrated and confused because of work - Rochelle, Chanida, Shabina, and friends I met at university during undergraduate year and the graduate school breakfast club. Thanks to my fellow GTA, Sophie Oduyale, whose friendship and 'inability to deal with me' has made me laugh and keep going. A huge and special thanks to Jonathan Stroud, for his stable support and affection, that has brought me joy, comfort, and motivation to continue onwards. Lastly, I thank and acknowledge all the sources that have influenced my faith, and kept me resilient, to ultimately bring this work to completion.

Declaration

I, Flavia Ghouri, confirm that this is my own work and the use of all material from other sources has been properly and fully acknowledged.

The thesis contains published work that has been contributed by other co-authors.

Flavia Ghouri

March 2021

Dissemination of Findings

Research Publications

Book Chapter

1. Ghouri, F., Hollywood, A., & Ryan, K. (2021). Pregnancy, urinary tract infections and antibiotics: pre-natal attachment and competing health priorities. Chapter Five in *Living Pharmaceutical Lives*. Ballantyne, Peri and Ryan Kath (Eds). Abingdon, Oxfordshire, UK: Routledge.

Journal articles

1. Ghouri, F., & Hollywood, A. (2020). Antibiotic Prescribing in Primary Care for Urinary Tract Infections (UTIs) in Pregnancy: An Audit Study. Medical Sciences, 8(3), 40. https://doi.org/10.3390/medsci8030040.
2. Ghouri, F., Hollywood, A., & Ryan, K. (2020). 'There is no choice apart from antibiotics…': Qualitative analysis of views on urinary infections in pregnancy and antimicrobial resistance. Health Expectations, hex.13044. https://doi.org/10.1111/hex.13044.
3. Ghouri, F., Hollywood, A., & Ryan, K. (2019). Urinary tract infections and antibiotic use in pregnancy - qualitative analysis of online forum content. BMC Pregnancy and Childbirth, 19(1), 289. https://doi.org/10.1186/s12884-019-2451-z.
4. Ghouri, F., Hollywood, A., & Ryan, K. (2018). A systematic review of non-antibiotic measures for the prevention of urinary tract infections in pregnancy. BMC Pregnancy and Childbirth, 18(99), 1–10. https://doi.org/https://doi.org/10.1186/s12884-018-1732-2.

Conference abstracts

1. Ghouri, F., Hollywood, A., & Ryan, K. (2018). Managing urinary tract infections in pregnancy: A qualitative analysis of online forum content [abstract]. Research in Social and Administrative Pharmacy, 14(8), e47. https://doi.org/10.1016/j.sapharm.2018.05.096.

2. Ghouri, F., Hollywood, A., & Ryan, K. (2018). A systematic review of non-antibiotic measures for the prevention of urinary tract infections in pregnancy [abstract]. International Journal of Pharmacy Practice, 25(Supplement 1), 49–50. https://doi.org/https://doi.org/10.1111/ijpp.12443.

Conference Presentations

1. Ghouri, F. Hollywood, A. & Edwards, A. Tackling urinary tract infections and antimicrobial resistance in pregnancy. Pharmacy Virtual PhD Conference, 2nd-3rd July 2020, University of Reading, UK.
2. Ghouri, F. Hollywood, A. Ryan, K. Managing urinary tract infections in pregnancy: a qualitative analysis of online forum content. Annual Conference of the European Health Psychology Society 3-7th September 2019, Dubrovnik, Croatia.
3. Ghouri F, Hollywood, A. Ryan, K. Managing urinary tract infections in pregnancy: A qualitative analysis of online forum content. International Social Pharmacy Workshop, 23-23 July 2018 Leuven, Belgium. *Research in Social and Administrative Pharmacy.* 14(8), e47. https://doi.org/10.1016/j.sapharm.2018.05.096.
4. Ghouri, F. Hollywood, A. Ryan, K. A systematic review of non-antibiotic measures for the prevention of urinary tract infections in pregnancy. Health Services Research and Pharmacy Practice Conference, 12th-13th April 2018, University of Newcastle, UK. *International Journal of Pharmacy Practice.* 25(S1):49-50. https://doi.org/10.1111/ijpp.12443.

Relevant training

1. Behavioural Insights Summer School (BISS). Aug 2019, University of Erfurt & World Health Organisation Regional Office for Europe, Erfurt, Germany.
2. Improving the Quality Use of Medicines and Pharmacy Practice with Behaviour Change. Sept 2018, University of Bath, UK.
3. Conceptualization and Operationalization in social research, sessions 1 & 2. May 2018, University of Reading, UK.
4. NVIVO 11 Training workshop. Feb 2018, University of Reading, UK.
5. Doing and Communicating Qualitative Research. Summer School Jul 2017, Kingston University, London, UK.
6. Our inner biases: Identifying and overcoming them. Jun 2017, University of Reading.
7. Interview Structures and Techniques. May 2017, University of Reading.

Table of Contents

Abstract……2

Acknowledgements……4

Declaration……5

Dissemination of Findings……6

Relevant Trainings……8

Table of Contents……9

List of Tables……13

List of Figures……13

Abbreviations……14

1. Chapter One: Introduction……16
    - 1.1. Antimicrobial Resistance (AMR)……16
    - 1.2. Strategies to tackle AMR……19
    - 1.3. Tackling AMR through Behaviour Change……22
    - 1.4. Theoretical models of health behaviour……23
        - 1.4.1. Health Belief Model……23
        - 1.4.2. Protection Motivation Theory……24
        - 1.4.3. Theory of Reasoned Action and Theory of Planned Behaviour……24
        - 1.4.4. Social Cognitive Theory……25
        - 1.4.5. The COM-B model of behaviour……25
    - 1.5. Pregnancy……28
    - 1.6. Urinary Tract Infection……29
    - 1.7. Risks of a UTI during pregnancy……30
    - 1.8. Risks of antibiotics use during pregnancy……31
    - 1.9. Overview of thesis……32
2. Chapter Two: Research Methodology……37

2.1. Introduction……37

2.2. Research paradigms……37

2.2.1. Positivism……38

2.2.2. Constructivism……38

2.2.3. Transformative……39

2.2.4. Pragmatism……39

2.3. Qualitative and Quantitative Methodologies……39

2.4. Overview of studies……40

2.5. Methodological approaches……41

2.5.1. Quantitative research……41

2.5.1.1. Systematic Literature Review……42

2.5.1.2. Clinical Audit……43

2.5.2. Qualitative research……46

2.5.2.1. Online forum data……46

2.5.2.2. Semi-structured interview data……48

2.6. Qualitative methods for data analysis……51

2.6.1. Conducting thematic analysis……53

2.7. Trustworthiness and rigour in qualitative research……54

2.8. Reflexivity in qualitative research……57

3. Chapter Three: A systematic review of non-antibiotic measures for the prevention of urinary tract infections in pregnancy……61

3.1. Introduction……61

3.2. Published article……63

4. Chapter Four: Urinary tract infections and antibiotic use in pregnancy - qualitative analysis of online forum content……73

4.1. Introduction……73

4.2. Published article……75

5. Chapter Five: 'There is no choice apart from antibiotics…': Qualitative analysis of views on urinary infections in pregnancy and antimicrobial resistance……83

5.1. Introduction……83

5.2. Published article……85

6. Chapter Six: Antibiotic Prescribing in Primary Care for Urinary Tract Infections (UTIs) in Pregnancy: An Audit Study……92

6.1. Introduction……92

6.2. Published article……93

7. Chapter Seven: Exploring antimicrobial prescribing for urinary tract infections in pregnancy – a qualitative interview study……102

7.1. Introduction……102

7.2. Preliminary research article……104

8. Chapter Eight: Discussion……121

8.1. Key findings of research……121

8.2. Implications of findings for antibiotic use and AMR……124

8.3. Implications for research and practice……127

8.4. Strengths and limitations……130

8.5. Conclusion……131

References……133

Appendices……154

Appendix 1: Study One – Search strategy for systematic review……154

Appendix 2: Study Two and Three – Ethics approval UREC Ref. 17/30……158

Appendix 3: Study Two – Permission to collect data from www.mumsnet.com……160

Appendix 4: Study Three – Participant Information Sheet……163

Appendix 5: Study Three – Consent Form……168

Appendix 6: Study Three – Interview schedule……..170

Appendix 7: Study Four – Ethics approval SCFP Research Ethics Committee Ref. 12/19……..172

Appendix 8: Study Four – Data collection form to assess prescribing of antibiotics for UTIs in pregnancy……..174

Appendix 9: Fifth Study – Ethics approval HRA & HRCW Ref. 20/HRA/0163……176

Appendix 10: Fifth Study – Ethics approval UREC Ref. 20/06……..183

Appendix 11: Fifth Study – Participant Information Sheet……188

Appendix 12: Fifth study – Consent Form……193

Appendix 13: Fifth Study – Interview schedule……194

Appendix 14: Book Chapter – Pregnancy, urinary tract infections and antibiotics: pre-natal attachment and competing health priorities. Chapter Five in Living Pharmaceutical Lives……197

Appendix 15: COVID-19 Impact Statement.....215

List of Tables

Chapter 3, Table 1	PICOS Inclusion criteria
Chapter 3, Table 2	Search strategy
Chapter 3, Table 3	Quality appraisal using CASP checklist for cohort studies
Chapter 3, Table 4	Quality appraisal using CASP checklist for case-control studies
Chapter 3, Table 5	Quality appraisal using CASP checklist for randomised controlled trials
Chapter 3, Table 6	Characteristics of included publications
Chapter 4, Table 1	Number of threads per search term
Chapter 5, Table 1	Participant demographics
Chapter 6, Table 1	Data collection tool
Chapter 6, Table 2	Distribution according to ethnicity
Chapter 6, Table 3	Antibiotic prescribing according to trimester of pregnancy
Chapter 6, Table 4	Proportion of antibiotic doses according to guideline

List of Figures

Chapter 1, Figure 1	Schematic representation of thesis
Chapter 1, Figure 2	The Behaviour Change Wheel
Chapter 3, Figure 1	Identification of publications
Chapter 4, Figure 1	Thematic map

Abbreviations

AMR	antimicrobial resistance
ASB	asymptomatic bacteriuria
BAME	Black and Minority Ethnic
CASP	Critical Appraisal Skills Programme
COM-B	Capability, Opportunity, Motivation, and Behaviour
Defra	Department for Environment Food and Rural Affairs
DH	Department of Health
EAU	European Urological Association
E.*coli*	*Escherichia coli*
EMA	European Medicines Agency
ESPAUR	English Surveillance Programme for antimicrobial utilization and resistance
ESRC	Economic and Social Research Council
HCRW	Health and Care Research Wales
HRA	Health Research Authority
GP	general practitioner
MSSU	midstream urine sample
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
OTC	over the counter
PICOS	Population, Intervention, Comparator, Outcome, Study Design
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT	randomised controlled trial
SCFP	School of Chemistry, Food and Pharmacy
SIGN	Scottish Intercollegiate Guidelines Network
TARGET	Treat Antibiotics Responsibly, Guidance, Education, Tools

UK	United Kingdom
UREC	University of Reading Ethics Committee
US	United States

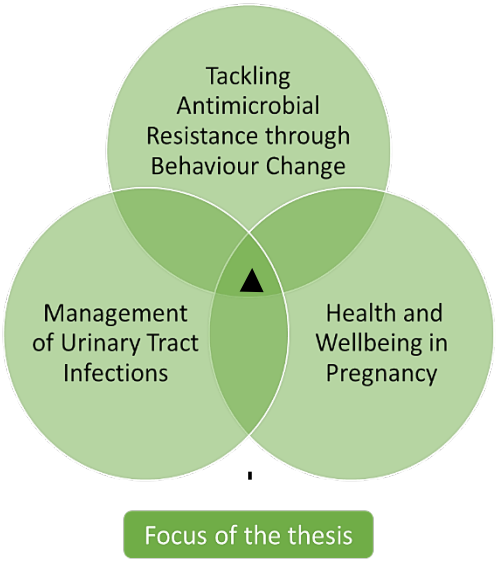
CHAPTER ONE

1. Introduction

This thesis explores the problem of antimicrobial resistance (AMR) in the context of urinary tract infections (UTIs) in pregnancy, using principles of behavioural science. Behavioural science refers to the study of how people behave and make decisions (European Commission, 2021).

The aim of this introductory chapter is to provide the reader with an orientation to the problem of AMR in healthcare and why it is an issue in the management of UTIs in pregnancy. The chapter begins by introducing AMR, models of health behaviour, pregnancy, and UTIs, followed by a discussion of its significance as a healthcare problem. Figure One shows a schematic representation of how the topics are interlinked in this thesis. The latter part of the chapter explains the rationale for conducting the research and proceeds with laying out the research questions that have been explored in the work incorporated in this thesis.

Figure 1: A schematic representation of the thesis



1.1. Antimicrobial resistance

Antimicrobials are medicines used to kill or inhibit the growth of disease-causing

microorganisms such as bacteria, viruses, and fungi (Merriam-Webster Dictionary, 2021). Antibiotics are antimicrobials that are used to prevent and treat infections caused by bacteria (EMA, 2021). Antimicrobial resistance (AMR) is the term used to describe the phenomenon of microorganisms evolving and developing characteristics that make them resistant to antimicrobial treatment. AMR is a broad term that is used to refer to resistance occurring in micro-organisms such as bacteria, viruses, fungi etc. whereas the term 'antibiotic resistance' is used to refer specifically to bacterial resistance . The term AMR will be used in this work from this point on to refer to antibiotic resistance. Resistance to antimicrobial medications, e.g., antibiotics used to treat bacterial infections, gives microorganisms the ability to cause life-threatening infections thus making it a major health concern. Different definitions exist to indicate the varying levels of resistance that bacteria exhibit. Antibiotics are classified into different drug classes based on the similarity of their chemical structures and the mode of action by which they eradicate bacteria. 'Multi-drug resistance' is the term used to characterise bacteria that are resistant to at least one antibiotic in three or more antimicrobial drug classes. The next level of resistance is when bacteria are defined as 'extensively drug-resistant' which means they are non-susceptible to at least one antibiotic in all except one or two antimicrobial drug classes. The next and highest level of resistance is termed 'pandrug-resistance' which is used to refer to bacteria that are resistant to all antibiotics in all antimicrobial drug classes (Magiorakos et al., 2012).

AMR is a natural evolutionary process that can occur spontaneously as well as in response to an antimicrobial agent. Random mutations in the genetic structure of bacteria can allow them to naturally develop resistance characteristics and survive antimicrobial treatment. However, when treated with antimicrobial agents, eradication of susceptible bacteria can leave behind bacteria that are inherently resistant to the antimicrobials. The inherently resistant bacteria are left behind in favourable conditions where they are no longer restricted in competition for

nutritional resources by the sensitive bacteria which were killed by the antimicrobial agent. This phenomenon allows the resistant bacteria to proliferate, colonise, and cause further infections resulting in a rise in AMR. Thus, although AMR is a natural phenomenon, the use of antimicrobial medicines is strongly associated with an acceleration in the emergence of resistant microogranisams (Fair & Tor, 2014). Excessive and inappropriate use of antibiotics istherefore the biggest driver and contributor towards the problem of AMR.

Patients who are ill with resistant infections experience greater morbidity and mortality compared to someone who is ill with a non-resistant infection. The healthcare costs associated with the treatment of resistant infections is also higher compared to susceptible infections due to longer and more severe periods of illness. It has been estimated that AMR will result in an additional 1.2 trillion US dollars per year in healthcare costs by 2050 (WHO, 2021). The World Health Organisation (WHO), a non-governmental organisation committed to global public health, listed AMR as one of the top ten health challenges facing the world in 2019 (WHO, 2019) and have also published a global action plan to tackle this important issue (WHO, 2015). In the United Kingdom (UK), a major review of AMR was commissioned by former Prime Minister David Cameron owing to the pressing nature of the problem, and the danger it continually poses to individual and public health around the world (O'Neill, 2016).

The most common use of antimicrobial medicines is in the healthcare industry to treat infectious illnesses in hospitals and in the community. The expansion in the world's population and subsequent increase in the elderly and immunocompromised groups of people result in a rise in antimicrobial use, thus contributing towards the development and spread of AMR. As well as being used to treat common infections in the community, antibiotics have also been used prophylactically to prevent infections in high risk medical and surgical procedures.

Examples of routine use of antibiotics are widely seen in the context of chemotherapy for patients with cancer and those undergoing organ transplantations (Ventola, 2015). Such life-saving medical procedures would not be as effective or even entirely possible without the

availability of antibiotics.

The rising rate of AMR is coupled with the fact that research and development for new antimicrobial medications has slowed down considerably in the past two decades (Payne et al., 2007; Renwick et al., 2016). This declining trend in the development of new antibiotics leaves behind a limited number of medicines to treat infectious illnesses. Most infections are acute in nature meaning that their duration is short-term. Antimicrobial regimens are generally used fora shorter period compared to chronic illnesses, like heart disease, where medication treatment might be used lifelong. The acute nature of infections makes the development and use of antimicrobials less profitable compared to medicines developed for chronic illnesses. Newly developed antibiotics are also reserved for use as a last line to preserve their effectiveness for as long as possible. Medicines that are newly developed and marketed carry a patent which excludes competitors from manufacturing and profiting from their sale for a limited period (Mayfield, 2016). While delaying the use of new antibiotics to safeguard their effectiveness is a useful approach from a clinical point of view, it reduces the revenue that can be generated in comparison to the investment put towards its development. Thus, the widespread use of antimicrobial medications alongside the slow development of newer agents exacerbates the problem of AMR. AMR poses a huge risk to human health and its effects have been seen and experienced drastically in recent years. However, the effects of AMR go beyond human health affecting livestock and agriculture, thus having implications on economic growth and productivity (Van Boeckel et al., 2015). Infectious illness due to resistant bacteria affecting humans and animals are harder to treat which increases treatment costs. Sickness due to prolonged infections also increase hospital stays which results in greater use of human and material resources adding to the economic impact. AMR is thus a widespread global problem that directly affects human health but also goes beyond that to impact the economic and social structures of society across the world.

1.2. Strategies to tackle AMR

In 2015, the WHO developed and published a Global Action Plan on Antimicrobial Resistance to tackle AMR (WHO, 2015). The global action plan outlined five key strategies through which AMR can be tackled. These strategies include:

i. Improving awareness and understanding of AMR

The aim of this strategy is to focus on increasing the awareness and knowledge about the risks of AMR through public campaigns and behaviour change programmes targeting all sectors of society.

ii. Strengthening knowledge through surveillance and research

Increasing efforts to monitor AMR patterns and research into how best to manage the problem which can then be utilised in day to day practice to minimise the risks associated with AMR.

iii. Reducing the incidence of infection

Focusing on identifying and evaluating infection prevention measures which can be adopted to reduce the incidence of infection. This approach reduces the need for antimicrobial drugs which allows longer-term preservation of their effectiveness.

iv. Optimising the use of antimicrobial agents

Antimicrobial drugs have been overused in multiple sectors of society thus efforts should be in place to reduce their unnecessary use by weighing up the risk of AMR against the benefit of antimicrobials.

v. Ensuring sustainable investment in tackling AMR

AMR has an economic impact on society and therefore it is imperative that investment in strategies developed to tackle the problem are economically viable and effective to address the issue holistically.

The WHO Global Action Plan also provided a framework to encourage individual countries to

develop their own national action plans to tackle AMR. The UK has a five year national action plan (Global and Public Health Group, 2019b) aligned with WHO's Global Action Plan that aims to tackle the issue both within the UK as well as drive positive change to combat AMR across the globe. The UK also has a 20-year vision for the world to have effectively managed the threatfrom AMR by 2040 (Global and Public Health Group, 2019a). The UK's national action plan focuses on three main ways of managing AMR:

i. Reducing the need for, and exposure to, antimicrobial drugs.

ii. Optimising the usage of antimicrobial drugs.

iii. Investment in improving access and supply of antimicrobial drugs.

The global and national strategies described above refer to interventions and actions that can be taken across all sectors of society to promote antimicrobial stewardship both on a community and an individual level. Antimicrobial stewardship can be defined as 'an organisational or healthcare-system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness' (NICE NG63, 2017). Community level strategies refer to those that target policies in organisations to affect mass change in practice whereas individual strategies refer to the steps that individuals can take to tackle AMR personally. Examples of community level strategies in the UK include antimicrobial stewardship efforts through campaigns such as pledging to be an Antibiotic Guardian (Kesten et al., 2017), use of the Royal College of General Practitioners TARGET (Treat Antibiotics Responsibly, Guidance, Education, Tools) toolkit in General Practitioner (GP) consultations (RCGP, 2021), and the Start Smart then Focus campaign in hospitals (Ashiru-Oredope et al., 2012). The Antibiotic Guardian campaign is an initiative where members of the public and healthcare professionals can take an online pledge to use antibiotics responsibly. The TARGET toolkit consists of resources that give information about AMR and can be used by healthcare professionals to aid their decision-making as well as educate and inform patients. The Start Smart Then Focus campaign is used in hospitals to encourage prescribers to use antimicrobial guidelines when

starting antibiotics and then review and tailor the treatment based on laboratory results. In addition to the campaigns, special research grants focusing on AMR research are also amongst some of the community level strategies developed to tackle AMR. Examples of individual level strategies include encouraging individuals to stay up to date with vaccinations, health campaigns promoting hand washing for infection prevention and encouraging the public to use antibiotics only as prescribed by a healthcare professional.

1.3. Tackling AMR through Behaviour Change

It is evident from the global and UK action plans that amongst the strategies to tackle AMR, targeting people's perceptions and behaviours is one approach towards optimising antibiotic use. Before antibiotics are consumed, they are prescribed and dispensed in response to a person seeking medical help in response to an illness. These are all behaviours that can be facilitators or barriers to responsible use of antimicrobials. In the words of Professor Dame Sally Macintyre, a medical sociologist,

> *"The mechanisms which lead to antimicrobial resistance are biological. However, the conditions promoting, or militating against, these biological mechanisms are profoundly social."* (ESRC Working Group, 2014)

Studying people's perceptions and behaviours therefore provide insight into the factors that hinder or facilitate appropriate antibiotic use. Behaviour can be defined as 'the internally coordinated responses (actions or inactions) of living organisms (individuals or groups) to internal and/or external stimuli', excluding responses more easily understood as developmental changes' (Levitis, Lidicker, & Freund, 2009). Behaviours can be either intrinsic/automatic or intentional/rationalised and are determined by multiple factors which might be internal or external to an individual. Behavioural science is an area of social science which is concerned with the study of human and animal behaviour. This field of study provides scientific insights to behaviours that can be observed around us. Behavioural science systematically develops and applies scientific hypotheses to understand behaviour (Pinder et al., 2015). Health behaviours

can be defined as ‘overt behavioural patterns, actions and habits that relate to health maintenance, to health restoration and to health improvement’ (Gochman, 1997). Predicting and understanding the determinants of health behaviour can lead to design of health interventions that can be used to employ behaviour change. Behavioural science is therefore highly valuable in understanding how health behaviours relating to antibiotics can be identified and changed to tackle AMR.

1.4. Theoretical models of health behaviour

Different theories have been developed and studied to understand and predict people’s health behaviours. Literature describes structured models that have been constructed using theory to predict health behaviours. Theoretical models of health behaviour are used to characterise, understand, and predict the determinants of behaviour and behaviour change. They describe theoretical constructs and variables that shape an individual’s health cognitions which in turn helps to predict the likelihood of them performing related behaviours. There are several different models that have been used to predict health behaviour. Commonly used examples include the health belief model, protection motivation theory, and theories of reasoned action and planned behaviour. These models use constructs that conceptualise people’s health cognitions and are aligned with the social cognitive theory (Bandura, 1986). The qualitative research presented in subsequent chapters was analysed using a data-driven approach, specifically inductive thematic analysis (see Section 2.6). Therefore, the research did not adhere to a specific model to allow for a flexible and authentic interpretation of the data. The analysis presented however explains the data by drawing on the theoretical constructs, e.g., self-efficacy, that form these models. An introductory description of the relevant health models is therefore presented below.

1.4.1. Health Belief Model

The health belief model describes a set of variables that determine the occurrence of a behaviour (Becker, 1974; Rosenstock, 1966). The variables are susceptibility to illness, severity

of the illness, the costs or barriers involved in performing the behaviour, the benefits of performing the behaviour, the motivation of the individual, and cues or triggers to perform the behaviour. In summary, the model suggests that an individual is likely to perform a health behaviour if they perceive themselves as being susceptible to an illness that they consider to be severe and where the benefit of performing that behaviour outweighs the barriers involved.

Additionally, the model posits that the performance of the behaviour is dependent on how motivated an individual is and internal (e.g., symptoms of an illness) or external (e.g., information from a health campaign) cues of action.

1.4.2. Protection Motivation Theory

Protection Motivation Theory was originally developed by Rogers (1975) and focuses on fear appeals (warnings to discourage harmful behaviours) together with four other variables to predict behaviour. The variables in this model are similar to the health belief model and include severity of illness, personal susceptibility to illness, response effectiveness of the behaviour, self-efficacy and fear. The model describes two appraisal processes that occur in response to a health threat which are termed threat appraisal and coping appraisal. In the threat appraisal process, individuals become motivated by fear to perform a health protective behaviour because of the perceived severity and their personal susceptibility to an illness. The likelihood of the behaviour is also determined by the coping appraisal process if they consider the behaviour to be effective (response effectiveness) and believe in their own ability to perform it (self-efficacy). The two appraisal processes lead to coping responses which can be adaptive and beneficial or maladaptive and harmful to health.

1.4.3. Theory of Reasoned Action and Theory of Planned Behaviour

The Theory of Reasoned Action was first developed by Fishbein and Azjen (1975). It focused on a person's intention as a central determinant of their behaviour. The theory describes two factors that shape a person's intention to perform a behaviour. These two factors are their own attitude towards the behaviour and the subjective norms (i.e., what they perceive as socially

acceptable in their world). The Theory of Planned Behaviour was developed by extending the theory of reasoned action by adding in a third element that influenced a person's intention to perform a behaviour. This third element is perceived behaviour control which is a measure of how capable a person considers themselves of performing a specific behaviour. In summary, the theory predicts that a person's intention is a reliable predictor of whether they will perform a behaviour and that it is influenced by attitudes, subjective norms and perceived behaviour control.

1.4.4. Social Cognitive Theory

Social cognitive theory was developed by Bandura (1986) and focuses on two variables to predict health behaviours. These two variables are termed outcome expectancy and self-efficacy. Outcome expectancy refers to the outcomes or consequences of performing a behaviour. Self-efficacy refers to individuals own confidence in their ability to perform a behaviour. Self-efficacy has been a key theoretical construct in health behaviour change theories and studied extensively in health literature. In summary, social cognitive theory predicts that an individual is likely to perform a behaviour if they perceive the outcomes to be advantageous and have confidence in their ability to execute that behaviour.

1.4.5. The COM-B model of behaviour

Despite their wide use in research and practice, the theories described above have faced criticism on their predictive utility. Some of the criticisms include arguments that the models offer overly simplistic explanations, the constructs overlap between the models, and that they focus more on individual factors and less on social contexts that can provide opportunities for change (Ogden, 2003; Sutton, 1998).

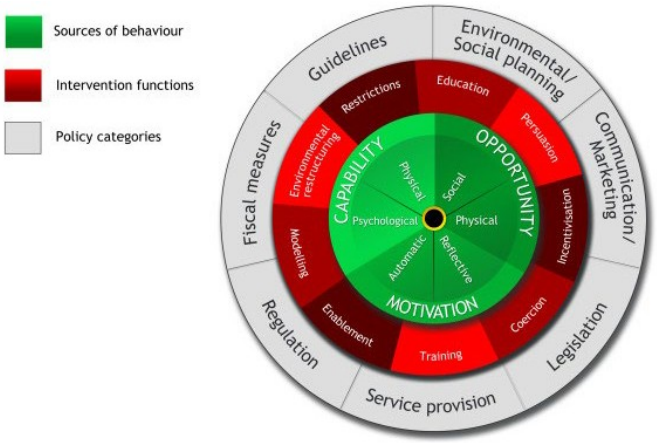
A more recent and comprehensive model developed to identify how behaviour change occurs is called the COM-B model (Michie et al., 2011). The COM-B model describes three conditions that collectively form a system which interact and result in a specified behaviour. COM-B stands for Capability, Opportunity and Motivation which posit that for a behaviour to occur, an

individual must have the capability, the opportunity, and the motivation to perform that action. Capability can be subdivided into the physical or psychological ability of the individual.

Opportunity can be further subdivided into physical opportunity which relates to the environmental structure in which the individual operates or social opportunity which relates to the cultural interplay that influences behaviour. Motivation can also be further subdivided into reflective motivation where an individual evaluates and plans actions or automatic motivation which relates to impulsive and habitual behaviours which do not undergo conscious forethought.

The COM-B model has proven to be useful for designing health interventions through the Behaviour Change Wheel framework (see Fig 2.) . The behaviour change wheel was developed from 19 frameworks of behaviour change (Michie et al., 2011). At its core the wheel identifies the preconditions (capability, opportunity, motivation) that result in behaviour. This core is useful in intervention design as it helps to diagnose what needs to change i.e., whether capability, opportunity or motivation needs to be targeted. Surrounding the core are nine intervention functions which are used to influence and target capability, opportunity and/or motivation for behaviours to occur. For example, the intervention function 'training' can help to increase physical or psychological capability and thus affect change in behaviour. The outermost layer of the wheel describes seven policy categories which influence behaviour by supporting the interventions. For example, a guideline (policy) can support enforcement of training (intervention) which can increase capability (core) and cause behaviour change.

Figure 2: The Behaviour Change Wheel (Michie et al., 2011)



Research presented in this thesis refers to theoretical constructs from the behaviour change models that have been described above to highlight the implications of the findings. Despite its clear value however, behaviour change in the context of AMR is a complex issue because it is the quality of two different populations who might have different expectations and norms of behaving (Edgar, 2012). These two populations are the patients (or public) and the healthcare professionals who prescribe antibiotics or are involved in patient care. Research on the behaviours of prescribing healthcare professionals in the UK with regards to the management of UTIs, specifically in pregnancy, is limited. However, there are studies that have investigated prescribing behaviours for UTIs in the general population. For example, a study conducted by Duane et al (2016) with general practitioners (GPs) shows that prescribers acknowledge the risks from AMR but focus on improving antimicrobial prescribing for respiratory infections. Antibiotics for UTIs on the other hand are viewed as a necessity which drives prescribing. GPs can also be influenced by a misperception that patients expect antibiotics for UTIs which can also lead to higher rates of prescribing (Lecky et al., 2020; Van Der Zande et al., 2019). The GPs in the study by Lecky et al (2020) also expressed concerns about delayed help seeking by patients which can lower the threshold for prescribing antibiotics owing to a fear of complications. Responsible behaviours to tackle AMR involves both judicious prescribing on the part of healthcare professionals and adherence to treatment and prevention advice on the part of patients and the public. To be effective there, strategies informed by behavioural science need to be context specific with the health problem and target population clearly defined. This thesis aims to do this

by focusingon exploring behaviours and providing insights into perceptions of AMR within the context of UTIs in pregnancy. The following section provides background information on pregnancy and UTIs followed by a description of the risks that UTIs and antibiotics pose during pregnancy.

1.5. Pregnancy

Pregnancy is the period in which a foetus grows and develops inside a female uterus. The conception rate for women in 2018 in England and Wales was 75.4 conceptions per 1000 women aged between 15 to 44 years old (Office for National Statistics, 2020). The human pregnancy period lasts approximately 40 weeks which is divided into three trimesters. The first trimester lasts from week 1-12 with the foetus being fully formed by the end of this period. The second trimester begins from week 12 and lasts until week 28. During this period, the foetus grows bigger in size and its organs start to develop. The last trimester of pregnancy starts at week 29 until the baby is born and this is the period where the foetus continues to grow and begins to move down towards the pelvis in preparation for birth. Birth before 37 weeks is classed as pre-term and babies born prior to this period can face developmental problems and health issues (Reich, 2012). Pregnancy reaches full term at week 37 and therefore most babies born after this period are well developed to survive outside the womb.

The first indication of pregnancy for women is usually missing their regular monthly period. Early symptoms of pregnancy include nausea and vomiting in the morning which can occur until around weeks 4-6 of pregnancy. Nausea and vomiting in the first trimester of pregnancy is often termed morning sickness, although it can occur at any time of the day. In some women, hyperemesis gravidarum i.e., extreme nausea and vomiting can also result in dehydration and be accompanied by a urinary tract infection (UTI). Other early symptoms of pregnancy include breast tenderness, tiredness, food cravings and a sensitivity to smell. In addition, there are several common minor ailments that might affect women throughout the different stages of pregnancy. Women may experience constipation and haemorrhoids (enlarged swollen blood

vessels around the rectal and anal areas) due to hormonal changes. The growing foetus and the enlarged uterus put pressure against the stomach which can cause symptoms of a heartburn.

Hormonal changes can also cause indigestion which might be experienced as abdominal discomfort. Pregnancy also increases the amount of vaginal discharge that is produced which can be quite uncomfortable for some women. The physical changes in the body due to the growing uterus can cause a strain on the back and result in backpain throughout the pregnancy. In summary, women can experience several uncomfortable physiological changes and acute ailments during the pregnancy period which might cause them to seek medical treatment. A multinational study of medication use during pregnancy shows that antibiotics are among the most frequently used class of medications (Lupattelli et al., 2014). In terms of the proportion of antibiotics that are prescribed, the most frequent indication in the UK is a UTI (Petersen et al., 2010).

1.6. Urinary Tract Infections (UTIs)

A urinary tract infection (UTI) is one of the most common types of bacterial infection that can affect humans. It is caused by bacteria that colonise and infect the urinary tract. Females have a short urethra compared with men and it is also in proximity to the rectum. The rectum is colonised by bacteria from the gastrointestinal tract which can transfer to the urinary tract and cause a UTI in females. Consequently, the prevalence of UTIs is more common in women than in men. It has previously been estimated that 40-50% of women experience a UTI during their lifetime and about one third of females experience at least one UTI by the time they are 24 years old (Butler et al., 2015; Foxman, 2002).

The most common symptoms of a UTI are feelings of stinging and burning when passing urine, associated with an increased frequency of urination. The urine can also appear to be cloudy along with the presence of blood. These symptoms can progress in severity to back pain, nausea, vomiting, chills and a high temperature. UTIs can be characterised according to the severity of symptoms as asymptomatic bacteriuria (ASB) which is bacteria in the urine without

symptoms, lower UTI which is an infection along with the presence of symptoms, and pyelonephritis which affects the kidneys and is accompanied with some of the more severe symptoms like fever and chills. An infection can occur along any part of the urinary tract and is termed urethritis when the urethra is affected, the commonly used term cystitis when affecting the bladder and pyelonephritis when occurring in the kidneys in the upper regions of the urinary tract.

Bacteria that cause a UTI are normally commensal i.e., they are normally found in the body and live in the gastrointestinal tract especially around the rectal area. *Escherichia coli* (*E.coli*) is the most common bacterial species to cause a UTIs followed by *Klebsiella pneumoniae* and *Proteus mirabilis* (Farrell et al., 2003; Hounsom et al., 2011). Notable examples of antimicrobial resistant bacteria that cause UTIs include *Klebsiella Pneumoniae*, *Acinetobacter baumannii* and *Escherichia coli*. Untreated UTIs can cause a significant disruption to people's quality of life due to the painful symptoms associated with this type of infection (Butler et al., 2015; Flower et al., 2014). Other health risks include kidney injury and infection of the bloodstream (sepsis) which is associated with significantly negative health outcomes including mortality (Tandogdu et al., 2016).

The European Association of Urology (EAU) classifies UTIs as complicated, uncomplicated, recurrent, catheter-associated and urosepsis. Acute or recurrent UTIs in non-pregnant women fall under the uncomplicated category if they do not have any co-morbidity or abnormality of the urinary tract. UTIs in men, pregnant women and in individuals with renal diseases or other abnormality of the urinary tract are classed as complicated UTIs. Catheter-associated UTI, as the name suggests, is infection in people who have had a catheter inserted for the removal of urine. Catherization is a well-known risk factor for UTIs, and catheter associated UTIs are linkedto a greater risk of sepsis (Melzer & Welch, 2017).

As UTIs are caused by bacteria, treatment consists of taking a course of antibiotics. The antibiotic used for treatment is selected based on patient characteristics (i.e., their age, sex,

etc.) and is guided by local antibiotic recommendations which are based on the sensitivity patterns of the bacteria. The National Institute for Health and Care Excellence (NICE) in the UK publishes evidence-based guidelines that provide recommendations on the optimum treatment options available for a variety of clinical conditions. The NICE antimicrobial guideline recommends a three-day antibiotic treatment duration in women and a seven-day course in men (NICE NG109, 2018). The first-line antibiotics to treat an acute episode of a UTI include nitrofurantoin and trimethoprim. Amoxicillin, cefalexin, pivmecillinam and fosfomycin are examples of some of the second-line available options.

1.7. Risks of a UTI during pregnancy

UTIs are usually an acute infection that can be treated with an antibiotic course without any lasting complications. In pregnancy, however, both asymptomatic and symptomatic UTIs are associated with several negative outcomes. The most well-established risk of UTIs during pregnancy is the risk of the pregnant woman developing a kidney infection (pyelonephritis) which is reported to happen in up to 30% of women with asymptomatic bacteriuria (Smaill & Vazquez, 2019). Pyelonephritis during pregnancy can require prolonged hospital admission to clear the infection and result in severe maternal morbidity. As well as this, a strong association between UTIs during pregnancy and pre-eclampsia has been reported in literature (Easter et al., 2016; Schieve et al., 1994). This finding has been mirrored in other studies (Bánhidy et al., 2007; Mazor-Dray et al., 2009) which have also found an association of UTIs with an increased chance of having a caesarean delivery, developing iron deficiency, and abnormal volume of amniotic fluid (fluid surrounding the foetus in the uterus). In addition to having harmful effects on the woman, UTIs during pregnancy can also adversely affect the foetus if left untreated. Risk of intra-uterine growth restriction (delayed growth) to the baby as well as a higher chance of having a low birth weight and being born pre-term have also been reported in literature (Matuszkiewicz-Rowińska et al., 2015; Sangkomkamhang et al., 2015).

In view of the risks of UTIs in pregnancy, bacteriuria i.e., the presence of bacteria in the urine

with or without symptoms is treated with an antibiotic course in pregnant women. NICE guidelines for lower UTIs (NICE NG109, 2018) makes specific recommendations for the choice of antibiotics in pregnant women. The first choice according to the guideline is nitrofurantoin, which is highly effective and safe for use in pregnancy unless the woman is in the third trimester and at term i.e., 37 weeks and beyond. Other options which are commonly used during pregnancy include the beta-lactam antibiotics, amoxicillin and cefalexin, which are used if nitrofurantoin is contraindicated or ineffective due to resistance.

1.8. Risks of antibiotic use during pregnancy

Although beneficial to treat infections, antibiotic use is associated with a rise in AMR which is a global health issue as described earlier. Antimicrobial resistant infections are a universal health concern but in pregnancy the risks are cross-generational and affect both women and their offspring. The risk of AMR in pregnancy is also unique because it limits an already restricted range of antibiotics that are available to treat infections in pregnancy because of the need to ensure foetal safety. Unlike the general population, the choice of antibiotic used to treat any infection in pregnancy needs to be effective (i.e., the bacteria should be sensitive to it) and not cause any adverse effects on the foetus. For example, one of the most common antibiotics used to treat a UTI is trimethoprim. However, it is associated with malformations in the developing foetus, especially if used in the first trimester (Andersen et al., 2013). Therefore, trimethoprim should be avoided during pregnancy even though it might be a suitable treatment option in the general population.

Resistant infections during pregnancy are also a concern because of the impact on the baby once it is born. Individuals who use antibiotics for respiratory or urinary tract infections can carry resistant bacteria for up to a year (Costelloe et al., 2010). Pregnant women who use antibiotics and carry resistant bacteria can pass these to the neonate during birth by vertical transmission. Vertical transmission refers to the transfer of a pathogen from the mother to the child and can occur at any time point prior to birth, during the delivery process and/or after

birth (Arora et al., 2017). This poses a risk to neonatal health as the neonatal period is a vulnerable time for acquiring infections because of relatively underdeveloped immunity compared to an adult human. Studies have previously reported an increase in ampicillin resistant neonatal infections with increased maternal use of ampicillin (Mercer et al., 1999; Towers et al., 1998). The impact of AMR is serious enough that it is now thought to be responsible for 30% of neonatal deaths that occur from severe infection (Laxminarayan et al., 2016). Excessive use of antibiotics and its association with AMR therefore has far reaching consequences for the health of women, their offspring, and the wider health of society.

Antibiotic use in pregnancy is also associated with other risks, in addition to AMR, that can have an impact on health. Antibiotic use in pregnancy has implications on the health of the foetus as the medicine can cross the placenta and potentially affect its development. This is termed teratogenicity which refers to the toxic effects a substance can have on the development of the foetus. There have been several studies which have found the use of antibiotics in pregnancy to be associated with risks to the offspring. A recent study investigating antibacterial exposure in pregnancy found that the use of certain antibiotics was associated with an increased risk of miscarriage (Muanda et al., 2017). These included the broad spectrum and widely used penicillin and cephalosporin classes of antibiotics. Another study assessing the effects of the antibiotics nitrofurantoin, trimethoprim-sulfamethoxazole, and cephalosporins found an increased risk of birth defects such as oral clefts, oesophageal, and anorectal abnormalities (Ailes et al., 2016). As well as causing immediate adverse effects, studies have also found an association with antimicrobial use in pregnancy and adverse outcomes in children later in life. A large trial called ‘the ORACLE II trial’ investigated the long-term effects of using erythromycin and/or co-amoxiclav in pregnancy (Kenyon et al., 2008). This trial showed an association with antibiotic use during pregnancy and functional impairment in children. The results also demonstrated a link between cerebral palsy in children with the use of maternal antibiotics during pregnancy. Another study which investigated the effects of antibiotic administration on

vaginal bacterial colonisation found that antibiotic use altered the vaginal tract bacteria in women. This reduced the diversity of bacteria colonising neonates and increased morbidity rates (Stokholm et al., 2014). Results from the study by Stokholm (2014) linked antibiotic use for UTIs to increased colonisation of the vagina by *Staphylococcus* bacterial species which has also been previously found by another study (Norinder et al., 2006). Increased colonisation with Staphylococcus in mothers, due to use of antibiotics for UTIs, is concerning because it is linked to a greater risk of children developing asthma (Benn et al., 2002; Stensballe et al., 2013). The study investigators were able to conclude this through studying different cohorts and looking at antibiotics used for non-respiratory infections to avoid the results being affected by the mothers' asthma phenotype. In addition, Collier et al (2013) also found a positive relation between antibiotic use and childhood asthma especially if the antibiotic was used for UTIs, and a systematic review also supports the link between prenatal exposure to antibiotics and a child's risk of developing asthma (Murk et al., 2011).

Estimates suggest that over 40% of women are given antibiotics for an infection prior to their delivery (de Tejada, 2014). European estimates suggest that one in five women are given at least one antibiotic during pregnancy whilst this figure is doubled in the United States (Kuperman & Koren, 2016). Antibiotics are in fact the most widely used class of medication in pregnancy (Nahum et al., 2006), accounting for 80% of all medicines prescribed to pregnant women (Bookstaver et al., 2015). This widespread use of antibiotics has been questioned by experts in obstetric care because of the health risks that they pose due to AMR as well as additional risks associated with their use (Ledger & Blaser, 2013). It is therefore important, considering the risks of AMR and the adverse effects on neonates and children, that antibiotics in pregnancy are used judiciously with every feasible step taken to safely minimise their usage. As mentioned earlier in Section 1.5, antibiotics are the most frequently used class of medication in pregnancy (Lupattelli et al., 2014) with UTIs being the most common indication in the UK for use by pregnant women (Petersen et al., 2010). The conception rate in England and Wales is estimated to be 7.5% (Office for National Statistics, 2020) and a population

survey in England reported a UTI incidence rate of 11% in females in a year (Butler et al., 2015). The data on the exact prevalence of UTIs in pregnant women in the UK is lacking, however review studies provide an estimate ranging between 2-10% (Meads, 2011) for asymptomatic infections. The overall prevalence of UTIs during pregnancy is therefore likely to be higher as it would include symptomatic infections. Data on demographic factors associated with UTIs in the UK is also lacking, however studies from other countries suggest a higher frequency in women with diabetes or those associated with a lower socioeconomic group (Meads, 2011). Although the data on prevalence rates in the UK is limited, there is there is evidence from national and international studies that antibiotics are overused for UTI during pregnancy (Mosedale et al., 2013; Sekikubo et al., 2017). Antibiotics for UTIs during pregnancy has implications for AMR and is therefore the topic of focus in this thesis.

1.9. Overview of thesis

This research project explores behavioural insights into antimicrobial resistance and UTIs in pregnancy. The aim of the research was to provide behavioural insights into antibiotic use for UTIs in pregnancy and provide recommendations on interventions that can optimise this use. The objectives of the research were to study how UTIs can be treated or prevented without antibiotics and explore women's and prescribers' perspectives on AMR and UTIs in pregnancy. The first study was a systematic review of non-antibiotic measures described in the literature to prevent UTIs in pregnancy. The research question for this study was 'what non-antibiotic measures can be employed in pregnancy to prevent UTIs and minimise antibiotic use?'. The thesis then focuses on the patient perspective by exploring the perceptions and views of women. The second study explored women's perceptions of UTIs and antibiotic use during pregnancy by analysing data from an online health forum. The research question for this study was 'what are women's perceptions of UTIs and antibiotic use in pregnancy?'. The third study explored women's perceptions of AMR by interviewing women who had experienced a UTI during pregnancy. The research question was 'how do women view AMR in relation to UTIs in

pregnancy?'. The thesis then progresses to provide a complete insight into the phenomenon by focussing on the healthcare professionals' perspective by focusing on their practices and views. The fourth study was an audit of antibiotic prescribing for UTIs in pregnancy that was conducted in primary care. The question guiding the fourth study was 'does antibiotic prescribing for UTIs in pregnancy meet defined standards?' with the standards drawn from the NICE antimicrobial guideline for lower UTIs. The final study explored the prescribing practice of antibiotics for UTIs in pregnancy. The primary research question was 'what influence does AMR have on prescribers' decision-making process when prescribing antibiotics for UTIs in pregnancy?'.

The thesis is organised as a collection of papers consisting of eight chapters. This introductory chapter provided a background to AMR, pregnancy, UTIs along with the problems associated with using antibiotics in pregnancy. This is followed by a methodology chapter that explains the methods and the research philosophy underpinning the research. The next five chapters comprise the research articles corresponding to the studies that form this thesis. The final chapter provides a discussion on the overall implications of the research findings, the strengths and limitations of the work and recommendations for future research.

CHAPTER TWO

2. Research Methodology

2.1. Introduction

Research is a systematic investigation into a problem which involves collecting data and interpreting it to arrive at a solution and create new knowledge (Burns, 2000). The philosophy of research underpins why, how, and which problem is investigated guided by a research paradigm or philosophical worldview. The research paradigm can be defined as 'the philosophical intent or motivation for undertaking a study' (Mackenzie & Knipe, 2006).

Research paradigms guide scientific enquiry by influencing four main elements, namely the ontology (study of being or existence), epistemology (study of knowledge), axiology (study of the values and ethics) and the methodology (the science of methods) of a research study (Kivunja & Kuyini, 2017).

Ontology is a branch of philosophy which is concerned with the concept of reality or the existence of things. It asks questions pertaining to what is real and what is the nature of that reality. Epistemology, as a branch of philosophy, is concerned with how we can know reality or the truth and therefore is concerned with the question of 'what counts as knowledge?' (Cooksey & McDonald, 2011). The axiology of a research paradigm is concerned with the ethical issues that might arise in research. Axiology is the branch of philosophy that focuses on the ethical values that govern the decisions made in the research process. Methodology refers to the overall approach used in the design and conduct of a research study and can be defined as the 'collection of methods or rules by which a particular piece of research is undertaken' (Somekh & Lewin, 2005, p346).

These four elements (ontology, epistemology, axiology, and methodology) are important because they determine the philosophical assumptions made in the research process to

formulate the research question and how it will be addressed. Several research paradigms are described in the field of philosophy, which differ in terms of the approach that is used to define and investigate a problem and in terms of how new knowledge is created and subsequently advanced. The following is a summary of the different research paradigms which are commonly described in literature followed by a focus on the research paradigm that guided this doctoral project.

2.2. Research paradigms

2.2.1. Positivism

Positivism assumes the existence of a single objective measurable reality. It employs a philosophy which relies on empirical evidence to validate cause and effects in an investigation (Park et al., 2020). Studies based on a positivist research paradigm are mostly quantitative in nature and focus on tightly controlling variables to minimise effects on outcomes. Qualitative studies may also however be rooted in positivism and are characterised by minimising the influence of the researcher and research participants' subjective values and experiences.

Positivism has traditionally been viewed as 'the scientific method' of conducting research (Mertens, 2005, p8) by confirming theories and generating hypotheses to further develop knowledge.

2.2.2. Constructivism

Research based on the constructivist paradigm, also termed interpretivism, views reality as a social construct arising from human experience (Cohen et al., 2018, p34). Studies founded on a constructivist paradigm predominantly use qualitative methodologies (Rees et al., 2019) and place significance on the experiences of both the researcher and the research participant.

Major emphasis is placed on considering the social context within which the research is conducted. Researchers aligned to the constructivist paradigm tend to work towards generating theories inductively in contrast with the positivist paradigm which focuses on testing

hypotheses (Creswell, 2003, p9).

2.2.3. Transformative

The transformative research paradigm, or critical theory, is concerned with bringing about social transformation and political change (Chyderiotis et al., 2013). To this end, researchers whose work is based on this paradigm tend to engage collaboratively with the participants. Transformative research seeks to enhance inclusivity and diversity in research outputs by incorporating different viewpoints into how studies are conducted. Transformative researchers may use both qualitative and quantitative methods to conduct research, although a mixed approach may be advocated to provide a 'complete and full portrait' of the subject under investigation (Somekh & Lewin, 2005, p275).

2.2.4. Pragmatism

Pragmatism focuses on the nature of the research problem to answer the research question (Creswell, 2003, p11). It does not, therefore, strictly adhere to a single way of conducting research but instead relies on the practicality and feasibility of a method to solve a particular research problem (Mackenzie & Knipe, 2006). Most research studies based on pragmatism tend to use a mixed methods approach, whereby both qualitative and quantitative methods are employed to investigate an issue. The mixed methods approach also allows triangulation which increases the validity and credibility of research because it offers a balanced explanation using a variety of methods (Noble & Heale, 2019) . In essence, researchers aligned with pragmatism focus on what is practically meaningful and important to know, then use methods of inquiry that they consider most appropriate and relevant to their research (Morgan, 2014).

2.3. Qualitative and Quantitative Methodologies

Research paradigms or worldviews described above can adopt quantitative, qualitative or a combination approach to conduct the research. Quantitative research asks 'specific and narrow questions' (Creswell & Guetterman, 2021, p37) that can be measurably observed and analysed statistically with a careful effort to minimise influence from external variables, including but not

limited to the researchers' own biases. Research using quantitative methods aims to generate knowledge that is objective and generalisable across different settings. Quantitative studies prefer large sample sizes and the techniques used to collect quantitative data include experimental work and structured surveys or questionnaires. Qualitative research, on the other hand, leans towards open and exploratory questions to study a central phenomenon as it is concerned with conceptual rather than numerical analysis of data (Fitzpatrick & Boulton, 1994). Qualitative data is usually collected or generated through techniques such as individual or group interviews and may be in different forms such as auditory or visual media. The context in which qualitative research is also very important to how the results are communicated and generalised across other settings. Although the research paradigms mentioned earlier tend to gravitate towards the use of either quantitative or qualitative methods, there are no strict rules on how they align with either of these methodologies. In general, however, research based on a positivist paradigm favours quantitative methods whereas constructivism relies on the use of qualitative methods. Transformative and pragmatic research paradigms may use mixed or multiple methods, adopting either or both quantitative and qualitative methods to conduct research.

2.4. Overview of studies

The research paradigm that the work in this thesis overall aligns with is the pragmatic epistemological framework. This framework identifies a problem and then considers options on how to practically research a solution. The research project was designed by initially studying the literature on excessive antibiotic use in pregnancy and the role of behaviour in tackling this issue, to gain familiarity with the problem. Upon further study and reflection, the project was refined to focus on UTIs in pregnancy as this is where the majority of antibiotic use occurs in this population. Thereafter, the perceptions of women and prescribers were considered vital in addressing the problem of AMR due to excessive antibiotic use. Multiple methods have been used for this project, mainly utilising qualitative methods but also using a quantitative method

of analysis where it was considered most appropriate.

The first study in this thesis was a systematic literature review of measures that could be employed to prevent UTIs in pregnant women. Results from this research were collated and presented using a narrative synthesis. The second and third studies both focused on the views of women who had experienced a UTI during pregnancy. The second study analysed the views and experiences of women relating to UTIs during pregnancy as expressed on an online pregnancy forum. This qualitative data was analysed using thematic analysis. The third study also employed qualitative methodology and was conducted to explore women's views on AMR in relation to experiencing a UTI during pregnancy. Data for the third study was collected by interviewing women using a semi-structured interview schedule and then analysed using thematic analysis. The fourth and fifth studies were designed to focus on prescribing practice. The fourth study was an audit that was conducted in a primary care setting and the aim of this work was to assess antibiotic prescribing for UTIs in pregnancy against set standards. A quantitative approach was used to analyse the data and descriptive statistics were used to collate and report the results. The final study in this thesis was designed as semi-structured interviews with prescribers to explore their prescribing in the management of UTIs in pregnancy. Data was collected by interviewing prescribers and the analysis was conducted qualitatively, using thematic analysis. These methods are described in further detail in the following section.

2.5. Methodological approaches

Different methods were considered when designing each of the studies. The method employed was chosen based on its appropriateness and feasibility in addressing the research question. As previously stated, the first study was a systematic literature review, followed by analysis of online forum content and interviews with women, a clinical audit, and a final qualitative interview study with prescribers.

2.5.1. Quantitative research

2.5.1.1. *Systematic Literature Review*

The first study was a systematic literature review of non-antibiotic measures that could prevent UTIs in pregnancy. A systematic literature review was considered most appropriate to ensure that a thorough examination of published literature was performed to identify evidence-based measures. A systematic literature review is different to a traditional literature review (also known as a narrative review) as it answers a specific and focused question as opposed to only summarising information about a topic (Robinson & Lowe, 2015). Systematic reviews are conducted to identify and provide an evidence based summary of findings about a health topic and doing so is beneficial because it makes 'the available evidence more accessible to decision makers' (Ganeshkumar & Gopalakrishnan, 2013). In a systematic literature review, the search process is designed in a logical and systematic way using pre-defined inclusion criteria to search different databases. Search results are selected based on the inclusion criteria, also the methodological quality of the selected studies is critiqued and evaluated using a quality appraisal tool. In a literature review, the search process can be random and not as precisely defined compared with a systematic review. Literature reviews do not have specific inclusion criteria and although reviewers may comment on the quality of evidence available, this process is less formal process compared with the systematic literature review. The difference between a literature review and a systematic literature review can be summarised in this respect that the former provides an overview about a topic whereas the latter strengthens existing evidence about a topic by synthesising results from primary research literature.

Systematic literature reviews can synthesise results either qualitatively or quantitatively. When data from studies are quantitatively pooled together, it is called a meta-analysis (Montori et al., 2003) whereas integration of data solely from qualitative studies is called a meta-synthesis (Lachal et al., 2017). A meta-analysis collates and statistically analyses data from studies that are conducted using quantitative methodology. There can however be instances where studies included in the systematic review might be quantitative but differ to a degree where it is not

possible or appropriate to combine the results for a statistical meta-analysis. In such a case, results can still be reported together in the form of a textual explanation to summarise the findings and such an approach is called a narrative synthesis (Popay et al., 2006; Ryan, 2013). The aim of the first study was to review the literature systematically to identify non-antibiotic measures that could prevent UTIs in pregnancy. A search across 10 databases was conducted to identify studies that fit the inclusion criteria. The inclusion criteria were based on the acronym PICOS which stands for Population, Intervention type, Comparator, Outcome and Study Design as per the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement for reporting systematic reviews (Liberati et al., 2009). The PRISMA statement is a set of recommended items that should be reported in systematic reviews, as a minimum, to facilitate their clear and transparent reporting. The inclusion criteria according to PICOS were; Population: pregnant women, Intervention: non-antibiotic prevention measures, Comparator: any e.g., a placebo, Outcome: incidence of bacteriuria or UTI, Study Design: any (randomised, observational etc.). The search terms used were pregnan*, prevention or control or management, urinary tract infection or UTI or bacteriuria or cystitis. After excluding non-eligible studies, eight were included in the systematic review which reported five different non-antibiotic measures to prevent UTIs in pregnancy. The eight included studies were appraised for quality using the Critical Appraisal Skills Programme (CASP) checklists (2019). Although there are several checklists available for quality appraisal (e.g., SIGN and Joanna Briggs Institute checklists), the CASP checklists were chosen because these were available for the different study designs (i.e., cohort, randomised controlled trials etc.) that were included in the systematic review . As the included studies differed considerably in their design and in terms of the measures that they reported, it was not appropriate to pool the results from these studies together to conduct a statistical meta-analysis. A narrative synthesis approach was therefore used to explain and summarise the results.

2.5.1.2. *Clinical Audit*

The fourth study was a clinical audit which can be defined as a process which is conducted to 'find out if healthcare is being provided in line with standards and lets care providers know where their service is doing well, and where there could be improvements' (NHS England, 2021). It is a quality improvement process to seek and improve healthcare outcomes (NICE, 2002). The conduct of an audit follows a five-stage cyclical process that starts from a phase of planning and preparation and continues towards a phase of sustaining the improvement brought about by the audit. In the first phase, termed the preparation phase, the topic to be audited is chosen and the aims and purpose for conducting the study are defined. The second phase is when the standard criteria are set against which current practice is assessed. The third phase is the data collection phase where the agreed procedure is followed to collect data. Data can be collected in two ways, either prospectively or in retrospect. In the fourth phase the collected data is analysed to see how current practice matches with the audit standards. This is also the phase where recommendations are made on how to make improvements to practice in areas that do not comply with the audit standards. The fifth phase is where an evaluation of the effectiveness of the audit process takes place. The fifth phase ensures that improvements are sustained through re-audits and a repeat of the audit cycle, if considered necessary (Esposito, 2014).

The aim of the audit study was to assess the prescribing of antibiotics for UTIs during pregnancy against recommended standards. In a strict sense, audit is not considered to be research and its primary focus is on addressing the question of whether best practice is being followed (Hughes, 2012). Research on the other hand generates new knowledge and focuses on establishing what constitutes best practice. In clinical settings however, both audit and research serve very similar functions by acting as drivers for change and positive improvements to current practice (Twycross & Shorten, 2014). In fact, since both research and audit are conducted systematically and seek to solve specific issues, it has been stated that the legitimate difference between them cannot be characterised concretely (Wade, 2005). Antimicrobial prescribing for UTIs in

pregnancy has not been previously studied in a primary care setting. The audit was therefore designed to be conducted prior to interviewing prescribers to gauge the current norms in antimicrobial prescribing practice. The goal was to use the results from the audit to design the interview structure for the final research study where prescribers' perceptions and decision-making could be explored.

A primary care setting i.e., GP surgery was chosen because this is usually the facility that pregnant women access when they experience acute UTI symptoms or are diagnosed with asymptomatic bacteriuria at antenatal appointments. The GP surgery where the audit was conducted is part of a health group in London that provides primary care services in the community. The audit standards were taken and adapted from the antimicrobial prescribing NICE guideline for lower UTIs (NICE NG109, 2018). NICE guidelines were chosen as they are developed based on the best quality evidence available. The audit was conducted retrospectively by reviewing the medical records of women who had experienced a UTI during pregnancy. The inclusion criteria were records of women who had been prescribed antibiotics for a UTI while they were pregnant.

The study received favourable opinion for conduct by the University of Reading School of Chemistry, Food and Pharmacy Ethics Committee (Ref. Study 12/19). The Chief Pharmacist, who is the Clinical Director at the chosen health group, also approved the study and permitted access to the premises to retrieve clinical data. As the project was a retrospective audit, there was no anticipated risk of harm to patients or the researcher as previously recorded data were accessed in read-only mode. The main ethical consideration was maintaining patients' confidentiality and protecting their anonymity in any reports generated from this study.

Individual patients were therefore assigned codes which along with any other identifiable data were not taken out of the surgery premises to ensure patients' anonymity. A data collection form was designed to collect the data for analysis, and this was stored on a secure encrypted server and remained accessible only to authorised individuals. Data were analysed

quantitatively using descriptive statistics which was the most appropriate method of analysis to summarise the extent to which antimicrobial prescribing aligned with the audit standards.

2.5.2. Qualitative research

2.5.2.1. Online forum data

The second study analysed the experiences of women who had a UTI during pregnancy, as expressed on an online forum which is part of a popular parenting website in the UK (www.mumsnet.com). Online forums are websites where people can have digital conversations on a topic of their choosing. Forums comprise of 'threads' that relate to communications regarding a specific topic so that discussions are organised and distinguishable by topic.

Threads of conversations consist of posts by individuals in response to the topic under discussion. A typical online forum has threads of conversations which are usually started off by an original post that starts a conversation. Individual subscribers then respond to the original post with their views or comments to the original post. There is generally no specific limit to the length or number of responses to an original post, however threads might be moderated and can be closed by the website or forum admins.

Online internet forums are an invaluable source of data for qualitative research as they provide data that are rich, easily accessible, and naturalistic (Giles, 2017). Forums allow exploration of views and perceptions that are generated naturally by individuals without the researchers' influence. They not only provide data from individuals but also allow observation and exploration of social norms by studying the interaction between community members.

Subscribers of online forums may also view them as a safe environment to discuss sensitive information as the internet provides anonymity that is not available in face to face interactions. Data from online health forums can therefore be deep, untouched, and authentic in a way that is markedly different compared with other traditional face to face data collection methods.

Online searches for information, and using online communities for help and advice about

health problems, occurs frequently in pregnancy (Prescott & MacKie, 2017). Studies show that women rely significantly on the internet and specifically on online communities to access support, validation, and information to help them in making decisions about their health in pregnancy (Lagan et al., 2010, 2011; Wexler et al., 2020). An online forum was therefore selected as a valuable resource to explore women's experiences of a UTI during pregnancy. The website, www.mumsnet.com, was selected because it is a popular parenting website in the UK that is accessed by pregnant women. The website has a designated space called 'Talk' where people can have conversations about different topics. Topics on 'Talk' are organised into categories and there is an advanced search function that allows for a specific search of topics. The search function was used to retrieve conversations under the pregnancy topic where women talked about experiencing a UTI whilst pregnant.

The ethics of accessing online forums to retrieve conversations as data for research can be controversial and has been a subject of debate in literature. Giles (2017) discussed two opposing arguments on the ethics of conducting research using online discussion forums. The first argument disapproves unrestricted use of online forums since the data is generated by people who do not explicitly contribute their views for the purpose of research. Researchers who hold this view attribute conversations on online forums as the intellectual and private property of the individuals and therefore deem their explicit consent to be vital for ethical conduct of research. The second argument views posts on online forums as publicly available information that is freely accessible by anyone with an internet connection. Researchers who argue the second position point to the naturalistic depth and richness that online data provides. In most cases, it is not feasible to request and obtain consent from individuals on online forums as their offline identity is masked on the internet. The context of the research therefore is important on how researchers retrieve and use data from online forums. On evaluation, I hold the position that using an online forum to explore women's experiences of a UTI during pregnancy was ethical and justifiable and the following is an explanation of this view.

One of the main issues with collecting data from on an online health forum is whether it is a private or public space (Roberts, 2015). In the case of 'Talk', it is an online space that is not password protected and freely available to be viewed by any person using the internet thereby constituting as an online public space. Contact details of individual subscribers were also not known so it was not possible to contact them and obtain permission directly. Users also posted their views using fictitious usernames which were further changed for additional identity protection when reporting the findings. Another issue with using data from online forums is whether it should be considered as research conducted with human participants or supplementary analysis of textual narratives (Bradley & Carter, 2012). The terms of use of www.mumsnet.com specifically state that it has copyright to any content on the website and any data that is generated by individuals users may be edited and reproduced for any purpose whether commercial or otherwise. Permission was therefore obtained from www.mumsnet.com to download and use the data for research. The overall risk of harm to the website subscribers was considered minimal as their views had been shared voluntarily, under a pseudonym, and were publicly accessible. To ensure ethical rigour however, approval was obtained from the University of Reading's Research and Ethics Committee (Ref. 17/30) prior to the conduct of this study. The forum content was then downloaded on to a Microsoft Word document and analysed using thematic analysis with the aid of NVivo 11® software.

2.5.2.2. Semi-structured interview data

The third and fifth studies consisted of qualitative interviews with women and prescribers respectively. The purpose of a research interview is to richly describe and analyse people's beliefs, motivations and experiences beyond mere quantitative categorisation (Gill et al., 2008). Interviews are traditionally one of the most utilised technique to collect data for qualitative research (Holloway & Galvin, 2017a) and can be conducted one-to-one or in a group setting (focus group). Individual interviews allow for an in-depth exploration of beliefs and perceptions whereas focus groups differ in that they can also highlight shared experiences and perceptions

as influenced by social dynamics. Both individual one-to-one interviews and focus groups were considered for data collection for the two interview studies, however the individual interview technique offered the advantage of greater insight into personal experiences. The one-to-one individual interview approach was also more feasible due to interview scheduling constraints and therefore guided by a pragmatic paradigm, the individual interview approach was selected as the method of choice for data collection.

When designing an interview study, there are three main types of interview schedules which can be employed. These are categorised as structured, semi-structured and unstructured/in-depth interviews (Britten, 1995). Structured interviews generally produce quantitative data and are used for survey and questionnaire studies (DiCicco-Bloom & Crabtree, 2006). They are characterised by a list of pre-determined questions that generate fixed answers and are administered in the same order to each research participant. Semi-structured interviews also consist of a set of pre-determined questions, but these are usually broad and open-ended to extract the research participants' views. The answers to this type of interview questions provide varied and rich detail into the participants' points of view. The questions are organised topically rather than sequentially and therefore may not necessarily be asked in the same order for each participant. Additional prompts and probing questions are also used in semi-structured interviews, based on the participants' responses, to gauge further depth and clarity in the response (Tolley et al., 2016). The third type of interview, i.e., an unstructured interview, does not have a list of pre-determined questions but instead focuses on one or two broad questions around a topic. Participants interviewed through an unstructured interview schedule are encouraged to talk freely around the chosen topic. This allows research participants to generate detailed descriptions that are guided by their own perceptions of what they consider worth mentioning with minimal interference from the researcher (Britten, 1995).

Semi-structured interviews are the most common type of interview employed in qualitative studies (Holloway & Galvin, 2017a). Both the third and fifth studies used a semi-structured

interview schedule to explore the views of the research participants. As the goal of both the studies was to elicit and analyse the views of participants, a structured interview was not considered to be the best option for data collection and instead the suitability of semi-structured was compared with unstructured interviews when designing the studies. A semi-structured interview was chosen because it has the advantage of allowing in-depth exploration of participants' views through open-ended questions without generating excessive dross i.e., the amount of material that does not contribute anything meaningful towards the researcher's analysis (Holloway & Galvin, 2017a). In addition, the semi-structured technique allowed the researcher to direct the conversation to elicit relevant data on a topic that has not been significantly studied before (i.e., AMR and UTIs in pregnancy). The use of an unstructured approach in this case therefore may not have generated sufficiently detailed data and caused potential uncertainty for the participants due to the novelty of the research topic.

The interviews for the two studies were conducted via telephone. Telephone interviewing is a practically convenient medium to conduct interviews and has been utilised in both quantitative and qualitative research (Carr & Worth, 2001). Conducting the interviews via telephone has been described as a participant-centred approach (Trier-Bieniek, 2012). Telephone interviews were beneficial both for the participants and the researcher. Interviewing women, most of whom had young children, in the convenience of their home via the telephone was practical and circumvented the challenge of finding an appropriate time and space for an interview.

Similarly, for study three, prescribers in primary care who work long hours during the day were able to be interviewed via telephone at a time and place of their convenience which would not have been possible if the study design was limited to face-to-face interviews. Despite the obvious practical convenience, telephone interviews have been traditionally viewed as inferior to face-to-face interviews because it is thought that they do not provide the insight one gets from non-verbal cues such as body language (Novick, 2008). Despite this concern however, literature comparing telephone interviews with face to face is favourable (Lechuga, 2012;

Opdenakker, 2006; Sturges & Hanrahan, 2004) and does not point to a loss in the quality of the research. In fact, as well as the practical time and cost benefits, telephone interviews can increase disclosure due to the relative anonymity afforded by the geographical distance (Novick, 2008).

Ethical considerations were duly performed when designing and conducting the research interviews. In both studies, there was a risk of distress to the participants if they had a difficult experience of illness or treating illness during pregnancy. For this reason, participation in the interviews was voluntary and participants were provided with an information sheet and given the opportunity to clarify concerns prior to the interview. Ethical approval for both the studies was obtained from the University of Reading's Research and Ethics Committee (Study Three: Ref. 17/30, Study Five Ref. 20/06) before commencing data collection.

2.6. Qualitative methods for data analysis

There are several diverse methods or approaches when analysing qualitative data. However, what is common to all these methods is that the process is iterative, and the researcher might oscillate repeatedly between the generation and conceptualisation of the data (Fitzpatrick & Boulton, 1994). Qualitative methods of analysis can be broadly characterised as 'language oriented', 'descriptive/interpretative' and 'theory-building' (Tesch, 1991). Language oriented methods focus on how people communicate, descriptive/interpretative oriented methods focus on describing and interpreting research observations and theory-building oriented methods focus on generating a theory to explain a social phenomenon. The qualitative work included in this thesis used the descriptive/interpretative approach for analysis. There are many different methods or approaches to qualitative data analysis; some examples include grounded theory, phenomenology, discourse analysis, narrative inquiry, and thematic analysis.

Grounded theory is a qualitative analysis approach first used by Glaser and Strauss (1967) in which the researcher systematically collects and analyses data to generate a theory which is firmly based on that data. Phenomenology on the other hand is primarily a philosophical

approach that aims to explain social phenomenon exactly as they happen by focusing on the subjective lived experiences of people (Eberle, 2014). While the goal of grounded theory is to describe what is going on, the purpose of phenomenological enquiry is to describe the 'world-as-experienced'(Baker & Mn, 1992). Discourse analysis is another method used for qualitative analysis which is distinct because its primary concern is with how people use language to communicate meaning which in turn informs how they achieve and make sense of personal or social endeavours (Starks & Trinidad, 2007). Narrative inquiry is a much broader method and can encompass the approaches described above because it is concerned with peoples' stories (Holloway & Galvin, 2017b). However, it is also used as a stand-alone qualitative method because it is essentially concerned with storytelling to assists with understanding peoples' experience (Lai, 2010). Thematic analysis is a method of analysis that is foundational to qualitative research because of its flexibility. However, it is one that has been poorly described or referred to as a tool for analysis rather than a method in its own right (Braun & Clarke, 2006). Essentially, thematic analysis is 'a method for identifying, analysing, and reporting patterns (themes) within data (Braun & Clarke, 2006) and because of this, the way it is conducted overlaps with the other methods of analyses described above. In fact, all the above-mentioned methods adopt a data analysis approach which is similar to thematic analysis.

Regardless of how the data is generated or collected and the theoretical paradigm underpinning the research, raw qualitative data eventually takes the form of text. This requires the researcher to read and gain familiarity with the data and then proceed with its organisation and interpretation for sensemaking which are key characteristics of performing a thematic analysis. Multiple methods might be simultaneously appropriate for a study, but the choice of methodological approach is ultimately guided by the research paradigm, the aim of the study and the anticipated desired research outcomes.

Thematic analysis was the method employed when analysing data for the qualitative studies in this thesis. The common aim for the qualitative studies in this thesis was to describe and

interpret perceptions and thematic analysis is a flexible approach that allowed this to be done efficiently. Although other methods such as grounded theory, discourse analysis etc. may also describe patterns across data, they need to be rooted in a theoretical framework whereas thematic analysis is flexible and can be conducted without being bound to a theory (Braun & Clarke, 2006). As the topic of research in this thesis had not been explored before, this characteristic of thematic analysis to not be necessarily bound by a theory made it an appropriate method of choice for these studies. Although thematic analysis is not strictly bound to theory, there are two distinct ways of conducting thematic analysis namely inductive or theoretical (deductive). Inductive thematic analysis is a 'bottom up' approach of conducting analysis in which the coding of data for themes is driven by the data independently of any pre-existing theory. Theoretical or deductive thematic analysis is a 'top down' approach where a pre-existing theory is used that drives the coding and development of themes. Analysis using an inductive approach provides a rich interpretation of the data whereas the deductive approach has the advantage of being in-depth when a specific aspect is being studied. As mentioned earlier, the research topic has not been explored before and therefore an inductive approach was used for the studies, to allow a rich description of the data. At this point, it is important to point out that adopting an inductive approach does not imply that theory can be ignored or is not vital for analysis (Clarke & Braun, 2018) but that this approach allows the flexibility to explore the relationship between the data and the diverse range of existing theoretical constructs.

2.6.1. Conducting thematic analysis

Braun and Clark (2006) described a stepwise phased approach to conducting a thematic analysis. The process begins by familiarising oneself with the data which can be either through multiple reading of the data or listening to audio recordings when transcribing verbal data into text. This is followed by careful reading of the text and generating initial codes. Codes identify important aspects of the data that the researcher finds interesting or relevant for answering

the research question. Codes are then examined and grouped to interpret broader meanings which are termed themes. The phase following theme generation is the review phase in which the themes are cross checked with the data to ensure they provide a reliable account of the data. Themes may be discarded or refined at the review stage followed by finalising a name and defining a description for what the theme entails.

Data from both the online forum and interview studies were uploaded onto the NVivo 11® software at the beginning of the analysis. Data for the interview studies however was first transcribed from the audio recordings prior to being uploaded on the software. The phased approach described above was then followed to conduct the analysis. NVivo 11® was used to systematically facilitate the digital organising and managing of the data into initial codes.

2.7. Trustworthiness and rigour in qualitative research

Qualitative research contributes 'richness, context and dimension to the study of human beings and their environments' but has been the subject of criticism for producing studies lacking in rigour and scientific integrity (Jones, 2013). Unlike quantitative research, findings from qualitative work are not statistically reproducible and therefore not generalisable across different settings which can appear to strengthen the critic's arguments. Despite these criticisms, qualitative research has become of established importance in health care research (Al-Busaidi, 2008) especially when answering questions relating to the meaning behind social phenomena. It is imperative for this reason that qualitative researchers facilitate and safeguard the trustworthiness and rigour of their research.

There has been extensive debate and opposing ideas on how to evaluate the rigour of qualitative research (Hadi & José Closs, 2016). The different and sometimes opposing research paradigms that underpin qualitative work mean that there is a lack of a unified approach to judge its rigour (Rolfe, 2006). Nevertheless, there are several techniques that a qualitative researcher might adopt to ensure the rigour and trustworthiness of their work. Firstly however it is important to define the criteria for trustworthiness which can be subdivided into credibility,

transferability, dependability and confirmability (Guba, 1981). Credibility refers to the 'truth value' of the research questions or simply put the confidence in the plausibility of the findings. Transferability refers to the applicability of the findings in other research settings.

Dependability refers to the consistency of the findings in terms of how likely is it that similar findings will be reproduced if the work is repeated in the same research setting. Lastly, confirmability relates to the objectivity or neutrality of the findings in terms of how the findings are influenced by the researchers' biases. The techniques used to safeguard rigour are prolonged engagement, persistent observation, member checking, triangulation, peer debriefing, negative case analysis, thick contextual description, an audit trail, and reflexivity (Amin et al., 2020). These are briefly explained as follows with reference to the trustworthiness criteria that they influence.

Prolonged engagement involves the researcher spending adequate time in the context within which they are carrying out their work and therefore lends credibility and confirmability to the findings. It allows the researcher to become familiar with the culture and the norms that exist within that setting and allows them to resolve and/or identify their own preconceived notions (Johnson et al., 2020). Persistent observation involves the researcher identifying and focusing on the aspects of the research which are directly relevant to the research question. Although appearing to be similar to prolonged engagement, which helps shape the scope of the research, persistent observation provides depth into the specific characteristics that influence the topic of study (Amin et al., 2020) and therefore also contributes to increasing the credibility of the findings. Member checking also grants credibility to the research by involving the participants in the analysis and interpretation of the data. This technique can be used by asking the research participants for their comments on the raw data and/or the preliminary research outputs (Rolfe, 2006). Triangulation involves using more than one approach to explore a research problem by using different methods to collect and/or analyse data so that there is multiplicity in shaping the final perspective (Patton, 1999). Depending on how triangulation is used, it can

lend to the credibility, dependability and confirmability of data (Guba, 1981). Peer debriefing is when the researcher discusses the research with a peer who is not directly invested or involved in the conduct of that piece of work. The discussion has the advantage of challenging the researcher's assumptions which facilitates improved research outputs (Hadi & José Closs, 2016) and ensures credibility by keeping the researcher accountable and honest about their presumptions. Negative case analysis refers to the action of seeking out instances in the data that do not support the overall findings (Patton, 1999). The benefit of looking out for deviant cases is that it allows the researcher to strengthen the credibility of their analysis by assessing whether deviations are explainable or there are deeper phenomena that need to be further explored. Thick contextual description allows the reader insight into the setting (sampling criteria, data collection methods etc.) where the research is conducted (Johnson et al., 2020). It involves collecting thick descriptive data about the context to allow generalisation to a different setting. There are no set rules on what is meant by a thick description but in essence the description should be sufficiently detailed in terms of the study design and procedures used to allow the reader to evaluate how the findings might be applicable to other settings. An audit trail refers to the documentation of the entire research process and includes how procedures are conducted and decisions made at every phase (Rolfe, 2006). An audit trail allows the researcher to justify and demonstrate to an auditor that their conclusions have been systematically and logically developed and therefore ensures dependability and confirmability of the findings. Reflexivity refers to the researcher's discussion of how their epistemological and ontological assumption shapes the design and outputs of a research study. It allows the researchers to manage and discuss the influence of their own inherent beliefs and ideas when exploring a research problem (Jootun et al., 2009). As a technique, reflexivity is unique because it is highly comprehensive in that it contributes to the enhancement of all the criteria used to evaluate trustworthiness (i.e. credibility, transferability, dependability and confirmability) (Amin et al., 2020).

The content above describes why rigour is important and how it can be facilitated. The

numerous techniques described above all contribute to rigour however their simultaneous application is not always feasible or even necessary. It has been suggested that any given research study should use at least two of the strategies described above (Hadi & José Closs, 2016). Strategies which were relevant and feasible were duly applied during the conduct of the qualitative research studies in this thesis. Prolonged engagement with the online forum and interview data helped with achieving familiarity to aid the analysis. Peer debriefing was also used as a technique to ensure the rigour and trustworthiness of the research. This was done informally with fellow postgraduate colleagues at a departmental meeting for the second study which used data from an online forum. This strategy was also used for all the qualitative research in this thesis through conference presentations where any comments from peers were used to challenge and inform the final analysis. Peer debriefing was also a key strategy adopted in academic meetings with research supervisors who questioned and provided critique on the research outputs. Negative case analysis was a specific strategy that was employed in the conduct of the second study, to understand the differing points of view to antibiotic use during pregnancy. This strategy facilitated collective analysis and interpretation of the phenomenon behind deviant points of view with regards to antibiotic use. The third and fifth studies which were interviews with women and healthcare professionals involved note keeping which provided an audit trail to assist with decision making in the process of conducting the research. The notes assisted with reflection of the interview process, coding of data and identification of data saturation in the thematic analysis process. Lastly, the trustworthiness and rigour of the entire collection of research in this thesis was ensured by adopting reflexivity in the undertaking and the following is my personal account of this process.

2.8. Reflexivity in qualitative research

I started this research three months after qualifying as a pharmacist following completion of the pre-registration training programme in a hospital setting. During the pre-registration year, I had the opportunity to shadow the ‘Women and Children’s Health’ pharmacist and gained

insight into some of the health challenges unique to this group. In that time, I also undertook an audit on prescribing practice within the hospital. One aspect of the audit focused on antibiotic use to tackle antimicrobial resistance. The experience of working in an obstetric setting and exploring issues relating to AMR led to my interest in this topic and I started work as a Graduate Teaching Assistant at Reading School of Pharmacy. From studying as an undergraduate pharmacy student to working in a clinical setting in hospital, I was trained to adopt an evidence-based approach in my role as a pharmacy healthcare professional. I was then, and even now, firmly convinced that this indeed should be the standard when designing and providing healthcare services to patients. However, I did not consciously realise that my education and training as a pharmacist had meant that I viewed research and science from a realist and objective lens of enquiry. I believed that there was a reality that existed which could and should be studied objectively. My position has shifted radically now through the process of conducting research with people and exploring their perceptions and behaviours. I have come to view natural physical reality in the world, and the social reality of people as different kinds of phenomena which require different methods of enquiry and this is what has shaped the pragmatic nature of this doctoral research project.

The direction of the research to focus on women and prescribers was influenced by my previous experience of conducting an audit and working as a trainee pharmacist in an antenatal hospital ward. Pregnant women are frequently provided health advice by midwives and health visitors. However, my experience of witnessing instances of inappropriate antimicrobial prescribing whilst conducting the audit led to the focus on prescribing practice and subsequent antibiotic use. During the conduct of my PhD study, I endeavoured to remain neutral to minimise the effectsof my own preconceived views when collecting and analysing the data for this research. The process of evaluating my work however has meant that I have become aware of the contribution of my own views and experiences in shaping the final analyses in this thesis.

Whilst enrolled as a PhD candidate, I continued to work in a patient facing role as a locum community pharmacist. When analysing the views of women on the online forum and when interviewing them, I found the switch from pharmacist to researcher to be unnatural at times. It meant that I had to consciously root myself in my role as a researcher who was exploring the participants' perceptions and restrain myself from counselling or giving information during the interviews, especially when asked to do so by the participants. My training as a pharmacist meant that I have been strongly convinced about the risks of AMR to individuals and society. It has also meant that I regularly counselled patients on appropriate use of antibiotics and the risks of AMR. I have also asked prescribers to review and alter antibiotic prescriptions for this same reason. I had to set these personal and professional convictions aside to delve into the participants' reality and how they constructed their own meanings. Without doing so, I found myself quickly going down a reductionist path, describing interview data at face value as singular objective truth in contrast to seeking and identifying the deeper patterns and complexities that construct peoples' beliefs, motivations, and eventually their behaviour. I recognised this process when conducting my analyses especially in my discussions with my supervisors and the peer-review process when publishing work in scholarly journals. I tried to minimise and overcome my tendency to adopt a reductionist approach by attending different training events on analysing qualitative interview data (see relevant trainings, page 8) , studying qualitative health literature, and by prolonging my engagement with raw data to refine my final analyses.

For the interview studies, I did not specifically hide or specify my professional pharmacist qualification with the research participants and whilst this might have had some impact on how women shared their views with me, it certainly influenced the interaction in the interviews that I conducted with prescribers. Pharmacists in clinical settings often identify and query errors in prescriptions and I experienced some unease from participants in the initial interviews that I conducted with prescribers. I consciously made an effort to reduce this unease by affirming my

position solely as a researcher at the beginning of the interview and explaining and reiterating the rationale for conducting the study which they had previously been informed about in the participant information leaflet. On a personal level, I did not however completely abandon the views that I hold about AMR and felt that my interaction with participants, both women and prescribers, was a beneficial opportunity for them and myself to reflect on how we, collectively as society, can tackle AMR through our individual behaviours.

Throughout the process of designing and conducting the research presented in this thesis, I have maintained contact with the broader social science literature on health and medicine use. This has helped me to familiarise and appreciate the uniqueness and benefit of conducting research using qualitative methods of data collection and analysis. I have presented at national and international conferences (see conference presentations, page 7) and received valuable feedback and critique that has improved how I design and develop exploratory questions to advance and benefit health research.

CHAPTER THREE

3. A systematic review of non-antibiotic measures for the prevention of urinary tract infections in pregnancy

Chapter Three presents the publication:

Ghouri, F., Hollywood, A., & Ryan, K. (2018). A systematic review of non-antibiotic measures for the prevention of urinary tract infections in pregnancy. *BMC Pregnancy and Childbirth*, *18*(99), 1–10. https://doi.org/https://doi.org/10.1186/s12884-018-1732-2.

3.1. Introduction

This publication presents the findings of a systematic literature review on non-antibiotic measures that can be used to prevent UTIs. Prevention of UTIs minimises their incidence and consequently reduces the use of antibiotics which is vital to tackling AMR. Using non-antibiotic measures to manage and prevent infections is also a highly valuable strategy in reducing antibiotic use and managing AMR. A review of the literature reveals several non-antibiotic strategies to manage or prevent UTIs but not all these have been studied in pregnancy. This systematic review was conducted to identify non-antibiotic measures that could prevent UTIs specifically in pregnant women. The rationale for conducting this review was to summarise evidence-based non-antibiotic measures that could be encouraged in pregnancy to prevent UTIs which would subsequently mean that antibiotics could be avoided.

The results from the systematic review identified five different measures which include behavioural measures, cranberry juice, vaccination, ascorbic acid and a herbal medicine made up of rosemary, lovage and centaury. Although all these measures were reportedly safe in pregnancy, behavioural measures were the only feasible option supported by evidence that could be recommended in practice. The following chapter presents the systematic review as an

article that was published in the peer-reviewed journal titled *BMC Pregnancy and Childbirth*. The work following on from this article is based on studying behaviours of women and prescribers in the context of UTIs in pregnancy. Behavioural management of UTIs in pregnancy to prevent infection and minimise antibiotic use in response to AMR is therefore the key topic linking the studies in this thesis.

BMC Pregnancy and Childbirth

RESEARCH ARTICLE Open Access

A systematic review of non-antibiotic measures for the prevention of urinary tract infections in pregnancy

Flavia Ghouri, Amelia Hollywood* and Kath Ryan

Abstract

Background: Urinary tract infections (UTIs) are common in pregnancy and account for the highest proportion of primary care antibiotic prescriptions issued to pregnant women in the UK. It is well known that antibiotic use is associated with increased antimicrobial resistance and therefore measures to minimise antibiotic use for UTI prevention have been studied. The efficacy and safety of these measures in pregnancy have not been addressed and therefore the aim of this study was to systematically review the literature to identify and evaluate potential measures to prevent UTIs in pregnant women.

Methods: Ten databases (EMBASE, AMED, BNI, CINAHL, Medline, PubMed, PsycINFO, Cochrane Trials, Scopus and Science Direct) were systematically searched in July 2017 for studies reporting non-antibiotic measures to prevent UTIs in pregnancy. The terms ("urinary tract infection" or UTI or bacteriuria or cystitis) AND (prevention) AND (pregnan*) were used. The quality of the publications was appraised using the Critical Appraisal Skills Programme (CASP) checklists for cohort study, case-control study and randomised controlled trial. The results were synthesised using a textual narrative approach.

Results: Search results yielded 3276 publications and after reviewing titles and removing duplicates, 57 full text articles were assessed for eligibility and eight were included in the review. Five different approaches (hygiene measures, cranberry juice, immunisation, ascorbic acid and Canephron® N) have been identified, all of which are reported to be safe in pregnancy.

Conclusion: The quality of the evidence varied considerably and only hygiene measures were supported by evidence to be recommended in practice. Future work needs to concentrate on strengthening the evidence base through improved design and reporting of studies with a focus on immunisation, ascorbic acid and Canephron® N.

Keywords: Systematic review, Non-antibiotic measures, Prevention, Urinary tract infection, Antimicrobial resistance, Pregnancy, Behaviour change

Background

Urinary tract infections (UTIs) account for the highest proportion of primary care antibiotic prescriptions issued to pregnant women in the UK [1]. Pregnant women have an increased susceptibility to UTIs because of physiological changes. The growing uterus can result in urinary retention which predisposes the woman to infection. In addition, hormonal fluctuations relax the ureteral muscle and cause accumulation of urine in the bladder which also increases the chance of developing a UTI [2].

Treatment of UTIs is recommended in pregnancy if bacteria are detected in the urine even if there are no accompanying symptoms i.e. in asymptomatic bacteriuria (ASB) [3]. Both ASB and symptomatic UTIs in pregnancy are risk factors for the development of pyelonephritis which can result in severe maternal morbidity [4]. It is estimated that 20–30% of women with bacteriuria in the first trimester go on to develop pyelonephritis in later trimesters [5]. Therefore, although ASB on its own is not treated in the general population, guidelines

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published by the European Urological Association (EAU) [3] and Scottish Intercollegiate Guidelines Network (SIGN) [6] recommend screening and treating bacteriuria with or without symptoms. The current management strategy according to these guidelines is to use a short course of antibiotics.

Whilst antibiotics are vital in eradication of UTIs, antimicrobial resistance due to their use is a global health threat [7, 8]. Antimicrobial resistance means that bacteria can survive antibiotic treatment and cause serious or life threatening infections. Use of antibiotics is strongly associated with increasing emergence of resistant bacteria and subsequent redundancy of antibiotics i.e. previously effective antibiotics are losing their efficacy [8, 9]. Unlike the general population, the choice of safe antibiotics in pregnancy is limited because of teratogenic potential e.g. quinolones should be avoided in pregnancy because of a risk of joint malformations in the foetus. Therefore antibiotics becoming ineffective due to antimicrobial resistance is a particular concern in pregnancy as it further limits the range of drugs available to treat infections safely [10]. An example of this in practice is the replacement of trimethoprim with nitrofurantoin as the first line antibiotic to treat UTIs [11] because of an increase in resistance due to its widespread use in the UK [12]. Use of antibiotics can also result in carriage of resistant bacteria by individuals for a period of several months to a year after completing a course of antibiotics [13]. The resistant bacteria can transfer to close physical contacts and may colonise and infect subsequent hosts. This is especially of concern in pregnancy as women can pass on resistant bacteria to the neonate during birth, which is when they are most vulnerable to infection. An example of resistance specific to obstetric practice is the increase in ampicillin resistant neonatal infections due to maternal use of ampicillin [14, 15].

As well as contributing to antimicrobial resistance, antibiotic use in pregnancy also carries the risk of being harmful to the foetus. Recently, a study has found a link between antibiotic use and increased risk of spontaneous miscarriages [16]. Another study assessing the effects of nitrofurantoin, trimethoprim-sulfamethoxazole and cephalosporins which are used to treat UTIS, found an increased risk of birth defects such as oral clefts, oesophageal and anorectal abnormalities in the offspring [17]. In addition, research has also found an association with antibiotic use in pregnancy and functional impairment in children later on in life [18].

In light of the risks, it is essential that the use of antibiotics in pregnancy is carefully considered with a balance struck between the risks and benefits of these drugs. The UK's 5 year antimicrobial resistance strategy [19] developed by the Department of Health (DH) and Department for Environment Food and Rural Affairs (Defra) identifies seven key areas where action is needed to tackle antimicrobial resistance. One of these key areas is 'improving infection prevention and control practices' which will lead to a reduction in the use of antibiotics as infection rates will be minimised. Improving infection prevention is also one of the main recommendations of 'The Review on Antimicrobial Resistance' (2016), chaired by economist Jim O'Neill [8]. Non-antibiotic measures to minimise antibiotic use for UTI prevention have been studied but the efficacy and safety of these measures in pregnancy have not been addressed [20]. Therefore, the aim of this systematic review is to identify alternate measures reported in scientific literature which may be used to prevent UTIs in pregnancy. The benefits of non-antibiotic measures to prevent UTIs in pregnancy are two-fold. Firstly, the reduced use of antibiotics will mean that they remain effective for longer, and secondly, medication which is potentially harmful in pregnancy can be avoided.

Methods

Ten databases (EMBASE, AMED, BNI, CINAHL, Medline, PubMed, PycINFO, Cochrane Trials, Scopus and Science Direct) were searched and the final search string was conducted in July 2017. The inclusion criteria according to PICOS (see Table 1) consisted of studies reporting non-antibiotic measures for the prevention of UTIs in pregnant women.

Studies conducted exclusively in non-pregnant groups or in conditions such as diabetes or spinal cord injury were excluded. Search terms were; **P**: (pregnan*), **I**: (prevention or control or management), **O**: ("urinary tract infection" or UTI or bacteriuria or cystitis) as shown in Table 2.

The search terms 'control' or 'management' were initially used but these terms did not yield relevant results therefore this paper focuses on prevention only. The final search strategy is available in Additional file 1.

A manual search of references from included studies was also conducted. The quality of the publications was appraised using the Critical Appraisal Skills Programme (CASP) checklists for cohort study, case-control study and randomised controlled trial [21–23]. The results

Table 1 Inclusion criteria (PICOS)

Population	Pregnant Women
Intervention	Non-antibiotic prevention measures
Comparator	Any e.g. a placebo
Outcome	Incidence of bacteriuria or UTI
Study Design	Any e.g. randomised control trial (RCT) or observational study

Table 2 Search strategy

Database	Search terms	Results
EMBASE	("urinary tract infection" or UTI or bacteriuria or cystitis) AND (prevention or control or management) AND pregnan*	744
AMED	("urinary tract infection" or UTI or bacteriuria or cystitis) AND (prevention or control or management) AND pregnan*	0
BNI	("urinary tract infection" or UTI or bacteriuria or cystitis) AND (prevention or control or management) AND pregnan*	10
CINAHL	("urinary tract infection" or UTI or bacteriuria or cystitis) AND (prevention or control or management) AND pregnan*	66
Medline	("urinary tract infection" or UTI or bacteriuria or cystitis) AND (prevention or control or management) AND pregnan*	397
PubMed	("urinary tract infection" or UTI or bacteriuria or cystitis) AND (prevention or control or management) AND pregnan*	942
PsycINFO	("urinary tract infection" or UTI or bacteriuria or cystitis) AND (prevention or control or management) AND pregnan*	4
Cochrane Trials	("urinary tract infection" or UTI or bacteriuria or cystitis) AND (prevention or control or management) AND pregnan*	102
SCOPUS	(TITLE-ABS-KEY ("urinary tract infection" OR UTI OR bacteriuria OR cystitis) AND TITLE-ABS-KEY (prevention or control or management) AND TITLE-ABS-KEY (pregnan*) AND NOT TITLE-ABS-KEY (catheter OR catheter AND associated) AND NOT TITLE-ABS-KEY (antibacterial* OR antibiotic* OR antimicrobial*) Note: additional terms searched using 'NOT' due to too many results	1008
ScienceDirect	("urinary tract infection" or UTI or bacteriuria or cystitis) AND (prevention or control or management) AND pregnan*	3
Manual search		0
Total		3276

were analysed and discussed using a narrative synthesis approach.

Results

Search results yielded 3276 publications and after reviewing titles and removing duplicates, 56 full text articles and one conference abstract were assessed for eligibility by FG and eight were included in the review as shown in Fig. 1. The results identified five different measures (hygiene behaviour, cranberry juice, immunisation, ascorbic acid and Canephron® N) which can be used for the prevention of UTIs in pregnancy. Quality appraisal of the included publications using the CASP checklists is shown in Tables 3, Table 4 and Table 5.

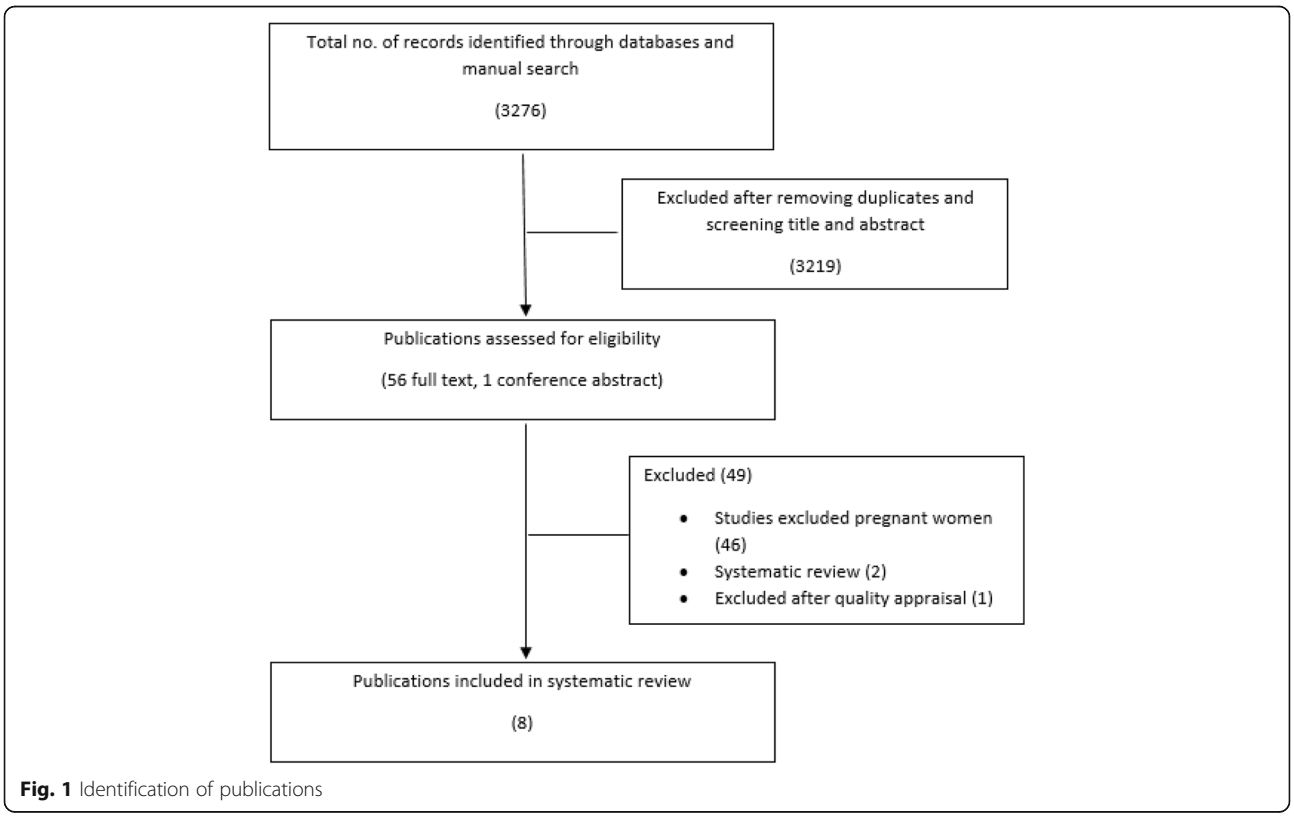

Fig. 1 Identification of publications

Table 3 Quality appraisal using CASP checklist for cohort studies

CASP cohort study checklist	Elzayat et al. 2017 [26]	Baertschi et al. 2003 [29]	Ordzhonikidze et al. 2009 [32]
Did the study address a clearly focused issue?	Yes	Yes	Yes
Was the cohort recruited in an acceptable way?	Yes	Yes	Can't tell
Was the exposure accurately measured to minimise bias?	Yes	Yes	Can't tell
Was the outcome accurately measured to minimise bias?	Yes	Yes	Can't tell
(a) Have the authors identified all important confounding factors?	Yes	Yes	Yes
(b) Have they taken account of the confounding factors in the design and/or analysis?	Yes	Yes	Yes
(a) Was the follow up of subjects complete enough?	Not applicable	Yes	Yes
(b) Was the follow up of subjects long enough?	Not applicable	Yes	Yes
How precise are the results?	Can't tell (no CI given)	Can't tell (no CI given)	Can't tell (no CI given)
Do you believe the results?	Yes	Yes	Yes
Can the results be applied to the local population?	Yes	Yes	No (study population not clearly defined)
Do the results of this study fit with other available evidence?	Yes	Yes	Yes
Does the study have implications for practice?	Yes	Yes	Yes

CI Confidence interval. Significance: $p \leq 0.05$

The characteristics of the publications are included in Table 6.

Hygiene behaviour

Three observational studies were identified which investigated the association between sexual and genital hygiene behaviours of pregnant women and the incidence of asymptomatic bacteriuria (defined as $>10^5$ colony forming units/ml of urine) or symptomatic UTIs. One study by Badran et al. [24] was not included in the review due to repetition of results from a previously conducted study.

Table 4 Quality appraisal using CASP checklist for case-control studies

CASP case-control study checklist	Amiri et al. 2009 [25]
Did the study address a clearly focused issue?	Yes
Did the authors use an appropriate method to answer their question?	Yes
Were the cases recruited in an acceptable way?	Yes
Were the controls selected in an acceptable way?	Yes
Was the exposure accurately measured to minimise bias?	Yes (but questionnaire completed by midwives)
Have the authors taken account of the potential confounding factors in the design and/or in their analysis?	Yes
Were the results and risk estimate precise?	Yes
Do you believe the results?	Yes
Can the results be applied to the local population?	Yes
Do the results of this study fit with other available evidence?	Yes

The study by Amiri et al. [25] was a case-control study which included 100 cases matched to 150 controls i.e. total of 250 pregnant women. The two groups were compared in terms of differences in genital hygiene or sexual activity. The study by Elzayat et al. [26] was an observational cohort study that included 170 pregnant women between the ages of 18–41. Participants in this study were administered a questionnaire about their hygiene behaviours and a urine sample was tested to determine the prevalence of bacteriuria. Both studies show that hygiene behaviours are associated with the incidence of UTIs.

Cranberry juice

There were two studies that assessed the effectiveness of cranberry juice in preventing UTIs during pregnancy. Wing et al. [27] conducted a randomised controlled trial with 188 pregnant women under 16 weeks of pregnancy and compared the efficacy of cranberry juice with a placebo. There was a 57% reduction in bacteriuria and 41% reduction in all UTIs reported in this trial. Essadi et al. [28] conducted a randomised controlled trial that compared cranberry juice with water in 760 pregnant women. They also reported positive results for the effectiveness of cranberry juice and 70.5% of the participants who drank cranberry juice showed a significant

Table 5 Quality appraisal using CASP checklist for randomised controlled trials

CASP randomised control study checklist				
	Ochoa-Brust et al. 2007 [31]	Grischke et al. 1987 [30]	Wing et al. 2008 [27]	Essadi et al. 2010 [28]
Did the trial address a clearly focused issue?	Yes	Yes	Yes	Yes
Was the assignment of patients to treatments randomised?	Yes	N (although described as randomised)	Yes	Can't tell
Were all of the patients who entered the trial properly accounted for at its conclusion?	No	No	Yes	Yes
Were patients, health workers and study personnel 'blind' to treatment?	No	No (only patients were blinded)	Yes	No (able to differentiate between juice and water)
Were the groups similar at the start of the trial?	Yes	No (different pregnancy status)	Yes	Yes
Aside from the experimental intervention, were the groups treated equally?	Yes	Yes	Yes	Can't tell
How large was the treatment effect?	Significant ($p = 0.03$)	Significant ($p \leq 0.001$)	Not significant ($p = 0.71$)	Significant ($p < 0.05$)
How precise was the estimate of the treatment effect?	Precise (95% CI used)	Can't tell (no CI limits)	Precise (95% CI used)	Can't tell (no CI limits)
Can the results be applied in your context? (Or to the local population)	Yes	Probable	Yes	Yes
Were all clinically important outcomes considered?	Yes	Yes	Yes	Yes
Are the benefits worth the harms and costs?	Yes	Yes	N (due to stomach disturbances)	No (due to stomach disturbances)

CI Confidence interval. Significance: $p \leq 0.05$

reduction in UTIs compared to 32.16% of women who drank water.

Immunisation

Immunisation as a means of preventing UTIs in pregnancy was assessed by two studies. Baertschi et al. [29] conducted a before-after study using a bacterial extract in 62 women who were 16–28 weeks pregnant. Use of the extract significantly reduced the incidence of UTIs and recurrence rates fell from 52.5% prior to using the extract to 19.4% after women started using the extract. Grischke and Ruttgers [30] investigated the effectiveness of an intramuscular vaccine in an open randomised trial. A total of 400 women were included in the trial and a significant difference was seen in the incidence of UTIs in the trial (28 infections) and control groups (84 infections) suggesting a beneficial effect of the vaccine.

Ascorbic acid

Ochoa-Brust et al. [31] conducted a RCT to evaluate whether daily intake of ascorbic acid (100 mg) prevented UTIs in pregnancy. There was a total of 110 pregnant women, 55 in the trial group and 55 in the control group. The infection percentage was 12.7% in women who were given daily ascorbic acid compared with 29.1% in women who received the comparator.

Canephron® N

Ordzhonikidze et al. [32] conducted a cohort study in 300 pregnant women using Canephron® N which is a herbal product. Women were divided into two groups, those who had a current UTI and those who suffered with chronic urinary tract problems but did not have a current exacerbation. The results show that the frequency of pyelonephritis was 1.5 times less in the first group and 1.3 times less in the second group due to use of this product.

Discussion

The five different measures (hygiene behaviour, cranberry juice, immunisation, ascorbic acid and Canephron® N) highlighted in the review vary in the evidence supporting their use for the prevention of UTIs in pregnancy.

Hygiene behaviour

The EAU guideline for urological infections states that studies investigating hygiene behaviours have not found any association with the incidence of UTIs [3]. The two observational studies included in this review, however, provide evidence that hygiene behaviours are associated with the incidence of UTIs. Results show that increased sexual activity of greater than two or three times a week was linked to a high frequency of UTIs. However, washing the genital area and voiding the bladder after intercourse had a protective effect. The direction of wiping the genital area after voiding the bladder was also found to be important and women who wiped from back to front had a higher incidence of UTIs according to both studies. Lastly, Amiri et al. [25] also found that drinking

Table 6 Characteristics of included publications

Author, Year, Country	Wing et al., 2008, USA [28]
Design	Pilot randomised control trial comparing cranberry juice with placebo. Participants were divided into three groups and asked to drink 240 ml of either cranberry or placebo juice. A. cranberry juice three times daily B. cranberry juice once and placebo twice daily C. placebo three times daily Note: High withdrawal led to modification of dose frequency to twice daily in the middle of the trial. Randomisation was stratified by site.
Aim	To determine effectiveness of cranberry juice at reducing the frequency of ASB.
Participants	188 pregnant women < 16 weeks gestation
Key findings	Results report a 57% reduction in bacteriuria and 41% reduction in all UTIs. Authors concluded that cranberries provide protection against ASB as well as symptomatic infections.
Limitations	Small sample size as it was a pilot. About 39% participants dropped out due to gastrointestinal issues.
Author, Year, Country	Essadi et al., 2010, Libya [29]
Design	Randomised control trial comparing cranberry juice to placebo (water). Participants were divided into two groups and asked to drink 250 ml of cranberry juice or water. A: cranberry juice four times daily B: water four times daily Note: This publication is from a conference poster and full details were not available.
Aim	To determine the effectiveness of cranberry juice at reducing the frequency of UTIs.
Participants	760 pregnant women
Key findings	Results report that 70.5% of patients who drank cranberry juice showed a significant reduction ($p < 0.05$) in frequency of UTI compared to 32.16% who drank water. Of women who developed symptomatic UTI, 4.12% delivered prematurely. Authors concluded that cranberry juice has a protective effect in UTI prevention.
Limitations	There was no blinding as cranberry juice is distinguishable from water. High withdrawal rate of participants (28%) attributed to gastrointestinal upset. It is not clear whether authors used intention to treat analysis which may distort results in favour of cranberry juice.
Author, Year, Country	Elzayat et al., 2017, Egypt [26]
Design	An observational study to determine prevalence of ASB and the risk factors associated with it in pregnancy. Urine specimens were collected and analysed to determine ASB. A survey was conducted using a pre-tested questionnaire to gather data for the associated risk factors.
Aim	To determine the prevalence of ASB and identify risk factors associated with it in terms of socioeconomic status or personal hygiene.
Participants	170 pregnant women between the ages of 18–41.
Key findings	The prevalence of ASB was 10% (CI 95% 5.93% to 15.53%) in this sample of pregnant women. There was an association between sexual activity and incidence of ASB and 14% of women with ASB reported sexual activity > twice per week ($p = 0.01$). There was also an association between direction of wiping and 15% of women with ASB reported wiping their genitals from back to front ($p = 0.03$). No other significant association was found. Authors recommended educating women on the significance of personal hygiene to prevent UTI during pregnancy.
Limitations	This is an observational study and data was collected by questionnaire which is subject to accurate participant recall. Confidence intervals were not reported for all the categories.
Author, Year, Country	Amiri et al., 2009, Iran [25]
Design	An observational case-control study. Cases (women with UTI) and controls (no UTI) were matched and compared in terms of difference in genital hygiene or sexual activity. The women were administered a questionnaire by a midwife following which a urine sample was taken for analysis.
Aim	To determine association of genital hygiene and sexual activity with the frequency of UTIs in pregnant women.
Participants	250 pregnant women (100 cases and 150 controls)
Key findings	The authors investigated multiple factors. Of note is the significant association seen with: Sexual activity > thrice a week (OR = 5.62 95% CI: 3.10–10.10) Not voiding the bladder after intercourse (OR = 8.62 95% CI: 6.66–16.66) Washing genital area from back to front (OR - 2.96 95% CI: 1.66–5.28)
Limitations	This was an observational study and data was collected using a questionnaire which is subject to accurate participant recall. Matching of cases and controls is not reported in detail.
Author, Year, Country	Baertschi et al., 2003, Switzerland [33]
Design	A before and after study testing a bacterial extract's (OM-8930) efficacy and safety in preventing the incidence of UTIs during pregnancy.
Aim	To determine the effect of immunisation on the number of UTI recurrences, the number and duration of antibiotic treatment used and establish the safety of the vaccine (in women or new born).
Participants	62 women 16–28 weeks pregnant
Key findings	The extract significantly reduced the recurrence of UTIs from 52.5% to 19.4% ($p = 0.002$). Number of people needing antibiotic treatment reduced from 55.7% to 12.9% ($p = 0.0002$) Duration of antibiotic treatment reduced from a mean of 3.2 to 2 days ($p = 0.0016$) The authors concluded that OM-8930 reduced the number of UTI recurrences but a larger trial was needed to confirm this result.
Limitations	

Table 6 Characteristics of included publications *(Continued)*

	The study compares data from the trial to the 6 month period prior to the study instead of comparison with a control group. There is a risk of bias due to this because women's pregnancy status would likely be different at the two times. Also, The study was a pilot and had a small sample size.
Author, Year, Country	Grischke & Ruttgers, 1987, Germany [35]
Design	An open comparative randomised trial comparing effectiveness of a vaccine preparation, Solco-Urovac®, to standard antibiotic therapy for prevention of UTIs. The participants were divided into two groups Group 1: 200 participants given Solco-Urovac® (68 were pregnant) Group 2: 198 participants given nitrofurantoin or another appropriate antibiotic
Aim	To establish the effectiveness of Solco-Urovac® in reducing the frequency of UTIs.
Participants	400 pregnant and non-pregnant women
Key findings	There were 28 infections in the trial group and 84 infections in the control group – this was a significant difference ($p \leq 0.001$). Average duration of the infection was significantly longer than in the control group. No adverse effects were observed in the offspring.
Limitations	The study was not conducted exclusively in pregnant women and their proportion in each group is not specified. Randomisation was not done appropriately as the treating physician may have allocated patients with acute symptoms to the antibiotic group.
Author, Year, Country	Ochoa-Brust et al., 2007, Mexico [36]
Design	A randomised trial to assess the prophylactic role of ascorbic acid in preventing UTIs during pregnancy. Participants were divided into two groups. Group A: treatment with ferrous sulphate 200 mg, folic acid 5 mg and ascorbic acid 100 mg daily for 3 months Group B: treatment with ferrous sulphate 200 mg and folic acid 5 mg daily for 3 months.
Aim	To determine the role of ascorbic acid in reducing the frequency of UTIs.
Participants	110 pregnant women, 55 in each group.
Key findings	The infection percentage was 12.7% in Group A and 29.1% in Group B ($p = 0.03$, OR 0.35, CI 95% 0.13–0.91). The relative risk reduction was 56.5% and absolute risk reduction was 16.3%, The number needed to treat was 6. The authors concluded that pregnant women in areas with high rates of antimicrobial resistance should take ascorbic acid during gestation to prevent UTIs.
Limitations	Patients were excluded from study if they were not compliant, had serious side effects or if they had a UTI recurrence which may have distorted the results in favour of ascorbic acid.
Author, Year, Country	Ordzhonikidze et al., 2009, Russia [38]
Design	

Table 6 Characteristics of included publications *(Continued)*

	Two groups of pregnant women were treated with Canephron® N. Group 1: 160 women with an exacerbation of pyelonephritis were given Canephron® N in combination with standard therapy (antibiotics). Group 2: 140 women with chronic history of urinary tract disease who were given Canphron® N alone for prevention. The dose of Canephron® N was two tablets three times a day.
Aim	To assess the role of Canephron® N in the management of urinary tract diseases in pregnant women.
Participants	300 pregnant women
Key findings	Group 2 seemed to show more favourable results compared to Group 1. The percentage frequency of exacerbation of pyelonephritis was 10–6.25 in Group 1 and 3–2.1 in Group 2. The authors state in the results section that there was a 1.5-fold decrease in the frequency of infectious complications in the first group and a 1.3-fold decrease in the second group when comparing results to previous years.
Limitations	The methods, results and analysis have not been reported clearly. Canephron® N was not compared to a placebo or to antibiotics.

inadequate amounts of fluid and delaying voiding of the bladder also increased the likelihood of UTIs.

The overall evidence from these studies supports the adoption of protective hygiene behaviours, which may seem intuitive, as good hygiene is well known to protect against all types of infections. Women should be provided with specific recommendations because they may get upset if they get advised to 'just keep clean' as evidenced by a qualitative study conducted by Flower et al. [33].

Cranberry juice

Both RCTs [27, 28] assessing the efficacy of cranberry juice to prevent UTIs in pregnancy concluded that it has the potential to be effective. However, both studies had limitations which shed doubt on the effectiveness of this intervention. The study by Wing et al. [27] was underpowered with a small sample size (188 women). Essadi et al. [28] had a larger cohort (760 women) but compared cranberry juice to water which led to inadequate blinding giving rise to a risk of performance bias i.e. systemic differences between the groups. In addition, it is not clear if they used intention-to-treat analysis which may have distorted the results in favour of cranberry juice. A point to note with regards to Essadi et al. [28] is that it was published as a conference poster and full details were not available but it was included because the abstract reported data in sufficient detail to determine the significance of the results.

A limitation of cranberry juice seen in both studies was the high volume of juice that needed to be ingested (240 ml [27] and 250 ml [28]). Both trials had a high withdrawal rate mostly due to gastrointestinal disturbances which can limit its use on grounds of acceptability to women. These results point to a need to investigate a standardised content of cranberries in alternative formulations such as tablets and capsules which may help with improving adherence and tolerability of this intervention.

Both these trials view cranberry juice as potentially effective at preventing UTIs in pregnancy but a Cochrane review by Jepson et al. [34] included both these studies in a meta-analysis and found cranberries to be ineffective in preventing UTIs in pregnancy. Thus, although there has been interest in using cranberries for UTI prevention, the evidence does not support its efficacy. It can still be used as a self-care option, if preferred by women, because of its known safety in pregnancy [35, 36].

Immunisation

Both studies investigating the role of immunisation to safely reduce the recurrence of UTIs in pregnancy found favourable results, however both had significant limitations. Baertschi et al. [29] used a bacterial extract consisting of different strains of *Escherichia coli (E.coli),* which is the most common uropathogen [37], however this vaccine would not be effective against any other type of bacteria. Furthermore it was an open pilot study and did not have a control group to compare the effectiveness of the vaccine. Therefore, the results need to be confirmed by a RCT, as noted by the authors themselves. Grischke and Ruttgers [30] conducted their study in a sample where 68 pregnant women were given the intramuscular vaccine but the number of pregnant women in the control group was not specified. Blinding was not clearly described either and so there is an unclear risk of bias. Therefore, immunisation as an approach to prevent UTIs in pregnancy needs further exploration to assess its feasibility in practice.

Ascorbic acid

Ochoa-Brust et al. [31] concluded that daily ascorbic acid was beneficial especially in areas with a high incidence of UTIs and antimicrobial resistance. This is a promising result but requires additional trials to strengthen the evidence before it can be recommended. It is not clear whether the authors used intention-to-treat analysis because they did not specify the withdrawal rate and there was a selection bias as they excluded women who were non-adherent or had 'serious side effects' from the medication. Excluding these results from analysis may distort the results in favour of ascorbic acid. It is worth noting, however, that no harmful effects were observed in the offspring of women who ingested ascorbic acid daily.

Canephron® N

Canephron® N is a phytotherapeutic medicine with antibacterial properties and contains three herbs namely rosemary, lovage and centaury [38]. It is manufactured by a German company, Bionorica®, which focuses on researching and developing plant-based medicines. Ordzhonikidze et al. [32] conducted a study with pregnant women using this product, to optimise management of urinary tract diseases including ASB and pyelonephritis, which concluded that it could be recommended for prevention of urinary tract complications in pregnancy. The reporting of results was not comprehensive so it was not possible to determine how the study was conducted in sufficient detail (see Table 3). A review by Naber et al. [38] assessing the efficacy of Canephron® N suggests that there might be some benefit from its use in pregnant women because it included evidence from additional studies which have not been discussed here as they were conducted in pregnant women with co-morbidities and so did not meet the inclusion criteria of this review. It is worth noting that the safety of Canephron® N in pregnancy has been established [39, 40] but in order to make an evidence based recommendation, its efficacy needs to be confirmed by a randomised controlled trial.

Strengths and limitations

A total of ten databases were searched and search terms were mutually agreed by the authors and an independent colleague to ensure a comprehensive process. The studies included in the review were assessed independently by the authors using CASP checklists. Any disagreement was resolved by meeting and discussing the relevant studies. A limitation of this review is that only English language publications were included therefore there might be options which have not been identified. The results of this review have been discussed using a narrative synthesis approach due to the heterogeneous design of the included studies and the differing nature of the interventions identified.

Conclusion

All the approaches identified in this review are reported to be safe and effective. However apart from hygiene behaviours, the evidence behind these approaches is not robust enough to be recommended in practice. Future work needs to focus on strengthening the evidence base through improved design and reporting of clinical trials, in particular for the use of immunisation, ascorbic acid and Canephron® N. It is important that evidence based non-antibiotic measures to prevent UTIs in pregnancy are discovered to combat the danger that antimicrobial resistance poses to the health of this vulnerable patient group as well as the wider population.

Additional file

Additional File 1: Search strategy. The additional file 1 contains the search strategy used to retrieve publications from the databases. It also contains details of authors who were contacted to obtain full text articles. (DOCX 16 kb)

Abbreviations

ASB: Asymptomatic bacteriuria; Defra: Department for Environment Food and Rural Affairs; DH: Department of Health; EAU: European Association of Urology; RCT: Randomised control trial; SIGN: Scottish Intercollegiate Guidelines Network; UTI: Urinary tract infection

Acknowledgements

We would like to thank all the authors of the original studies, and Tim Chapman, the pharmacy division's liaison librarian at the University of Reading, for his support with conducting the literature search.

Funding

This work was supported by the University of Reading as a PhD studentship for F.G.

Authors' contributions

FG conducted the literature search and screened the papers for eligibility for this review. All authors (FG, AH and KR) screened the publications for quality assessment. The final manuscript was prepared by FG, then edited and approved by AH and KR.

Ethics approval and consent to participate

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Publisher's Note

Received: 1 February 2018 Accepted: 5 April 2018
Published online: 13 April 2018

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CHAPTER FOUR

4. Urinary tract infections and antibiotic use in pregnancy - qualitative analysis of online forum content

Chapter four presents the publication:

Ghouri, F., Hollywood, A., & Ryan, K. (2019). Urinary tract infections and antibiotic use in pregnancy - qualitative analysis of online forum content. *BMC Pregnancy and Childbirth*, *19*(1), 289. https://doi.org/10.1186/s12884-019-2451-z

4.1. Introduction

The following publication presents a qualitative study on women's perceptions of UTIs and using antibiotics in pregnancy. The data was collected using an online health forum on a popular parenting website in the UK (www.mumsnet.com) and then analysed qualitatively using inductive thematic analysis. This study was conducted following the systematic review which highlighted that behavioural measures to prevent UTIs were, at present, the only measure linked with reducing the incidence of UTIs and avoiding antibiotics. The general public can utilise options other than antibiotics, such as those available over the counter from pharmacies, to prevent and treat UTIs. Pregnant women however are given antibiotics once a UTI is diagnosed to prevent adverse outcomes that could affect them and their foetus. Behavioural measures therefore become increasingly important in pregnancy to prevent infections and avoid or minimise antibiotics in response to AMR. Behavioural insight into women's perceptions of their illness and medication use during pregnancy is therefore needed. The rationale for conducting this study was to explore women's perceptions of experiencing a UTI and using antibiotics during pregnancy which would then help healthcare professionals with understanding their beliefs and concerns with regards to this common health issue. Use of

the online forum for data collection provided access to discussions, relating to women's experiences, in a naturalistic setting. Studies focusing on women's experiences of a UTI and using antibiotics have been conducted before. However, they either excluded pregnant women or focused only on the general public. Pregnancy is a unique physiological state for women where their health concerns might differ from the non-pregnant population because of effects on the foetus. This study was therefore conducted to present women's perceptions of how they view UTIs and antibiotic use in pregnancy. UTIs are the most common infection and where the highest use of antibiotic occurs in this demographic. Ultimately, exploring women's perceptions of UTIs and antibiotic use during pregnancy is also important to help inform health interventions that could be designed to empower women for self-care in pregnancy and target how antibiotics are utilised in this population.

BMC Pregnancy and Childbirth

RESEARCH ARTICLE Open Access

Urinary tract infections and antibiotic use in pregnancy - qualitative analysis of online forum content

Flavia Ghouri, Amelia Hollywood* and Kath Ryan

Abstract

Background: Antibiotics are standard treatment for asymptomatic and symptomatic urinary tract infections (UTIs) in pregnancy. Their overuse, however, can contribute to antimicrobial resistance (AMR) and expose the foetus to drugs that might affect its development. Preventative behaviours are currently the best option to reduce incidences of UTIs and to avoid the use of antibiotics in pregnancy. The aim of this study was to explore women's experiences of UTIs in pregnancy to develop an understanding of their concerns and to optimise and encourage behaviours that facilitate appropriate use of antibiotics.

Methods: An online pregnancy forum in the United Kingdom (UK) was used to collect data on women's discussions of UTIs. A total of 202 individual threads generated by 675 different usernames were selected for analysis. The data was organised using NVivo 11® software and then analysed qualitatively using inductive thematic analysis.

Results: Women's perceptions of UTIs and antibiotic use in pregnancy were driven by their pre-natal attachment to the foetus. UTIs were thought to be common and high risk in pregnancy, which meant that antibiotics were viewed as essential in the presence of suspected symptoms. The dominant view about antibiotics was that their use was safe and of little concern in pregnancy. Women reported an emotional reaction to developing a UTI. They coped by seeking information about behaviour change strategies to assist with recovery and through emotional support from the online forum.

Conclusions: Women face dual risks when they experience UTIs; the risk from the infection and the risk from antibiotic treatment. Pre-natal attachment to the foetus is highlighted in the decision making process. The focus is on the shorter term risk from UTIs while undermining the longer term risks from antibiotic use, especially the risk of AMR. A balanced view needs to be presented, and evidence-based infection prevention strategies should be promoted, to women to ensure appropriate antibiotic use in pregnancy, to address the global challenge of AMR.

Keywords: Urinary tract infection, Prevention, Antibiotics, Online forum, Pregnancy, Pre-natal attachment, Antimicrobial resistance

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Background

Pregnancy can increase the susceptibility of urinary tract infections (UTIs) in women because of physiological changes [1]. The vast majority of primary care antibiotic prescriptions issued to pregnant women in the UK are for UTIs [2] which suggests a high prevalence. Evidence from studies shows that asymptomatic infection alone can affect 2–12% of women [3]. The current management of UTIs in pregnancy is with a short course of antibiotics whether or not the infection is symptomatic. Asymptomatic bacteriuria (ASB) is diagnosed and treated through routine screening during the first trimester [4] which is in contrast to non-pregnant women where asymptomatic infections are not treated with antibiotics [5]. ASB is treated in pregnancy because studies have shown that bacterial colonisation of the urinary tract in pregnancy can cause adverse health outcomes e.g. there are risks of kidney infection, intra-uterine growth retardation and pre-term birth [6, 7]. The authors of a recent randomised control trial however have questioned the benefit of routine screening for ASB in the first trimester of pregnancy [8]. Kazemier et al. (2015) [8] found no association between ASB and growth retardation or pre-term birth and although an association was observed between ASB and kidney infection, the absolute risk was found to be low.

Excessive and unnecessary use of antibiotics is strongly associated with a rise in antimicrobial resistance (AMR) which is the ability of bacteria to survive in spite of antibiotic treatment leading to life threatening infections [9]. There is evidence from the UK and internationally which suggests that antibiotics to treat UTIs are overprescribed in pregnant women [10, 11]. Although AMR is a global public health threat to everyone, in pregnancy it can be particularly concerning due to the risk of resistant bacteria passing on to the neonate during birth which can be a vulnerable stage of life with regards to contracting infections. In addition to this, antibiotic use in pregnancy may also carry the risk of potentially teratogenic effects including spontaneous abortion [12] . Therefore, in light of AMR and the risk of adverse effects from the use of antibiotics, it is important that maternal antibiotic use is appropriate without compromising the health of women if they experience a UTI.

While a number of non-antibiotic options for UTI management have been studied, research has mostly focused on non-pregnant populations. A systematic review by the authors of the current study reported that preventative hygiene behaviour, such as washing the genitals after sexual intercourse, is the only evidence-based intervention linked to a reduced incidence of UTIs in pregnancy and therefore the most effective method of avoiding antibiotics [13]. Therefore women need to be encouraged, through effective communication, to adopt these preventative behaviours to minimise antibiotic use. Qualitative exploration of women's perceptions can assist healthcare professionals by informing an in-depth understanding of their beliefs and concerns about experiencing UTIs during pregnancy. As this has not been researched before, this study aims to explore women's perceptions about UTIs specifically during pregnancy.

Method

Design

Research has shown that searching for information online increases during pregnancy and women find online communities useful because of their accessibility [14, 15]. The website www.mumsnet.com was used to access naturally occurring data with regards to women's perceptions about UTIs during pregnancy. Mumsnet is a popular parenting website in the UK and consists of conversational threads in a designated space called '*Talk*' where users have discussions on a wide array of topics. A Mumsnet census from 2009 showed that subscribers to the website are mostly white British women, 30–40 years old, with a degree qualification [16]. Although the demographic data is difficult to ascertain precisely and may have changed over the years, using the website as the medium for data collection provides access to naturalistic data where participants are open about their views due to the anonymous nature of posting on an online forum under a username. The data was analysed qualitatively using inductive thematic analysis [17].

Procedure

Conversation threads on the website were searched using the search tool and limited to 'thread title only' under the topic of 'pregnancy'. The search terms 'urinary tract infection or UTI', 'cystitis', 'kidney infection', 'bladder infection', 'E.coli', 'antibiotic', 'antimicrobial resistance', 'amoxicillin', 'co-amoxiclav', 'ciprofloxacin', 'nitrofurantoin' and 'trimethoprim' were used to extract comprehensive data about UTIs. The search was conducted between 01-01-12 to 30–11-17 to explore recent views. All relevant threads were selected and downloaded to a Microsoft Word® document and then organised using the qualitative analysis software, NVivo 11®. A total of 202 individual threads generated by 675 different usernames were downloaded and analysed as seen in Table 1.

Data analysis

The data was analysed using inductive thematic analysis, using the guide recommended by Braun and Clarke (2006). Thematic analysis is a method used to analyse qualitative data that provides flexibility in identifying, analysing and reporting patterns in data. Inductive thematic analysis is directed by the content of the data and

Table 1 Number of threads per search term

Search terms	No. of threads
Urinary tract infection or UTI	121
Cystitis	18
Kidney infection	12
Bladder infection	4
Water infection	18
E.coli	0
Antibiotic	19
Antimicrobial resistance	0
Amoxicillin	2
Ciprofloxacin	0
Co-amoxiclav	0
Nitrofurantoin	4
Trimethoprim	4
Total	202

was chosen to allow collective exploration and interpretation of women's perceptions of UTIs in pregnancy. The data was read by FG multiple times to achieve familiarisation and to generate detailed codes. Codes were then organised and developed by FG into themes by examining and reflecting on broader patterns in the data. Themes were reviewed by all authors and refined by referencing back to the data. A thematic map was generated which shows how the themes are linked. Illustrative quotes from the data have been used to evidence each theme. Quotes have been edited for clarification where appropriate.

Ethical consideration

Mumsnet is a website that provides a forum for discussions where users are required to create a username to post a comment and they are informed that their posts are visible to anyone on the internet. The terms of use of www.mumsnet.com explicitly state that the website and its content are copyright to Mumsnet and any submission of data by users can be edited or published by Mumsnet for any purpose, commercial or otherwise, that the website considers appropriate. Therefore Mumsnet was contacted to explore whether they deemed this study an appropriate use of their data. Mumsnet confirmed approval and gave permission for the researchers to download the data to conduct the study. Individual users could not be informed about the study or contacted for explicit consent to use the content that they have posted on the website as users post under a username and no contact details are provided. To ensure scientific rigour ethical approval was sought and obtained from the University of Reading's Research and Ethics Committee (Ref 17/30).

Public attitudes with regards to conducting research using social media are conflicting [18]. The rationale behind proceeding with the research was that data was not collected from a restricted space but an online open public forum accessible to anyone with an internet connection. There was a low risk of harm or distress because users had voluntarily shared their views. No identifiable information was collected or analysed during the conduct of this study protecting the identity and confidentiality of users. Users on the website posted using fictional usernames which were further changed to pseudonyms to anonymise quotes as an additional precaution to protect anonymity and confidentiality. Upon balancing the harms and benefits of this study, the authors believe that the study meets the British Psychological Society's guidelines for internet-mediated research [19] and the Association of Internet Researchers' recommendations for ethical decision making and internet research [20]. Exploring and voicing the experiences of women would lead to better understanding of healthcare needs by healthcare professionals and benefit women during pregnancy thus justifying this research ethically.

Results

Analysis of the data led to construction of three subthemes and an overarching theme as shown in Fig. 1. The primary theme relates to women's pre-natal attachment to the foetus which is reflected in the subthemes that describe women's perceptions of UTIs in pregnancy, the safety of antibiotics and coping mechanisms employed to deal with the impact of the illness. The themes with illustrative quotes are described below.

Pre-natal attachment

The primary overarching theme describes the pre-natal attachment or bond that women feel towards the foetus during pregnancy. Cranley (1981, pg. 282) described pre-natal attachment as 'the extent to which women engage in behaviours that represent an affiliation and interaction with their unborn child' [21]. Analysis of the data in this study strongly demonstrated women's attachment to their baby which was visible in the types of questions they asked each other and the language that they used in the discussion on the forum. The findings also show that while women discussed a range of issues, the main concern for most, with regards to experiencing a UTI, was concern for their baby.

> I'm just worried for my little nugget, think I'll ask to check the heartbeat when I go back for peace of mind. (Luna).

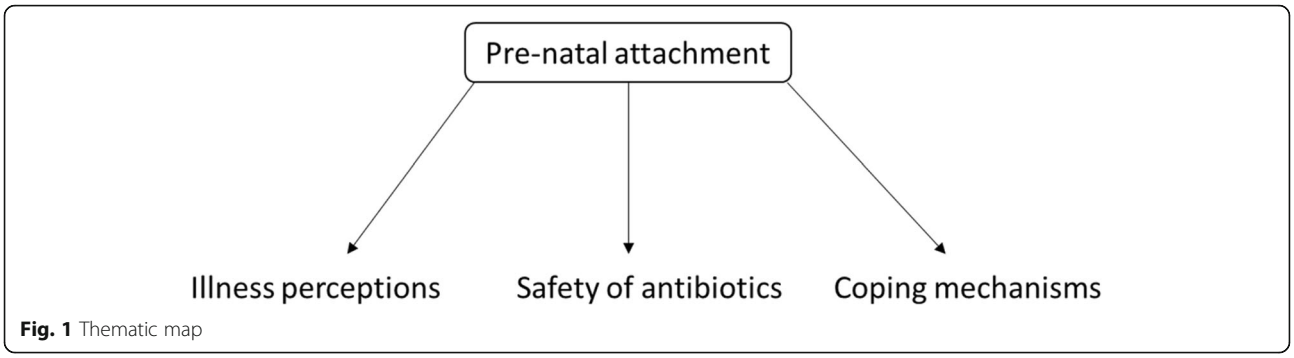

Fig. 1 Thematic map

> Hi I'm 6 + 4 and had a scan today…got to see a little heartbeat: -) only problem was traces of blood in my urine so they gave me antibiotics for what they suspect is a UTI…just worried now after seeing the heartbeat that taking the antibiotics will do something to baba?? (Sally).

The following section describes women's perceptions of UTIs and antibiotics in pregnancy and shows how pre-natal attachment is reflected in the three subthemes.

Illness perceptions

The risks of UTIs were viewed in terms of how the infection could impact the mother's health e.g. developing a kidney infection, and the risks to the pregnancy in terms of effects on the foetus e.g. pre-term birth or miscarriage. The majority of discussions, however, focused on the impact on the foetus.

> I'm really worried as I'm aware UTIs if left untreated can cause miscarriage, I feel like a sitting duck! I'm obviously glugging away at the water and cranberry juice but the pains are worrying me. (Rachel).

> Untreated UTIs can lead to permanent kidney damage for you and premature labour. I'm not trying to scare you and I'm sure you'll be fine but could you get in touch with your MW [midwife] and get their opinion. (Jane).

For most women it was the diagnosis of a UTI rather than the difficult symptoms per se that made them anxious, as even those who had an asymptomatic infection shared similar concerns about the UTI impacting pregnancy and harming the foetus.

> Had no symptoms but told I had a bad UTI, I'm now absolutely petrified that I've found out too late and my baby will be harmed (Shadane).

Most women also viewed UTIs as being very common in pregnancy. As Stella described, "Never had one outside of pregnancy, you are more prone to them unfortunately!" In fact, it was thought that pregnancy caused UTIs to the extent that any troubling symptom could be the sign of a UTI.

> "I always find in pregnancy that everything is put down to a UTI." (Linda).

At the same time UTIs in pregnancy were also viewed as harder to diagnose and more difficult to treat compared to when not pregnant. The reasons were thought to be due to an overlap between normal pregnancy symptoms and those characteristic of UTIs. For example, as Jane indicated, "symptoms of UTI are quite difficult in pregnancy as you have a lot of them anyway". Biochemical changes in the body due to pregnancy were also attributed to making diagnosis more difficult.

> I also had trouble getting diagnosed when pregnant and was told by the midwife that it's because there are so many things present in your pee and altering what's in your pee when pregnant that it can be hard to get a dip result indicating a UTI. (Bella).

Ultimately, a desire to protect their baby, arising from pre-natal attachment, led most women to view UTIs to be so risky that urgent treatment with antibiotics was considered an absolute necessity and delaying or ignoring any symptoms was deemed "irresponsible".

> I'm surprised they haven't given you any antibiotics straight away as it can cause early labour or a small baby if left untreated. Mine's been in my kidneys, the pain has been horrendous. Don't suffer if you need to ring and ask for antibiotics. (Aria).

> If you weren't pregnant you could maybe take your friend's advice to drink water and cranberry juice and wait it out, but given that you are pregnant it's irresponsible advice to be honest. (Nikita).

In summary, the majority of women perceived UTIs to be more dangerous in pregnancy compared to when not pregnant due to the risk of serious consequences such as miscarriage or pre-term birth. They also considered UTIs to be a fairly common occurrence with diagnosis and treatment of the infection more problematic in pregnancy. Pre-natal attachment to the foetus meant most women considered antibiotics to be absolutely essential for treatment and avoiding them, or a delay in seeking help was seen as irresponsible behaviour.

Safety of antibiotics

A few women expressed reluctance and questioned the use of antibiotics in pregnancy for the treatment of UTIs. The reasons varied from concerns about teratogenicity, effects on long term immunity or personally experiencing antibiotic side effects. For example, Liza was fearful about the effects on the foetus, "I'm petrified that taking amoxicillin will harm baby!" while another website user was concerned about longer term effects such as the development of allergies in the child.

> Personally I would be wary of it [antibiotic] because there is a link between taking antibiotics in late stage pregnancy and the baby having eczema and allergies. I took antibiotics in late pregnancy and my daughter has multiple food allergies and eczema (Tania).

In spite of these concerns, which were expressed by only a small proportion of women, most considered antibiotics to be generally safe.

> Antibiotics are one of the few things they are really sure about giving to pregnant women, precisely because we get infections. (Tula).

The majority of women compared the risks of a UTI with the risks of using antibiotics and viewed antibiotics as the safest option for normal progression of their pregnancy. They drew on their personal experiences of using antibiotics or viewed a prescription as proof that antibiotics were not dangerous. As Carey suggested, "Doc wouldn't prescribe if dangerous. It's more dangerous to leave a UTI, as at its worst it can cause kidney issues and miscarriage". This view also meant that some women thought that it was better to take antibiotics "just in case".

> The doc said it wouldn't do me any harm and better than not taking them just in case I had needed them (if that makes sense). I don't think you should feel guilty as the doc will have given you antibiotics that wouldn't affect your baby. (Usha).

Thus when discussing the safety of using antibiotics to treat UTIs, whether or not they viewed them as safe in pregnancy, women's primary motivation was to protect the foetus owing to pre-natal attachment. For a small proportion of women it was the uncertainty of how the antibiotic might affect the foetus or their child's immunity in the long term that led them to be wary but for the remaining majority, antibiotics were perceived as the safest and most effective management option.

Coping mechanisms

Pregnancy can understandably be an emotional time and unsurprisingly women on the forum described it in similar terms. Experiencing painful and frustrating symptoms of a UTI, coupled with a fear of how the infection might impact the pregnancy, had a considerably enhanced emotional impact on many women. Throughout the data, highly emotive language featured quite strongly to express discomfort and frustration. For example,

> I just really worry about taking things when pregnant and feel so emotional atm [at the moment]!! Tia [thank you in advance] x (Serena).

One particular quote highlights strong feelings of guilt alongside the frustration,

> I don't know why but it makes me feel like such a failure each time the results come back with an infection still present. I get angry with myself that I can't get my body to do its job to fight it and I'm putting my baby at risk. Stupid I know but I can't help it xx (Nadia).

The majority of women therefore used the forum as a way of coping via two main functions; by using the forum for emotional support or by seeking information and advice. Some women coped by expressing their thoughts and feelings and seeking people with similar experiences whereas others sought advice on the forum about measures they could take to ease their symptoms and clear the UTI.

Using the forum as an online social support system to cope emotionally was seen throughout the data. For example, as one person posted, "Not sure why I'm posting, may just need a bit of hand holding …" (Hope) and another person while consoling someone stated, "It's such a lonely illness try [to] get some company or people to talk [to] on the phone/text or Mumsnet of course" (Rachel). The emotional impact of the illness was particularly strong in women who experienced recurrent or resistant infections requiring multiple courses of antibiotics. They expressed frustration and feeling a lack of control as emphasised in the exchange below.

> Now dreading getting another UTI as it will prove difficult to treat according to my GP. Only 19 weeks along, so this better not happen again (Veda).

> I feel your pain - aside from the physical symptoms it was the "how will I ever get rid of this without Abs [antibiotics]?" question that really dragged me down (Response by Lynn).

As mentioned above, many women also used the forum to seek and give advice on measures to cope actively with their illness, especially if they experienced recurrent infections. Preventative measures such as drinking cranberry juice, using over-the-counter (OTC) cystitis relief remedies or following certain hygiene behaviours, like wiping the genitals from front to back etc., were some of the measures that women discussed. Perceptions around these measures, however, were varied and the suitability of some of the remedies was also often questioned. For example, one woman advised avoiding cranberry juice while another found it be effective and a better option than antibiotics especially for milder infections.

> As much water as you can drink. Mix some bicarb in water and have that if you have some, tastes awful but helps. Avoid cranberry juice. Avoid caffeine. I am a UTI veteran! (Alia).

> Cranberry juice is good as well. If it is mild this may flush the infection out and is gentler than antibiotics which will be likely to cause thrush… (Marina).

Similarly, there were differing views regarding the suitability of over-the-counter cystitis relief treatment.

> I can't have the sachets I normally drink to ease symptoms as they are unsuitable for pregnant women (Delia).

> My doctor said it was safe to use the cystitis relief sachets along with drinking plenty of water and cranberry juice and apparently it should go within 48 h (Irene).

To summarise, UTIs in pregnancy had an emotional impact on most women which left them feeling frustrated at a time when they were already going through physical changes in their bodies. They used the online forum to find ways to cope either through exchange of information and advice or for emotional support. The discussions, both when exchanging tips and when venting emotionally, centred significantly on the impact on the pregnancy which again highlights women's pre-natal attachment to the foetus.

Discussion

This study explored women's perceptions of experiencing a UTI during pregnancy as discussed on an online forum. The results indicate that women view UTIs in pregnancy primarily from the lens of being an expectant mother and pre-natal attachment to their unborn baby drives them to put the safety of the foetus at the very core of how they view the illness and how they behave at the onset of a UTI. Pre-natal attachment is a theoretical construct drawn from John Bowlby's theory of Human Attachment [22]. Its relevance to antenatal care lies in the fact that it is useful in motivating women to adopt practices that facilitate good health for themselves and their unborn child [23].

Previous studies [24, 25] exploring women's perceptions of UTIs report that the condition can significantly affect women's quality of life. The current study supports these findings, as described in the first subtheme relating to illness perceptions, and highlights how the state of being pregnant means that women view UTIs to be more common and linked to serious consequences compared to when not pregnant. The high risk perception and the view that UTIs are common in pregnancy encourages women to seek antibiotic treatment at the onset of any probable symptom even though it may be a normal pregnancy occurrence such as increased frequency of urination. The second subtheme, which relates to the safety of antibiotics, highlights that apart from a small proportion, most women on the forum favour antibiotic treatment which is in contrast to a study conducted with non-pregnant women [26]. The perception that antibiotics are generally safe in pregnancy is also unusual in light of other studies that report that women view antibiotics to be moderately harmful [27] and that women overestimate teratogenic risk from exposure to medicines [28]. The last subtheme, which describes coping mechanisms, highlights the negative impact that UTIs can have on women and how they cope by adopting two distinct approaches. These approaches are seeking advice on actions to take to cope with the UTI or using the forum for emotional support. Both of these approaches are reflected in health psychology literature and correspond to problem-focused or emotion-focused coping respectively which are two styles that people might adopt to cope with stressors [29].

Implications of study

The findings from this study have implications for how women should be encouraged to take care of their health during pregnancy with regards to urinary infections and the use of antibiotics. The data highlights how pregnant women are faced with dual causes of risk when they experience UTIs; the risks arising from the infection and

the risks from using antibiotics. This duality of risks leads most women to perform a cost-benefit analysis and pre-natal attachment means they prioritise safeguarding the foetus against the short term risks of a UTI while overlooking the longer term risk of AMR from using antibiotics. This might lead to increased demand and overuse of antibiotics and contribute to the problem of AMR, which can affect not just the foetus but women themselves and society at large.

Current data on the incidence and outcomes of UTIs in pregnancy in the UK along with improved diagnostics is needed to ensure antibiotics are not being overused. As well as this, women need balanced information from healthcare professionals not only about the risks of UTIs but also of excessive antibiotic use. Future research can investigate the usefulness of emphasising pre-natal attachment in interventions designed to promote responsible use of antibiotics.

Although pregnancy can increase women's susceptibility to a UTI, prevention measures can protect against it [13, 30, 31]. Information about prevention through hygiene behaviours needs to be standardised and emphasised as the best way of preventing UTIs in pregnancy. In addition, the perception that pregnancy causes UTIs, as seen in this study and promoted by the National Health Service [32], requires challenging as it reflects a medical model of illness that attributes the cause of illness to external factors beyond individual control. Instead, women should be encouraged to use a problem-focused coping style through the adoption of preventative hygiene behaviours so that they can appreciate the controllability of this illness rather than rely solely on a medical solution i.e. antibiotics. Promoting such a behavioural model of illness, which sees the individual's behaviour as the solution to a health problem, has also been reported to lead to practise of healthier behaviours and outcomes that are sustained over a long period of time [33]. Lastly, the emotion-focused coping seen on the forum highlights women's need for emotional support and a sensitive approach to their care during pregnancy in relation to UTIs.

Strengths and limitations of study

The strengths of this study lie mainly in the method used for data collection. The advantage of using an online forum to collect data was that it provided access to a wide range of participants across the UK. Online forum postings increase the perceived sense of anonymity in participants, which can increase disclosure compared to face-to-face interviews. Data was also immediately available for analysis and circumvented transcription errors arising from interviews.

Using an online forum, however, also contributed to the limitations of this study. Women used descriptive text and emoticons to express their feelings, but using an online forum could result in a loss of insight that facial expressions or verbal tone can offer to exploring perceptions. It was difficult to characterise the exact demographics of website users and only views of women who had access to the internet and had subscribed to the forum could be analysed. Different cultural groups in the UK may also have different norms of behaviour in pregnancy and the views of women from varying backgrounds may differ from what was captured from the forum. Therefore, the interpretation and transferability of the results should be made within this context and broad generalisations may not be appropriate.

Conclusion

UTIs are prevalent in pregnancy and can cause women considerable stress and anxiety. Their primary concern stems from how the infection or the antibiotics might affect their baby. Although some women question the safety of antibiotics, most women adopt a risk appraising process which leads them to regard antibiotics as absolutely essential and safe for use in pregnancy if they experience any suspected symptom of a UTI. Pre-natal attachment may cause women to focus solely on the risks of a UTI while under-appreciating the risks of antibiotics, particularly the threat from AMR, which is a major global challenge.

Abbreviations

AMR: Antimicrobial resistance; ASB: Asymptomatic bacteriuria; *E.coli*: *Escherichia coli*; UTI: Urinary tract infection

Acknowledgements

We would like to thank www.mumsnet.com for their permission to collect and analyse the data used in this study.

Author's contributions

The data was collected and organised by FG. All authors developed and reviewed the themes. The final manuscript was prepared by FG, then edited and approved by AH and KR. All authors read and approved the final manuscript.

Funding

This work was supported by the University of Reading as a PhD studentship for FG. The study design, collection, analysis and interpretation of data and writing of the manuscript was conducted independent of the funding body, with AH and KR acting as PhD supervisors.

Availability of data and materials

All datasets supporting the conclusions of this article were collected from www.mumsnet.com and are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Consent to use the publicly available data was obtained from Mumsnet, as the website has licence to use the content as they deem appropriate. Individual users could not provide consent due to the anonymity of the posts. Ethical approval was obtained from the University of Reading's Research and Ethics Committee (Ref 17/30).

Consent for publication

Not applicable.

Competing interests
The authors declare that they have no competing interests.

Received: 18 December 2018 Accepted: 6 August 2019
Published online: 13 August 2019

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Publisher's Note

CHAPTER FIVE

5. 'There Is No Choice Apart from Antibiotics…': Qualitative Analysis of Views on Urinary Infections in Pregnancy and Antimicrobial Resistance

Chapter five presents the publication:

Ghouri, F., Hollywood, A., & Ryan, K. (2020). 'There is no choice apart from antibiotics…': Qualitative analysis of views on urinary infections in pregnancy and antimicrobial resistance. *Health Expectations*, hex.13044. https://doi.org/10.1111/hex.13044

5.1. Introduction

This publication presents the findings of an interview study conducted with women who had experienced a UTI during pregnancy. Qualitative semi-structured interviews were conducted with women to explore their perceptions of AMR in relation to experiencing a UTI during pregnancy. This study was designed following the previous study which explored women's perceptions of UTIs and using antibiotics. The previous study provided insight into how women perceived the infection and their views of using antibiotics during pregnancy. The data for the previous study was collected from an online health forum and although it provided an in-depth view on how women perceived UTIs during pregnancy, it did not provide insight into how they viewed AMR. This study was therefore designed to interview women and probe their views on AMR.

Previous research on perceptions of AMR have highlighted misconceptions about how the public view AMR. However, these studies were conducted with the general public and do not provide insight into how women perceive AMR. A contextual understanding of AMR is needed to effectively tackle this issue and therefore this study was designed to explore the views of women who had experienced an infection, specifically a UTI whilst pregnant. The study

highlights the conflicts in health priorities that arise when using antibiotics for infections in pregnancy and focuses on behavioural measures as a potential solution as they offer protection through infection prevention. This has implications for women's own individual health but also the health of their foetus and the wider society, as infection prevention minimises antibiotic and is therefore an effective strategy to tackle AMR.

Received: 29 October 2019 | Revised: 13 January 2020 | Accepted: 11 February 2020

DOI: 10.1111/hex.13044

WILEY

ORIGINAL RESEARCH PAPER

'There is no choice apart from antibiotics…': Qualitative analysis of views on urinary infections in pregnancy and antimicrobial resistance

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Funding information
This work was supported by the University of Reading as a PhD studentship for FG.

Abstract

Background: Antimicrobial resistance (AMR) is a health risk as it can lead to life-threatening infections. There has been a rise in resistant urinary tract infections (UTIs) which is the most common infection in pregnancy. This can be challenging in pregnancy due to the additional need to safeguard foetal development. The study's aim was to explore views about AMR in women who experienced UTIs in pregnancy.

Design: Fifteen semi-structured interviews were conducted in the UK and analysed using thematic analysis.

Results: Results highlighted two themes: conceptualization of AMR and pregnancy as a deviation from the norm, with an overarching theme of 'self-efficacy'. Results show that participants were concerned about AMR but uncertain about the effect on society compared to individual's taking antibiotics and about completing antibiotic courses. Participants reported an unsparing use of antibiotics was justified in pregnancy, and behaviours like drinking adequate water were ineffective at preventing UTIs. In summary, women had low self-efficacy regards tackling AMR and managing their health.

Conclusion: Misconceptions about how AMR affects society vs the individual translated into viewing it as a future problem to be tackled by the health-care sector. Consequently, AMR requires reconceptualization as a current problem requiring collective action. This research also indicates women endorse a biomedical model of UTIs in pregnancy which attributes resolving illness to interventions such as medicines, implying an automatic reliance on antibiotics. Subsequently, there is a need for self-efficacy by focusing on a behavioural model which emphasizes behaviours for infection prevention, thus reducing the need for antibiotics.

KEYWORDS

antibiotic resistance, antimicrobial drug resistance, interviews, pregnancy, qualitative research, self-efficacy, urinary tract infection, women's health

1 | INTRODUCTION

Antimicrobial resistance (AMR) is a global health threat and can result in serious or life-threatening infections. Although AMR is a naturally occurring phenomenon, antibiotic use is its biggest driver because the use of these drugs causes positive selection of resistant bacteria. Antibiotic use can result in carriage of resistant bacteria by individuals for a period of several months to a year after completing a course.[1] The bacteria can transfer to people in close contact and thus result in a spread of resistant infections. The transmission of resistant bacteria is particularly concerning in pregnancy as they may infect neonates during the birthing process. The choice of antibiotics in pregnancy can also be limited compared to the general population because of the risk of teratogenicity, which is the risk of harm to the developing foetus. Teratogenicity can exclude or restrict the use of antibiotics[2] to specific trimesters; for example, trimethoprim is avoided in the first trimester due to a risk of neural tube defects and the risk of haemolysis precludes the use of nitrofurantoin at term.

Due to AMR, it is essential that antibiotics are used with a careful consideration of the benefits and risks. Antibiotics are the most commonly prescribed medicines in pregnancy,[3] and urinary tract infections (UTIs) account for the majority of their use.[4] In 2013, Public Health England established the English Surveillance Programme for antimicrobial utilization and resistance (ESPAUR) that monitors and publishes national data on AMR. The ESPAUR report from 2018 to 2019 shows that AMR in UTIs is established and an increasing burden in health care.[5] The National Institute for Health and Care Excellence (NICE), who provide national care guidelines in the UK, published an update on its antimicrobial guideline for lower UTIs in October 2018 in response to this growing issue.[6] Unlike respiratory infections, UTIs are caused by bacteria, and therefore, antibiotic treatment is usually required, especially if the infection is symptomatic. However, unlike the general population, antibiotic treatment is given in pregnancy if bacteria in the urine is detected even if the patient is asymptomatic.

A systematic review of interventions to prevent UTIs in pregnancy has shown that preventative hygiene behaviours are the only evidence-based method associated with a reduced incidence of UTIs.[7] Preventing the infection in the first place is therefore preferable to treatment through avoidance of behaviours associated with increased risk of UTIs, for example wiping from back to front after urination.[8,9] Although UTIs in pregnancy have been linked with risks such as pre-term birth,[10] there are also studies that suggest no such association.[11,12] A study analysing views from an online pregnancy forum shows that women associate UTIs with a high risk of negative outcomes, which might cause them to overlook the risks of AMR.[13] A systematic review about public views of AMR has demonstrated that people might have incorrect scientific knowledge or apathy about AMR.[14] The aim of the current study is to explore views on AMR in relation to UTIs by interviewing women who have experienced a UTI in pregnancy, and the research question is 'how do women view AMR in relation to UTIs in pregnancy?'. The anticipated outcome of the study is to have an impact on the optimization of antibiotics for UTIs in pregnancy through an improved understanding of women's views about AMR.

2 | METHOD

2.1 | Design and procedure

This study used a qualitative design and consisted of 15 semi-structured telephone interviews with women who had experienced a UTI in pregnancy. The inclusion criteria were women who were over 18 years old, resident in the UK and had experienced a UTI during pregnancy. The interviews mostly took place 2 years after the pregnancy where they experienced the UTI (the mode value for this data set was 2 years). All participants except one (participant four) took antibiotics for the treatment of the UTI. Participant four employed behavioural measures, such as drinking plenty of water, to resolve the UTI. The demographic characteristics of the participants can be seen in Table 1. Purposive sampling was used to recruit participants through advertisement of the study in online pregnancy forums (www.mumsnet.com and www.netmums.com) and social media (Twitter and Facebook posts). Interviews were conducted between July 2018 and January 2019. Most participants were recruited by advertising the study through the National Childbirth Trust social media account.

The participant information sheet and consent form were emailed to women who expressed an interest in participating in the study. Participants were encouraged to read the participant information sheet and contact the researchers if they had any questions or concerns. The telephone interview date and time was arranged once the participants had returned the signed consent form. Interviews were conducted by the lead researcher about women's beliefs on

TABLE 1 Participant demographics

Participant number	Age (years)	Ethnicity	Education	Employment
P1	31	White	Degree	Full time
P2	18	White	GCSE	Not working
P3	31	White	Degree	Full time
P4	33	Other	Degree	Full time
P5	32	White	Degree	Full time
P6	35	White	Degree	Full time
P7	32	White	Degree	Not working
P8	38	White	Degree	Full time
P9	43	White	Degree	Part time
P10	31	White	Degree	Part time
P11	29	White	Degree	Not working
P12	43	White	A level	Full time
P13	27	White	A level	Not working
P14	31	White	Degree	Not working
P15	31	White	GCSE	Full time

prevention strategies for UTIs and antimicrobial resistance. The interview schedule included the following open questions:

- How was your experience of getting a UTI during pregnancy?
- How do you think UTIs impact pregnancy?
- What do you think about using antibiotics to treat UTIs during pregnancy?
- What do you think about antimicrobial resistance?
- What do you think about using alternatives to antibiotics to treat or prevent UTIs in pregnancy?

The interviews were recorded using an audio recorder to aid transcription. Interview recordings were transcribed verbatim for analysis by the lead researcher, and an honorary research assistant with all transcriptions double-checked for accuracy. The average length of the interviews was 24.3 mins (SD ± 4.2) ranging from 18 to 29 minutes. Participants were gifted a £10 Amazon voucher at the end of the interview to thank them for their participation.

2.2 | Data analysis

Data collection and analysis occurred concurrently to recognize saturation of themes and to guide when recruitment should be stopped. The data were organized into codes using NVivo 11© and analysed using inductive thematic analysis.[15] Thematic analysis is a flexible qualitative method and was chosen to allow the identification, analysis and interpretation of patterns in the data. Interview transcripts were read multiple times by the lead researcher to become familiar with the data and form detailed codes. The codes were further developed into themes by careful reflection of the patterns recognized in the data. Themes were reviewed, discussed and approved by all the authors.

2.3 | Ethical approval

Participants were asked about their illness experience, so it was anticipated that there may be a risk of emotional distress. An information sheet was provided prior to the interview to notify participants of the topics that would be covered. They were also advised at the start of the interview that they were free to not answer any question if they were uncomfortable and could withdraw at any point during the interview. Documented consent was obtained from the participants prior to the interview. The study was reviewed and granted ethical approval by University of [Anonymised] Research and Ethics Committee (Ref. 17/30).

3 | RESULTS

Inductive thematic analysis of the interviews with women who had experienced a UTI in pregnancy yielded two main themes: how women conceptualize AMR and how pregnancy causes a deviation from the norm in terms of antibiotic use. Transcending these themes was an overarching theme of self-efficacy. The two themes highlight women's self-efficacy in terms of what can be done in response to AMR and how they can manage their health with regards to UTIs. Quotes from the data have been used to illustrate the themes with a reference number indicating the order of participation (P1 = participant no. 1) and the trimester of pregnancy in which they experienced the infection.

3.1 | Theme 1: Conceptualization of antimicrobial resistance (AMR)

Participants demonstrated a mixed understanding about AMR. Misconceptions that have already been identified through previous studies were also expressed by some women in this study. For example, several women thought that continual exposure to antibiotics makes the body resistant as opposed to the bacteria developing resistance and they indicated uncertainty in terms of how resistance is transferable. Some women, however, were aware that resistance is a characteristic of bacteria.

> *I am aware that if you overuse them [antibiotics], then they [antibiotics] will eventually stop, the body will stop working with them.*
>
> *(P15, 2nd trimester)*

> *Well I assumed that it was an individual that built up resistance because they were given a lot of antibiotics and that eventually it stops working on that person. I'm not sure how it works if you've never taken antibiotics and then you need them.*
>
> *(P1, 1st trimester)*

> *The drugs used to treat infections are becoming less effective because uhm, I mean, I am not a scientist, so I am probably not describing this properly, but the microbes within the infection are developing ways of overcoming the treatment.*
>
> *(P7, 3rd trimester)*

Despite some misconceptions, all the participants except one were aware of AMR and recognized it as a health threat because of overuse of antibiotics. They were aware that AMR meant that antibiotics might not be effective against infections; however, most of the participants spoke about AMR as a distant phenomenon, as something that might happen 'in the future' as opposed to a current problem.

> *I think I've heard in the media that they've been overprescribed in the past and – and, we might end up at*

a point where some of us are resistant to uh, like, they won't help us.

(P11, 1st trimester)

The most common solution cited by participants, in response to AMR, was to increase the public's understanding of the phenomenon. One participant mentioned the need for better diagnostics to optimize the use of antibiotics (P3), and two participants (P4 and P14) mentioned prevention as the primary way to avoid antibiotic use and tackle AMR.

I know it doesn't quite exist yet but sort of a definitive test to say, yes this is definitely a bacterial infection, yes we need antibiotics, and then later on down the line something to even tell you the best type of antibiotics so that you don't end up taking one course of antibiotic that your bug is resistant to and then needing a second course of another one.

(P3, 2nd trimester)

I think we have to solve the problem in a more natural way for instance through increasing our immune system so this would be much more beneficial for future as well.

(P4, 2nd trimester)

In summary, participants were aware of AMR but conceptualized it as a distant health threat. There was uncertainty about how people become infected with resistant bacteria even when they may not have used antibiotics themselves. Most participants were unsure about potential solutions but recognized a need for public awareness and suggested improved diagnostics and a focus on infection prevention to optimize antibiotic use.

3.2 | Theme 2: Pregnancy as a deviation from the norm

Participants highlighted their pregnancy as an exceptional state, compared to the general population, when referring to their use of antibiotics because of the risks of UTIs. Most described themselves as 'someone who does not like taking antibiotics' but felt it was the safest option and this was also the view communicated to them by health-care professionals.

I don't like taking antibiotics anyway, I don't – I'm not someone who takes antibiotics.

(P10, 2nd trimester)

Um, I – I think this is where she [pharmacist] just said, if – you know, if the infection goes from your urinary tract into the womb that it, it could be very very serious, that it could – the thing that was the trigger, was she [pharmacist] said you know, it could go wrong very quickly.

(P9, 1st trimester)

The reluctance to use antibiotics ranged from concern about side-effects to an awareness about AMR, and many women expressed an interest in alternative therapies, such as probiotics. However, they recognized that antibiotics were the only effective treatment currently available and any new treatment would still be a concern due to unknown teratogenic risks.

It's a very good idea, anything that reduces the need for antibiotics. It depends what they are in some respects so if you're talking about probiotics or food supplements or something like that, that's one thing, but if it's a novel drug then you're always concerned about new drugs in pregnancy.

(P3, 2nd trimester)

Most women were also aware of preventative hygiene behaviours but did not consider them effective.

Um well, you know, normal hygiene that everyone knows. Sort of wiping from front to back and general cleanliness – although I mean I suppose that doesn't make much difference.

(P12, 3rd trimester)

Thus, although participants described a preference for avoiding antibiotics, they felt they did not have a choice because of the unacceptable risks of UTIs in pregnancy. Pregnancy was interpreted as a deviation from the norm, where an unsparing use of antibiotics was required and justified. Furthermore, hygiene behaviours, such as the direction of wiping the genitals, were considered to have little impact on prevention of UTIs.

3.3 | Overarching theme: Self-efficacy

Salient across both themes was an overarching theme that highlighted women's perceptions of self-efficacy in terms of how AMR could be tackled and how they could manage their health in pregnancy. Self-efficacy, as defined by Bandura,[16] is 'the belief in one's capabilities to organize and execute the sources of action required to manage prospective solutions'.

The first theme showed that most participants described conflict regarding how AMR could be tackled because although antibiotics cause problems, they 'also save lives' (P8) which causes a dilemma around how they can be used appropriately. Women also referred to conflicting messages about which behaviours they should adopt, particularly in response to finishing a course of antibiotics.

You get the odd media report saying that, you know, you shouldn't finish the course and your doctor's telling you to finish the course, so I think there is a lot of misinformation about resistance.

(P3, 2nd trimester)

As a result, participants were unsure about how they could respond to AMR on an individual level and assigned the accountability for addressing the issue to health-care professionals.

I would say there is a bit of an issue with GPs over prescribing antibiotics and there needs to be more awareness at the health-care professional level.

(P7, 3rd trimester)

The second theme described women's views about UTIs and showed that most participants perceived UTIs as a result of reduced immunity in pregnancy. They viewed the cause of the illness as outside their control and attributed pregnancy rather than individual behaviour to causing the infection.

I guess your immune system is slightly weakened isn't it, umm, so you are more susceptible….

(P12, 3rd trimester)

You're so susceptible when you're pregnant because your immune system seems to be so uhm… compromised when you're pregnant.

(P1, 1st trimester)

Conflicting messages caused uncertainty and undermined women's confidence about what difference they could make thus resulting in low self-efficacy in relation to tackling AMR. Similarly, perceptions of UTIs, where the role of behaviour was undermined, reduced women's self-efficacy in managing their health through preventative hygiene behaviours. In summary, participants had low self-efficacy with regard to managing personal and societal health.

4 | DISCUSSION

This study qualitatively explored views on AMR in women who had experienced a UTI in pregnancy. The first theme demonstrates that participants were aware that antibiotics are overused at a population level, which can reduce their effectiveness and cause a health risk. However, misconceptions described by previous research,[17-19] such as the body becoming resistant at an individual level, were still prevalent. The results revealed uncertainty due to conflicting messages from their doctor and the media regarding when and how antibiotics should be used. There was also greater understanding of AMR affecting the individual taking antibiotics in comparison with all sectors of society. Consequently, consistent with the findings of Hawkings et al,[20] results from this research highlight that people prefer to delegate the responsibility of tackling AMR to health-care professionals. A survey about public views of AMR by Carter et al[21] reported that people did not consider AMR to be an important issue; however, in contrast, results from this study show that women were concerned about AMR but reported low self-efficacy rather than apathy about the problem.

The second theme describes perceptions of pregnancy as a unique physiological state in which immunity is reduced and preventative behaviours have little impact. High perceived susceptibility during pregnancy was thought to result in an increased incidence of UTIs. At the same time, the severity of UTIs was also perceived to be greater compared to when not pregnant. Ogden et al[22,23] described a model where causes and solutions to illness are attributed to external and/or internal factors. The model highlights a coherence between the causes and solutions of illness whereby people expect illnesses to be resolved through external sources, such as medicines, if they believe the cause of the illness is external. The perceptions of women in this study were reflected in the biomedical model[24] in which the cause of disease is attributed to medical or biological factors that were not necessarily under the control of the individual. The biomedical model therefore focuses on external interventions such as medicines sought for resolution of illness. Women's perceptions reflected this model and were combined with heightened perceived susceptibility and severity of UTIs. They also held medical advice in high esteem and therefore, to minimize any risks to their baby, reported an automatic reliance on antibiotics with reduced self-efficacy in managing their own health. The dependence on antibiotics overrode behaviours, such as drinking adequate water, which could prevent illness and assist with symptom resolution in the case of an active infection. Overall, women considered antibiotics to be acceptable because they perceived pregnancy to be associated with high susceptibility and severity of UTIs. Future work could explore whether this positive perception of antibiotics also exists in relation to other infectious conditions that might occur in pregnancy.

The overarching theme present in the two main themes, conceptualization of AMR and pregnancy as a deviation from the norm, is self-efficacy. Bandura's Social Cognition Theory[25] about behaviour change outlines key factors that influence behaviour. Perceived self-efficacy and outcome expectancies are two major constructs of the Social Cognition Theory. Self-efficacy relates to an individual's sense of agency about a behaviour while outcome expectancies relate to beliefs about the consequences of the behaviour. Luszczynska and Schwarzer[26] reviewed the Social Cognition Theory in the context of health behaviours and described how both these constructs can work in synchrony, which is seen in the present study. Women's outcome expectancy for preventative behaviours, such as drinking adequate water or the direction of wiping the genitals, was that they were ineffective. This outcome expectancy subsequently linked to low self-efficacy in terms of managing their own health in pregnancy and avoiding antibiotics to conserve them for the communal good.

With regard to public health, the results from this study have implications for how antibiotics are viewed and utilized by the public, particularly in pregnancy. There is a need to re-conceptualize AMR as a current, as opposed to a future, problem affecting society rather than just individuals, which requires action by both the public and health-care professionals. This study proposes that this can be achieved by enhancing people's self-efficacy through consistent messages about behaviours that are helpful to manage and reverse the risks of AMR. Bandura[27] has described sources of information (mastery experiences, vicarious experiences, verbal persuasion, and physiological and affective states) that enhance self-efficacy. Future research on health behaviours linked with AMR may find it useful to explore the role of these sources in enhancing self-efficacy for behaviour change. A consolidated approach, where infection prevention is prioritized and where people are empowered, is also endorsed by the World Health Organization (WHO).[28] The WHO global action plan on antimicrobial resistance emphasizes that the response to AMR needs to be through a focus on infection prevention, along with engagement and empowerment of health-care professionals and the public, across all sectors of society. Specifically, in pregnancy, there is scope for health-care professionals to develop women's perceptions of self-efficacy by highlighting preventative behaviours and linking them as a means of minimizing antibiotics for UTIs in response to AMR. This shift from a biomedical model to a behavioural model could lead to better and sustained health outcomes.[29]

The study provides unique insight into perceptions of AMR by focusing on women with personal experience of UTIs in pregnancy. Conducting an interview study had the advantage of exploring the issue in-depth by asking participants to expand or clarify their views through conversation. One of the main limitations of the study was that it focused on a small subset of the population using purposive sampling, which reduces generalizability. As the sample consisted predominantly of women who were White British, the views in this study may not be representative of women whose demographics differ significantly from the participants and need to be interpreted within this context. Future work will focus on exploring the views of health-care professionals to provide a comprehensive understanding of AMR and UTIs in pregnancy.

5 | CONCLUSION

In conclusion, women recognize the risks of AMR but demonstrated low self-efficacy and perceived control of UTIs in pregnancy. There is a need to re-conceptualize AMR and provide a consistent message to avoid uncertainties. Women might require reassurance specifically in pregnancy to feel confident about their ability to manage their own health with an emphasis on behaviours that can prevent UTIs to reduce the need for antibiotics.

ACKNOWLEDGEMENTS

We would like to thank all the participants for contributing their views and the National Childbirth Trust, www.mumsnet.com and www.netmums.com for their support in advertising the study. Thank you to Marcus Calway, an honorary research assistant, for his assistance with transcribing the interview recordings.

CONFLICT OF INTEREST

There are no conflicting interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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How to cite this article: Ghouri F, Hollywood A, Ryan K. 'There is no choice apart from antibiotics…': Qualitative analysis of views on urinary infections in pregnancy and antimicrobial resistance. *Health Expect*. 2020;00:1–7. https://doi.org/10.1111/hex.13044

CHAPTER SIX

6. Antibiotic Prescribing in Primary Care for Urinary Tract Infections (UTIs) in Pregnancy: An Audit Study

Chapter six presents the publication:

Ghouri, F., & Hollywood, A. (2020). Antibiotic Prescribing in Primary Care for Urinary Tract Infections (UTIs) in Pregnancy: An Audit Study. *Medical Sciences*, *8*(3), 40. https://doi.org/10.3390/medsci8030040

6.1. Introduction

The publication presented in this chapter focuses on the prescribing of antibiotics for UTIs in pregnancy. The audit study was designed to explore the current prescribing practice for UTIs and assess whether it met the recommendations of the antimicrobial guidelines published by the National Institute of Health and Care Excellence (NICE).

Antimicrobial guidelines are developed based on the best available evidence and facilitate antimicrobial stewardship efforts by providing recommendations on appropriate treatment options. The majority of antibiotic prescribing occurs in primary care and women who experience symptoms of a UTI consult their GP practice as the first point of medical help. Therefore, the audit was conducted in a primary care setting, using data from three GP surgeries. The rationale for conducting the audit was to assess the appropriateness of the prescriptions against the NICE guidelines and identify areas of improvement which could be used as feedback for prescribers to inform change in prescribing behaviour. As well as this, the results from the audit were used to develop a semi-structured interview schedule which was used in the next study, following the audit, which explored the perspectives of prescribers' with regards to AMR and antibiotic use during pregnancy.

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MDPI

Article

Antibiotic Prescribing in Primary Care for Urinary Tract Infections (UTIs) in Pregnancy: An Audit Study

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Received: 21 July 2020; Accepted: 10 September 2020; Published: 17 September 2020

Abstract: Urinary tract infections (UTIs) are associated with negative pregnancy outcomes and are treated with antibiotics. Although beneficial, antibiotic use causes antimicrobial resistance (AMR), and therefore their use needs to be carefully balanced. Antimicrobial guidelines are developed to facilitate appropriate prescribing of antibiotics. This study assessed antibiotic prescribing for UTIs in pregnancy against the National Institute for Health and Care Excellence (NICE) guideline NG109. Fifty antibiotic prescribing records dated from 1st October 2018 to 1st July 2019 were identified from three London-based GP practices. The results show that a mid-stream sample of urine, which is important for the review and tailoring of antibiotic treatment, was collected in 77.6% of cases. Prescribing the first-line antibiotic is important for adequate treatment and good antimicrobial stewardship and results show that 44% of prescriptions were for the first-choice antibiotic. Most prescriptions (56%) were for a second-line or non-recommended antibiotic. Providing self-care advice is key to empowering pregnant women in managing their own health but only 16% of records documented provision of self-care advice. This study highlights important areas of concern in the management of UTIs in pregnancy. However, due to the retrospective design, future work is needed to evaluate the role of AMR in the prescriber's treatment decision-making process.

Keywords: antibiotic prescribing; urinary tract infection; pregnancy; audit

1. Introduction

Urinary tract infections (UTIs) are caused by bacteria that colonise and infect the urinary tract. The infection commonly causes symptoms such as increased frequency of urination and burning pain when passing urine [1]. More severe symptoms can include nausea, vomiting, chills and a high fever [2]. Bacteria that cause a UTI are usually commensal within the body and normally transfer to the urinary tract from the gut [3]. UTIs are more common in women than in men, due to physiological differences, and estimates in the literature suggest that approximately 50% of women experience at least one episode of a UTI during their lifetime [4]. A shorter urethra in women makes it easier for bacteria from the gut to pass into the urinary tract and cause an infection. UTIs are classified as asymptomatic bacteriuria (presence of bacteria in the urine without symptoms), acute cystitis (affecting the bladder) or pyelonephritis (affecting the kidneys) [5].

UTIs are caused by bacteria and therefore antibiotic treatment is usually required to eradicate the infection. Asymptomatic infections in non-pregnant adults should not be medically treated, unless they are undergoing genitourinary surgery, whereas treatment of symptomatic UTIs consists of taking a short course of an antibiotic [6] such as nitrofurantoin or trimethoprim. In pregnancy, however, both symptomatic and asymptomatic UTIs are linked with adverse outcomes such as pyelonephritis. UTIs in pregnancy have also been associated with risks such as foetal growth retardation and pre-term birth [7,8]. They are the most common type of infection affecting pregnant women, with asymptomatic infections alone estimated to affect between 2 and 12% of pregnant women [9].

Clinical vigilance is therefore exercised in pregnancy through routine screening for bacteriuria at early antenatal appointments to detect and treat both symptomatic and asymptomatic UTIs with antibiotics [10,11]. The prescribed duration of the antibiotic course is also longer in pregnancy compared with non-pregnant women to ensure adequate eradication of the infection.

While antibiotics are highly effective at treating UTIs, they are also associated with antimicrobial resistance (AMR), which is a global health threat. AMR is the term used to describe the evolution of microorganisms to develop characteristics that make them resistant to antimicrobial treatment [12]. Antibiotic prescribing and consumption are directly associated with a rise in bacterial resistance and the development of antibiotic resistant infections [13]. Resistant infections can be difficult to treat and are associated with significant morbidity and mortality [14]. There is evidence to suggest that antibiotics to treat UTIs are overused in pregnant women [15,16], which can cause a rise in resistant UTIs. Resistant UTIs can be particularly concerning in pregnancy [17] because although they can be a challenge to treat in general, ensuring the combined safety of the woman and foetus adds further difficulty in pregnancy. Considering this, it is necessary to monitor the use of antibiotics in pregnancy to optimise prescribing and consumption of these valuable medicines and facilitate antimicrobial stewardship in antenatal care.

Primary care antibiotic prescribing during pregnancy has been studied in the UK and shows that UTIs accounted for the highest proportion of antibiotics in pregnant women [18]. The National Institute for Health and Care Excellence (NICE) published antimicrobial prescribing guidelines which recommend evidence-based treatment for infections to promote the judicious use of antibiotics. The present study was conducted to identify and assess the appropriateness of antibiotic prescribing for UTIs in pregnancy in line with the NICE antimicrobial prescribing guidelines for lower UTI [19]. The aim of the study was to assess the prescribing of antibiotics for UTIs in pregnant women.

2. Materials and Methods

The GP practices that were included in this study are part of a group in London that provide primary care services in the community. Three practices from this group were sufficient to achieve the required sample size. Collectively, the three practices have a total of 16 GPs, a team of pharmacy professionals and approximately 35,000 registered patients [20] from a range of ethnic backgrounds. The surgeries provide services that are typically representative of other practices in the area. The Chief Pharmacist, who is the Clinical Director at the health group, approved the study and permitted the researchers to access the premises and retrieve patient data. An ethics application was also submitted prior to conducting the study and was reviewed by the University of Reading School of Chemistry, Food and Pharmacy Ethics Committee and was given favourable ethical opinion for conduct (Study 12/19). The study used consecutive sampling to identify records of women who had been prescribed antibiotics while they were pregnant. The inclusion criteria were women who were pregnant and had been prescribed an antibiotic indicated for a UTI. A sample size of 50 sequential patient records was set as the target sample size; the rationale for this is that it is in line with a similar audit conducted previously [15]. Medical notes were assessed to collect data on antibiotic prescribing, and determine the appropriateness of the prescriptions according to the audit standards which were adapted from the NICE antimicrobial guidelines for lower UTI [19]. The standards are as follows:

1. A midstream urine sample (MSSU) is obtained and sent for culture before antibiotics are taken.
2. The choice of antibiotic prescribed is reviewed based on culture results and changed as appropriate to a narrow spectrum antibiotic.
    a. First choice antibiotic: nitrofurantoin 100 mg modified release twice a day (or 50 mg four times a day) for 7 days.
    b. If no improvement within 48 h or if first line is unsuitable: Second choice: Amoxicillin 500 mg three times a day for 7 days or cefalexin 500 mg twice a day for 7 days.
3. Provision of self-care advice on managing pain and maintaining adequate hydration.

A data collection tool was designed to collect demographic, clinical and treatment data from the medical notes. Table 1 summarises the key information that was collected using the data collection tool.

Table 1. Data collection tool.

Demographic Data			Clinical Data			Treatment Data			
Age	Ethnicity	Trimester	Allergy	Symptoms	MSSU (Y/N)	AntibioticDose	Duration	Self-care advice	Review (Y/N)

FG was given an induction of the SystmOne© GP prescribing software and trained on accessing patient medical notes prior to data collection. A search was conducted to retrieve medical notes of pregnant women using the read code for 'pregnancy', which was then combined with a search for antibiotics that are normally used for UTIs in the UK, regardless of pregnancy status. These antibiotics include nitrofurantoin, amoxicillin, cefalexin, which are recommended for UTIs in pregnancy, and trimethoprim, co-amoxiclav, fosfomycin and pivmecillinam, which are not recommended but can be used to treat UTIs in non-pregnant cases. Data were collected in July 2019 and the search criteria were limited between the dates of 1st October 2018 to 1st July 2019 to correspond with the publication of the NICE guidelines. The medical notes were examined to confirm that the antibiotics were for the treatment of a UTI during pregnancy. The medical notes were also used to establish the appropriateness of deviating from the guidelines' recommendation, e.g., the medical notes were consulted when a second line antibiotic was prescribed to determine whether it was because of contraindications to the first-line choice. Information from the medical notes was then documented on the data collection tool. Each of the 50 individual records were assigned a number to prevent identification and protect the anonymity of patients. The results were collated on Microsoft Excel® and are presented using descriptive statistics which summarises the proportion of prescriptions that met each standard as a percentage.

3. Results

The target sample size for the study was to assess fifty patients' records, which was achieved through consecutive sampling of data from the three GP practices. The records were reviewed, and information was recorded using the data collection form. The mean age of the women was 31.1 years (±4.3) and there was a range of ethnicities attending the practices, as seen in Table 2.

Table 2. Distribution according to ethnicity.

Ethnicity	Number of Records (n = 50)	Percentage (%)
White	21	42.0
Black	9	18.0
South Asian	7	14.0
Mixed	7	14.0
Other	6	12.0

3.1. Standard 1: A Midstream Urine Sample (MSSU) Was Obtained and Sent for Culture before Antibiotics Are Taken

A mid-stream urine sample (MSSU) was collected before antibiotics were prescribed in 38/49 (77.6%) of cases. An MSSU was not collected in 11/49 (22.4%) of instances and documentation was unclear in 1/50 (0.02%) prescriptions.

3.2. Standard 2: The Choice of Antibiotic Prescribed Was Reviewed Based on Culture Results and Changed as Appropriate to a Narrow Spectrum Antibiotic

- First choice antibiotic: nitrofurantoin 100 mg modified release twice a day (or 50 mg four times a day) for 7 days.

- If no improvement within 48 h or if first line was unsuitable:
    - Second choice: Amoxicillin 500 mg three times a day for 7 days or cefalexin 500 mg twice a day for 7 days.

Nitrofurantoin is the first choice of antibiotic according to the NICE guidelines unless there is a known contraindication to it—for example, the woman is in the third trimester of pregnancy or is allergic to nitrofurantoin. Nitrofurantoin was prescribed in 19/50 (38.0%) cases. Amoxicillin and cefalexin are the second-choice antibiotics which should be used if nitrofurantoin is contraindicated. These two antibiotics were prescribed in 27/50 (54.0%) of cases. Assessment of the medical notes and culture results revealed that 3/27 (11.1%) were prescribed amoxicillin or cefalexin because nitrofurantoin was contraindicated, therefore these were deemed as appropriate and meeting the guidelines. Trimethoprim and co-amoxiclav were two antibiotics which are not recommended for UTIs in pregnancy but were prescribed in 4/50 (8.0%) of cases. Therefore, the overall proportion of prescriptions that met the guidelines in terms of the first choice for empirical antibiotic therapy was 22/50 (44.0%). The proportion of prescriptions which are included in the guidelines for UTI treatment but are not the recommended as first choice was 24/50 (48.0%). The proportion of prescriptions which did not meet the guidelines completely was 4/50 (8.0%). The antibiotics prescribed according to the trimester of pregnancy can be seen in Table 3.

Table 3. Antibiotic prescribing according to trimester of pregnancy.

Antibiotic	Number of Prescriptions in each Pregnancy Trimester		
	First	Second	Third
Nitrofurantoin	10	9	-
Amoxicillin	4	9	3
Cefalexin	2	6	3
Trimethoprim	1	-	-
Co-amoxiclav	1	2	-

The dose and frequency of the antibiotic were according to the guidelines in 38/46 (82.6%) of prescriptions whereas 8/46 (17.4%) were prescribed a dose that did not meet the guidelines, as shown in Table 4.

Table 4. Proportion of antibiotic doses according to guideline.

Antibiotic	Dose		
	Optimum	High	Low
Nitrofurantoin	19	-	-
Amoxicillin	15	-	1
Cefalexin	4	5	2

The NICE guidelines recommend a seven-day course of antibiotics in pregnancy and 32/50 (64.0%) complied with this recommendation whereas 18/50 (36.0%) had a shorter duration (3 or 5 days) prescribed. Overall, 25/50 (50%) of antibiotic prescriptions did not meet the NICE guidelines either in terms of the choice of antibiotic and/or the dose or treatment duration that was prescribed.

3.3. Standard 3: Provision of Self-Care Advice on Managing Pain and Maintaining Adequate Hydration

This standard was considered to have been met if the medical notes mentioned provision of any advice on analgesics and/or emphasized maintaining adequate hydration. Self-care advice was provided in 8/50 (16.0%) occasions, but there was no documentation for the provision of self-care advice in the medical notes for 42/50 (84.0%) records.

3.4. Additional Clinical Data

Clinical data on the allergy status, whether the UTI was symptomatic or asymptomatic and the trimester of pregnancy were also collected. There were 5/50 (10.0%) instances where women were allergic to antibiotics, which included beta lactams and trimethoprim. Symptomatic infections accounted for 38/50 (76.0%) of UTIs treated, whereas asymptomatic infections occurred in 7/50 (14.0%) cases. The type of infection was not documented in 4/50 (8.0%) of cases. Due to screening for asymptomatic bacteriuria in the first trimester [21], it was expected that the overall incidence of UTIs would be highest in this period. However, the largest incidence of UTIs seen in this study was in the second trimester 21/50 (42.0%) followed by the first 18/50 (36.0%) and the third 11/50 (22.0%) trimesters.

4. Discussion

The study assessed 50 antibiotic prescriptions for UTIs in women who were pregnant. The women were from a range of ethnic backgrounds and at various stages of pregnancy in terms of trimesters. The following discussion highlights important criteria where the prescribing of antibiotics for UTIs in pregnancy did not meet the NICE antimicrobial guidelines for lower UTIs and the potential implications of deviating from recommended practice. These criteria correspond to the audit standards and include the collection of a MSSU, the choice of empirical antibiotic, the duration of the course and the provision of self-care advice.

The NICE guideline recommends the collection of a MSSU sample to test the susceptibility of the causative bacteria prior to the use of antibiotics. Culturing a MSSU sample is important as it can not only confirm the diagnosis of a UTI but also allows for the review and tailoring of the treatment by ensuring that the prescribed antibiotic is effective based on the antibiotic sensitivity of the causative organism [22]. Empirically prescribed antibiotics should be reviewed after the culture results are returned, which is typically within 48 h. Although an MSSU was obtained in the majority of cases, 22.4% of women were prescribed antibiotics without obtaining a urine sample, without a justifiable reason. Without a culture result, prescribers cannot review the choice of antibiotic prescribed which can lead to unnecessary and prolonged use of multiple antibiotics along with undermining antimicrobial stewardships efforts in primary care.

Nitrofurantoin is the first-choice antibiotic recommended by NICE as well as the European Association of Urology [23]. It is the first choice for treatment of UTIs based on evidence of its effectiveness [24] and because it has one of the lowest rates for resistance of E. coli [19], which is the most common uropathogen causing UTIs [11]. It is, however, contraindicated in pregnancy if the woman is at term, in the third trimester, because of the risk of neonatal haemolysis. It should also be avoided if renal function is impaired or if there is a known allergy or intolerance to it [25,26]. The second-choice antibiotic prescriptions recommended by NICE are amoxicillin and cefalexin. Both of these antibiotics are broad-spectrum with amoxicillin belonging to the aminopenicillin class, which has high rates of *E. coli* resistance globally [27]. Due to antimicrobial resistance, these antibiotics are not preferred as a first-line option but instead are used if symptoms do not improve after using the first-choice antibiotic for a minimum of 48 h or if the first choice cannot be used because of contraindications. The results show that amoxicillin and cefalexin were often prescribed as the empirical first choice despite the patient being suitable for nitrofurantoin. While clinically this may lead to the intended outcome of clearing the infection, it is not best practice when considering the broader problem of AMR. The medical notes indicate that a possible explanation for the preference of amoxicillin or cefalexin might be due to their perceived safety in pregnancy compared with nitrofurantoin, but this needs to be confirmed and addressed through future work.

The most concerning antibiotic prescriptions identified in this study were trimethoprim and co-amoxiclav. These are problematic because trimethoprim is a folate antagonist and unsafe in pregnancy, and short courses of co-amoxiclav have low effectiveness for treating UTIs [28]. The high proportion of second-line and non-recommended antibiotic prescribing is an important finding because they do not represent the optimal choice in terms of antimicrobial stewardship or antibiotic safety

in pregnancy. This result highlights that the choice of antibiotic is an important area where a change in prescribing requires a review. It is therefore recommended that a review of prescribers' perceptions of antimicrobial safety in pregnancy is conducted to elucidate their views to justify and inform future interventions.

The duration of antibiotic treatment in pregnancy is recommended to be seven days compared with three days in non-pregnant women. The results show that the course length was not long enough for 36% of prescribed antibiotics. There is no concrete evidence to suggest that a seven day course of antibiotics is essential [29,30] and the advice for patients to complete an antibiotic course has also been questioned [31]. However, traditionally it has been thought that shortening courses may not provide complete eradication of the infection. Therefore, unless new evidence emerges through randomised clinical trials, it is important that the course length of antibiotics is in line with the recommended seven days for adequate treatment.

Provision of self-care advice is a criterion where there was very low compliance with NICE guidelines. Comprehensive self-care advice includes several hygiene behaviours such as drinking adequate water, avoiding delay to use the toilet and wiping the genital area from front to back. However, in this study, self-care measures incorporated advice on suitable painkillers and emphasis on maintaining adequate hydration. Previous research shows that women require and value advice given by their GP for pain management in cystitis [32]. The result from this study shows that self-care advice was only reported in 16% of consultations. The importance of self-care advice lies not only in the empowerment of patients to manage their own condition but also in the protective role that preventative behaviours, such as drinking water, can provide. Preventative behaviours are associated with a reduced incidence of UTIs in pregnancy [33], and are therefore key in minimising reliance on antibiotics. Therefore, it is recommended that healthcare professionals emphasise these in consultations with women. An evidence-based intervention leaflet that encourages shared decision-making and self-care for uncomplicated UTIs has been developed [34]. It has also been endorsed by NICE [35] and contains helpful material that could be used in consultations with pregnant women to encourage preventative behaviours.

4.1. Future Work

Studies exploring the perceptions of women who experienced UTIs in pregnancy have shown that they were concerned but uncertain on how to tackle antimicrobial resistance [36,37]. One of the studies also showed that while women like to be informed and make decisions for their health, they trust and place high importance on the opinion of the healthcare professional involved in their care [36]. The authors have used the insights gained from this audit to design a research study to explore prescribers' decision-making practice for prescribing antibiotics to pregnant women. The barriers and facilitators to prescribing antibiotics according to guidelines will be identified to optimise the use of antibiotics in this population. The prescribing deviation from the guidelines seen in the results of this study is also valuable feedback for the prescribers. A pre and post analysis of prescribing patterns, once feedback is disseminated to the prescribers, is therefore also recommended for future work. In addition, future studies could also use a full year of data to mitigate monthly variation in prescribing patterns. This study also highlights the known gap in evidence for the optimal duration of antibiotic courses in pregnancy. Randomised controlled trials investigating shorter courses need to be conducted to provide evidence for effectiveness and safety as a step towards reducing antibiotics and promoting antimicrobial stewardship in antenatal care. At the same time, it is also important that patient safety is not compromised and therefore it is recommended that future work should investigate factors that prevent or delay antibiotic prescribing for UTIs in pregnant women.

4.2. Limitations of the Study

The data were collected retrospectively by searching through patient records and using consecutive sampling to identify women who had been prescribed antibiotics in pregnancy. Although the search

was conducted in consultation with an experienced user of the GP prescribing software, it is possible that some records were missed due to the way patients' details are recorded and read codes assigned in the system. Inconsistency between the provision and documentation of self-care advice has been noted in previous research [38], and was also seen in this study, as it relied on prescribers documenting the provision of self-care advice in the medical records. Therefore, the results may not completely reflect the care that is provided during the consultation. The study was conducted to assess antimicrobial prescribing for UTIs in pregnancy. It used data from three London-based GP practices and had a small sample size, and therefore it may not be representative of the patient and healthcare professional demographic and prescribing practice in other regions of the world. A larger sample size is recommended in the future to improve the design and lead to a better powered study. This study, however, highlights important issues for antimicrobial prescribing in pregnant women which would be relevant to healthcare professionals involved in antenatal care and interested in safeguarding appropriate antibiotic use.

5. Conclusions

The purpose of the study was to assess the appropriateness of primary care antimicrobial prescribing for UTIs in pregnancy. The results of the study highlight two important areas of concern. Firstly, the results show that the choice of first-line antibiotic is not optimal and second-line or non-recommended antibiotics are frequently prescribed to women. Secondly, self-care advice may need to be emphasised to women who are experiencing UTI symptoms during pregnancy. In conclusion, further work is required to review antibiotic use for UTIs in pregnancy and the provision of self-care advice, to facilitate a consolidated effort to optimise antibiotic use in response to the global threat of AMR.

Author Contributions: Both authors participated in the intellectual content, conception, design and writing of the manuscript. Conceptualization, F.G. and A.H.; methodology, F.G. and A.H.; formal analysis F.G.; writing—original draft preparation, F.G.; writing—review and editing, A.H.; supervision, A.H.; All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the University of Reading as a PhD studentship for F.G.

Acknowledgments: The authors would like to thank Graham Stretch for his assistance with accessing and identifying the relevant data for this study.

Conflicts of Interest: The authors declare no conflict of interest. The funder had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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CHAPTER SEVEN

7. Exploring antimicrobial prescribing for urinary tract infections in pregnancy – a qualitative interview study

7.1. Introduction

Chapter seven presents ongoing work that has been conducted to explore prescribers' perspectives with regards to antimicrobial prescribing for UTIs in pregnancy. This study was designed following the previous audit study, to gauge prescribers' perceptions on the issue of antimicrobial resistance and how it impacts their decision making when prescribing antibiotics to pregnant women.

Preceding research presented in this thesis provided insight into women's perceptions whereas this study is being conducted to provide insight into the perceptions of prescribers. In designing this final study, it was anticipated that studying the views of both women and prescribers would provide a comprehensive overview of antibiotic use and prescribing for UTIs in pregnancy. This groundwork could inform the design and conduct of further research interventions that can target perceptions and behaviours relating to antibiotic use to tackle AMR.

The work presented in this chapter is preliminary and subject to further analysis. The chapter begins by introducing the background and aim of the study which is followed by the method and a discussion of the preliminary results. Appendices 9 and 10 show the ethical approvals that were obtained for the conduct of this study. Appendices 11, 12, and 13 consecutively list the participant information sheet, the consent form, and the interview schedule that were used. Appendix 15 lists the COVID-19 statement of impact on this research study.

Exploring antimicrobial prescribing for urinary tract infections in pregnancy – a qualitative interview study

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Abstract

Background: A urinary tract infection (UTI) is the most common infection that occurs during pregnancy. It is treated with a course of antibiotics, however there is evidence to suggest that these are overused, which has implications for antimicrobial resistance (AMR). The aim of this study was to explore healthcare professionals' perspectives of antimicrobial prescribing for UTIs during pregnancy, which could provide insight into ways of minimising antibiotic use.

Design: Semi-structured interviews were conducted with healthcare professionals who work in primary care and have experience of consulting pregnant women. The interview questions explored their decision-making when prescribing antibiotics for the management of UTIs during pregnancy.

Results: The results highlight two themes that demonstrate how the participants viewed and managed UTIs during pregnancy. Fear of causing harm to the mother or baby leads to prescribers exercising a highly cautious approach to antibiotic prescribing and prefer to issue a prescription rather than delay or avoid antibiotic therapy. The cause of UTIs was also attributed to pregnancy and personal behaviours of women were viewed as inconsequential to the development of an infection. This results in little emphasis on self-care and preventative advice during consultations, with antibiotics offered routinely as a convenient solution.

Conclusion: The results have implications for AMR because these perceptions can result in an overuse of antibiotics for UTIs. Adopting a highly cautious approach means prescribers base their decisions on symptoms and women's pregnancy status, preferring to issue prompt antibiotic prescriptions. Routine prescribing of antibiotics without advising on prevention measures can also result in increased demand and reliance on antibiotics instead of changing beliefs and behaviours to avoid infection.

7.2. Background

Urinary tract infections (UTIs) are amongst the most commonly occurring infections in pregnant women. The estimated incidence of asymptomatic UTIs reported in studies from the United Kingdom (UK) range from 2-12% (Meads, 2011). In the UK, the highest proportion of antibiotic prescriptions issued during pregnancy is also for UTIs (Petersen et al., 2010). Untreated UTIs can carry considerable health risks in pregnancy, both for the woman and the foetus. Reported risks associated with UTIs include growth retardation of the foetus, pyelonephritis in the women and pre-term birth (Delzell & Lefevre, 2000). Antibiotic guidelines produced by the National Institute for Health and Care Excellence (NICE) therefore recommends a seven-day course of antibiotics for the treatment of UTIs in pregnancy (NICE NG109, 2018).

Although antibiotics are beneficial to effectively treat UTIs during pregnancy, there is evidence which suggests that they are overprescribed (Mosedale et al., 2013; Sekikubo et al., 2017).

Inappropriate use of antibiotics contributes to the problem of antimicrobial resistance (AMR) which is a global health threat. There is established evidence that resistance in pathogens that cause UTIs is increasing, which is a concern for health (Paul, 2018). The authors conducted an audit to assess the treatment for UTIs during pregnancy in three London based general practitioner (GP) surgeries (Ghouri & Hollywood, 2020). The outcomes of this audit highlighted that amoxicillin, a broad spectrum second line treatment option, was the most frequently prescribed antibiotic instead of nitrofurantoin. Nitrofurantoin is the preferred choice for empirical treatment because reports of resistance to it are low (Squadrito & del Portal, 2020). It is also exclusively used for UTIs, unlike amoxicillin which is used for multiple indications, and therefore is less likely to cause bacterial resistance in uropathogens (Huttner et al., 2015).

Resistant infections can be life threatening without adequate antibiotic treatment and they can be particularly challenging in pregnancy because chosen treatments affect both the woman and the foetus. Antibiotics prescribed during pregnancy need to be safe, without adverse effects on foetal development, in addition to being effective against the infection. Additionally, infections

in neonates due to vertical transmission of resistant pathogens at birth are also a concern associated with antibiotic use during pregnancy (Mercer et al., 1999). It is therefore important that appropriate antibiotic prescribing practices are encouraged and sustained.

A review by Pinder et al (2015) identified several studies exploring prescribers' knowledge and beliefs about AMR. However, no specific study has looked at prescribers' views on antibiotic use, or AMR, in pregnancy. It is important that AMR research is contextualised to identify and resolve specific issues relating to this health problem. Therefore, the current study aims to explore healthcare professionals' perspectives on antimicrobial prescribing for UTIs in pregnancy. This work will be beneficial in developing an in depth understanding of the factors relating to antimicrobial prescribing in pregnancy which can provide useful insight to identify and discourage inappropriate practices.

7.3. Aim and Objectives

The aim of the study was to explore the perspectives of GPs and non-medical prescribers on antimicrobial prescribing for UTIs in pregnancy.

The objectives of the study were to answer the following:

- What influence does antimicrobial resistance have on prescribers' decision-makingprocess when prescribing antibiotics for UTIs in pregnancy?
- What emphasis do prescribers place on behavioural measures to prevent or manageUTIs?

The intended outcomes of the study were to understand the decision-making behind prescribing antibiotics in pregnancy. Additionally, this research could help identify prescribing behaviours that can be targeted through behaviour change interventions.

7.4. Method

7.4.1. Design and procedure

This study was conducted using semi-structured interviews with prescribers who work in primary care and have experience of consulting pregnant women. Purposive sampling was used with the aim to recruit 10-20 participants by contacting GP surgeries in the southern region of England. The sample size for qualitative research depends on several factors such as the methodology and the research question. The proposed sample size for this study is in line with the recommendations for a study employing thematic analysis as there is no fixed sample size for qualitative research (Braun & Clarke, 2006). It was anticipated that the suggested sample size would allow for sufficient data quantity and quality to develop themes. Previous research has highlighted the challenges of recruiting GPs in England to participate in qualitative research (Patel et al., 2017) which has also been experienced in this study. Recruitment for this study has also been negatively impacted by the COVID-19 pandemic which reduced healthcare research activity (Nicola et al., 2020) and availability of primary care prescribers.

In line with the study protocol, participants were provided with a participant information sheet (see Appendix 11) prior to the interview to inform them about the study and provide them with an opportunity to ask questions or clarify information. Documented consent was also obtained from the participants after they read the information sheet and prior to conducting the interview. Interviews were conducted face to face or via telephone depending on the preference of the participants. The interviews were recorded using an audio recorder and transcribed for analysis. All transcriptions were anonymised prior to analysis to preserve confidentiality. Participants were asked about their prescribing practice for pregnant women using a semi-structured interview schedule. The questions focused on how they diagnosed UTIs, how they decided on the treatment, whether they considered AMR when prescribing antibiotics and what information they provided to women on self-care and prevention (see Appendix 13).

7.4.2. Data Analysis

The data were collected and analysed concurrently to inform saturation of themes which can guide when to cease recruitment. NVivo® 11 software was used to organise the transcribed data which were analysed using thematic analysis as recommended by Braun and Clarke (2006). Thematic analysis is a qualitative method which allows the exploration and interpretation of patterns in data. The interview transcripts were read multiple times to achieve familiarisation and form initial codes that were relevant to the research topic. The codes were then grouped and further developed to form themes which reflect the patterns in the data.

7.4.3. Ethical considerations

Participants were asked about their prescribing practice regarding antibiotics for pregnant women. There was a risk of distress to the participants in case they had experienced a difficult situation personally or with a patient because of a serious infection. However, participation in this study was on a voluntary basis, and participants were informed about the study through the participant information sheet and given the opportunity to discuss any concerns or ask questions prior to the interview. They were also assured that they did not need to answer questions if they felt uncomfortable and that they were free to withdraw at any point without specifying any reason. There were no risks anticipated to the interviewer due to their familiarity with the research topic and interviews being conducted on university premises during normal working hours. However, the research supervisors and University of Reading's Graduate School were available to provide support and guidance if any concerns arose during the conduct of this study. This study was reviewed and granted ethical approval for conduct by the Health Research Authority and Health and Care Research Wales (Ref. 20/HRA/0163), and by the University of Reading's Research and Ethics Committee (Ref. UREC 20/06).

7.4.4. Data protection and confidentiality

All data collected have been used for scientific research purposes only and confidentiality of the participants was ensured throughout. Contact details of the participants were collected to arrange

interview times, but this information was only accessible to the researchers and stored electronically on a secure encrypted server. An audio recorder was used to record the interviews and all recordings were deleted after transcription. The transcripts were anonymised and stored on a secure server to protect the confidentiality of the participants. Transcripts will be retained for a minimum of three years as per the University of Reading's Research Data Management Policy (University of Reading, 2021). All information remained accessible only to the researchers and all confidential data will be destroyed after completion of the study.

7.5. Results

The following results are from three interviews that have been conducted to date. These findings are preliminary as they are based only on the three participants that were interviewed. Two of the participants were medical doctors and the third participant was a pharmacist independent prescriber. All three participants worked in a primary care GP practice and had been in their current role for 7, 36, and 9 months, respectively. All participants had experience of prescribing medication to pregnant women. Two themes have been identified which describe prescribers' decision-making when prescribing antibiotics and the self-care advice they give towomen who are diagnosed with a UTI. The first theme relates to the careful approach that prescribers take when managing UTIs in pregnancy, while the second theme relates to the behavioural advice that prescribers give to women.

7.5.1. Erring on the side of caution

Prescribers treat UTIs more cautiously in women who are pregnant than they do in non- pregnant women. In fact, one participant referred to this being ingrained in them as part oftheir medical training.

> 'I think the other side of things is that you're kind of trained to think you know, you need to be really cautious. There are complications of urine infections and that kind ofbrought up thinking… means you do treat cautiously.' – Participant One

This cautious approach was a result of complications that are more commonly associated with aUTI during pregnancy. Participants quoted pre-term birth and pyelonephritis as the two most concerning adverse outcomes of a UTI in pregnancy .

> 'Urine infections in pregnancy can cause complications umm so I think it can cause pre-term labour and yeah I think… the problem is in pregnancy… that urine infections can cause pyelonephritis, it can be a real problem in pregnancy.' – Participant Two

When prescribing antibiotics for a UTI, the prescriber must ensure that the medication that they choose is effective and safe for both the foetus and the mother. In effect, this means that they treat an illness which affects two lives. They prescribe antibiotics according to the antimicrobial resistance profile of the causative bacteria as well as balance the risk of the antibiotic and the infection to the mother and the foetus. Treating an additional patient, i.e. thefoetus, means that prescribers urge more caution in pregnancy.

> 'You do treat cautiously I guess because there are two patients in a way…' –

ParticipantOne

The cautious approach to managing UTIs in pregnancy also means that a delay in starting empirical antibiotics is avoided, although this might be an approach that is adopted in non-pregnant patients as seen in the quote below.

> 'Uh but in pregnancy I would treat earlier with antibiotics than I necessarily would in anon-pregnant lady' – Participant Two

As well as this, prescribers base their decision to prescribe an antibiotic on the symptoms rather than relying on diagnostic tests such as dipsticks or waiting for a lab result to return.

> 'I wouldn't dip their urine as I don't think it's… I think the symptoms are probably more,more what drives your decision making rather than a dip showing something and I thinka dip is probably not very accurate in pregnancy anyway.' – Participant Three

> 'If I was happy that it wasn't a systemic infection then I'd go down the route of, I'd sendthe urine anyway, but I'd go down the route of giving them empirical antibiotics.' – Participant Two

In summary, prescribers urge more caution in pregnant women when treating a UTI. Prescribers may view prescribing in pregnancy as 'treating for two' and therefore adopt the more cautious approach. This might mean avoiding any delay in starting empirical antibioticsand relying on symptoms to aid diagnosis rather than any other diagnostic indicators.

7.5.2. Behaviour as inconsequential

The results indicate that the consultations focus on diagnosing the infection and prescribing antibiotics. Self-care advice is provided on the rare occasion focusing on drinking adequate amounts of fluid and advising on painkillers that can be taken during pregnancy. However, littleemphasis is placed on advising about prevention as stated by one participant,

> 'I generally don't say much about preventing them [urinary tract infections]' -Participant One

Nevertheless, in terms of the self-care advice that is provided, all three participants referred tomaintaining fluid intake as the most important behaviour which can be seen in the following quote.

> 'The most important prevention would be to maintain… ensure they are drinking enough fluids. Women have extra requirements for fluids anyway during pregnancy, 2-3L maybe even as a minimum amount that a woman should be having as they might begoing to the toilet lots and lots' - Participant Two

One participant also stated that while they might provide advice on preventative and self-carebehaviours, such as drinking enough fluids, they also reassure women about the cause of the UTI.

> 'With pregnancy I also kind of reassure them that often it's a common thing that occursin pregnancy and it might not necessary be something they have done or not done which has caused it.' – Participant Three

The quote above indicates a perception that UTIs are caused by the pregnancy of the woman rather than the result of individual behaviour. This conflict may have an impact on the self- efficacy of patients with regards to UTIs during pregnancy and reinforces a belief that the roleof behaviour is inconsequential to the development of UTIs.

7.6. Discussion

The aim of this study was to explore the perspectives of healthcare professionals on antimicrobial prescribing for UTIs during pregnancy. The results demonstrate that prescribers are motivated by a concern for the health of women and their foetus because UTIs are associated with adverse health outcomes in pregnancy. This means that avoiding an adverse outcome in patients, including both mother and baby, is viewed as a greater priority than minimising antibiotic use because of AMR. The results also demonstrate that clinicians rely on symptoms to a greater degree than diagnostic tests such as a dipstick, which is a chemically treated strip dipped in a urine sample to indicate an infection. This leads to basing a diagnosis on symptoms and initiating empirical antibiotics as a matter of urgency. Laboratory culture results from a urine sample can take a few days to be processed and therefore prescribing antibiotics is adopted as the preferred approach rather than delaying prescribing until culture results confirm an infection. A study conducted in Ireland by Vellinga et al (2011) shows that almost 70% of urine samples from patients did not return a positive culture result. This is similar to a multinational European study by Butler et al (2017) which found approximately 36%of urine samples revealed positive results upon culture. These two studies were conducted in the general population and a study specifically conducted with pregnant women may provide different results. However, symptoms of a UTI such as increased frequency of urination can be a normal

occurrence in pregnancy and hence might not be a reliable indicator of infection. Healthcare professionals' cautious approach therefore has implications for antibiotic use because it can lead to overuse and contribute to AMR. The results also indicate that prescribers attribute pregnancy as the cause of UTIs in pregnant women and therefore do not routinely offer prevention advice. This was seen in the audit studyby the authors (Ghouri & Hollywood, 2020) and is also in agreement with another study by Lecky et al (2020). This view reflects a biomedical model which has been described by Ogden (2012). This model suggests that illness is caused by factors which are biological or medical, e.g. bacteria or hormonal imbalances, and outside the behavioural influence of individuals. ViewingUTIs through a biomedical model undermines the role of behaviour in preventing infection.

Studies have shown the association between preventative behaviours and a reduced incidenceof UTIs (Amiri et al., 2009; Elzayat et al., 2017). Therefore, views reflected in a biomedical model can lead to reliance on, and overuse of, antibiotics. The results indicate that healthcare professionals need to reflect on how they can optimise therate of antibiotic prescribing for UTIs during pregnancy. Healthcare professionals consulting women in pregnancy require feedback on their prescribing of antibiotics for UTIs, which is an effective intervention to address prescribing rates (Duane et al., 2017; Vellinga et al., 2016).

Emphasis is also needed on educating patients about AMR which might not be done routinelywhen prescribing antibiotics for a UTI, as it is seen as an illness where a simple consult and prescribe antibiotic approach is considered sufficient (Duane et al., 2016). Healthcare professionals therefore need to divert their own and patients' focus toward

preventative behaviours to minimise the incidence of UTIs and thereby reduce antibiotic use.

7.6.1. Strengths and limitations

The focus of this study was on exploring perspectives of healthcare professionals in primary care with regards to antibiotic use during pregnancy. This has not been studied before and therefore provides novel insight which can be used to optimise antibiotic use in antenatal care. The work described in this chapter has limitations because it presents preliminary results. Recruitment for this study was paused because of the impact of the COVID-19 pandemic on the availability of healthcare professionals (see Appendix 15, COVID-19 impact statement, for more information). Additional data therefore needs to be collected which will be subject to further analysis and interpretation. Recruitment and data collection will therefore continue, and it is anticipated that the final work will be reported as a scientific article in a peer-reviewed scholarly journal.

7.6.2. Conclusion

The preliminary results of this study show that healthcare professionals adopt a highly cautious approach when consulting women who are pregnant and experiencing UTI symptoms. They preferto prescribe antibiotics promptly during consultations and do not emphasise preventative behaviours as they consider them ineffective. This can lead to excessive prescribing of antibiotics during pregnancy which has implications for AMR. A change in practice is therefore required where women are provided with advice and education on self-care and preventative measures to minimise infections rates and reduce antibiotic consumption to tackle AMR, which is a global health threat.

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CHAPTER EIGHT

8. Discussion

8.1. Key Findings of research

This chapter discusses the research presented in this thesis which includes four published articles and one with preliminary results. The aim of the research was to explore UTIs in pregnancy to tackle AMR using behavioural science.

The first study was a systematic review that was conducted to identify interventions that could prevent UTIs in pregnancy. A UTI is the most common type of infection that occurs in women during pregnancy. The first study oriented the research towards exploring the behaviours and perceptions of women and healthcare professionals with re agards to UTI management in pregnancy. This is because the main conclusion of the systematic review was that preventative behaviour is currently the only evidence-based intervention linked to a reduced incidence of UTIs in this population. Behaviours that can prevent UTIs include drinking adequate fluids which has a protective effect as it results in dilution and minimises colonisation of the bacteria responsible for causing the UTI (Hooton et al., 2018; Lotan et al., 2013). Maintaining hygiene after sexual intercourse, not delaying using the toilet when needing to urinate, and wiping from front to back when cleaning the genital area are additional behaviours which are associated with prevention and reduced incidence of UTIs (Amiri et al., 2009; Elzayat et al., 2017). Based on the importance of behavioural measures in reducing the incidence of UTIs in pregnancy, further research was subsequently designed and conducted to explore women's and prescribers' perceptions and behaviours. The rationale behind the research that followed the systematic review was that behavioural insights into how the infection and antibiotic treatment are perceived in pregnancy was crucial in addressing how antibiotic use could be optimised and safely minimised. As a result, the next two studies which were conducted after the systematic review were designed to explore perceptions and behaviours of women who had experienced a UTI in pregnancy.

Chapters two and three of the thesis present articles on the research relating to women's perceptions and behaviours within the context of experiencing UTIs in pregnancy. The study presented in chapter two focused on women's experiences of developing a UTI and using antibiotics during pregnancy. The next study presented in chapter three focused on exploring women's perceptions of AMR. This study was designed because whilst the online forum was valuable in providing a view into women's experiences of UTIs, it provided little insight on how they perceived AMR. The interview study provided the opportunity to ask women about their illness experience as well as probe them about their views on AMR. The findings from these two studies provide novel insights into the complexity of health issues faced by women when they experience an infectious illness in pregnancy and have also been published as a book chapter (see Appendix 14) in an edited collection of research based on how peoples' everyday lives are influenced by medications.

The article in chapter two presents results from thematic analysis of data which identified three themes under an overarching primary theme. The overarching theme concerns women's pre-natal attachment to their foetus which guides their concerns and motivations in relation to their health behaviours. Pre-natal attachment is a theoretical construct which has previously been described in literature as associated with health protective behaviours during pregnancy (Lindgren, 2001). The three themes in this article cover women's views of their illness (the UTI), their perceptions of the treatment (antibiotics), and their coping mechanisms. All of these were guided by the bond that they felt towards their unborn child. In seeking resolution of their illness, through medical or other means, women's focus remains on the safe development of the foetus. This study shows that pre-natal attachment is the primary driver in women's decision making on how they manage their illness. It causes women to focus on the short-term risks from a UTI and is the primary determinant that motivates them to use antibiotics in pregnancy.

Chapter three continues to explore the views of women and presents follow-up research with

women who were of a similar demographic background to those in the online health forum. The results highlight two themes with an overarching primary theme of self-efficacy. The first theme describes women's conceptualisation of AMR as a future health threat that affects individuals who take excessive antibiotics. AMR was also primarily perceived as a problem affecting the healthcare sector and therefore the onus was on healthcare professionals to manage and resolve the issue. The second theme described the uniqueness of pregnancy as a vulnerable state with regards to acquiring infection. In this way, pregnancy was described as different from the norm when treating health conditions because the health of both the woman and the baby need to be considered. The main finding from this study indicates that women viewed UTIs in pregnancy through a biomedical model where personal behaviours were considered to have little impact on the development of infection. Instead, pregnancy was attributed as the cause of the UTI. The overarching theme of self-efficacy describes how views reflected in a biomedical model might hinder adoption of preventative behaviours for infection prevention. As pregnancy was viewed to cause UTIs, most women did not feel that their behaviour impacted their health. This meant that they perceived little control over their health whilst pregnant and relied on medical solutions i.e., antibiotics to prevent illness. A shift to a behavioural model and increased self-efficacy for infection prevention is the key message for the safe reduction of antibiotic use in response to AMR.

Research in chapters four and five focus on the practice and perspectives of healthcare professionals in the context of UTIs during pregnancy. In chapter four, the article presents results from an audit that was conducted to assess current prescribing of antibiotics for UTIs during pregnancy. The audit was conducted in a primary care setting, specifically using data from three London based GP surgeries. The main results from the audit show that antibiotics that are for second-line use (amoxicillin, cefalexin) are often prescribed as the empirical first choice. The audit results suggest that this might be because of a perception that the second-line antibiotics are safer in pregnancy compared to the recommended first-line antibiotic

(nitrofurantoin). The results also show that patients are not routinely provided with self-care and prevention advice to help them manage their symptoms and prevent future infections. The fifth chapter presented preliminary results from a study conducted with prescribers to explore their perceptions of antibiotic prescribing for UTIs in pregnancy. The results show that prescribers are fearful of not prescribing or delaying antibiotics during pregnancy. They also have a lower threshold for prescribing antibiotics in pregnant women compared with non-pregnant women. It is important to note here that antimicrobial guidelines for UTIs do make a distinction between diagnosis and treatment of UTIs in women based on their pregnancy status (NICE NG109, 2018). According to the guideline, pregnant women should be treated for asymptomatic bacteriuria, unlike non-pregnant women. They should also be prescribed a longer duration of antibiotics (7 days) compared with non-pregnant women (3 days). Interview data with the prescribers however suggests that they had a lower personal threshold for treating pregnant women and perhaps a far more cautious approach than recommended by the guideline. This perception was rooted in an understandable fear that delay or withholding antibiotics could cause harm to the patient. At the same time, like the perceptions of women, prescribers demonstrated perceptions reflected through a biomedical model and did not consider behavioural measures to have a significantly protective effect.

8.2. Implications of key findings for antibiotic use and AMR

These research findings have important implications for antibiotic use during pregnancy and on a broader level for how AMR can be tackled in antenatal care using a behavioural approach.

The systematic review found five different approaches which had been investigated to prevent UTIs during pregnancy. Although literature describes additional non-antibiotic strategies, these have not been studied in pregnant women. Examples of non-antibiotic strategies which are mentioned in literature but have not yet been investigated for use in pregnancy include D-mannose (Kranjčec et al., 2014), probiotics, and non-steroidal medications (Beerepoot et al., 2013; Sihra et al., 2018). The findings from the systematic review therefore endorses the role of

behaviour as currently the most effective way of preventing a UTI in pregnancy which also reduces antibiotic use as a result. Infection prevention through behavioural measures thus supports antimicrobial stewardship efforts in antenatal care. Encouraging preventative behaviours and framing it as beneficial for tackling AMR helps achieve the public health priorities of tackling AMR and ensuring a healthy start at birth for mothers and children (Public Health England, 2019).

8.2.1. Women's perspectives

The research focused on women's perspectives shows that pre-natal attachment to the baby drives their decision-making to use antibiotics. Pre-natal attachment causes women to focus on the risks of UTIs and perceive antibiotics as a low-risk treatment option. This has implications for AMR as women are likely to seek antibiotics if they experience any symptom suggestive of a UTI. However, as UTI and physiological symptoms of pregnancy are quite similar, consultations for a UTI can lead to unnecessary and excessive use of antibiotics. The research with women also shows that their perceptions were reflected through a biomedical model of health which can also lead to overuse of antibiotics. Perceptions reflecting this model reduce the role of behaviour as ineffective for health because pregnancy rather than personal behaviours are attributed to causing a UTI. While pregnancy can increase the risk of developing a UTI, preventative behaviours are known to be protective and are associated with a lower incidence of infection during pregnancy (Amiri et al., 2009; Elzayat et al., 2017; Ghouri et al., 2018). The outcome expectancy that behaviours are not effective are linked with low self-efficacy in performing preventative actions to maintaining health which leads to a reliance on antibiotics. This means that women rely on a medical solution, i.e., the antibiotic, rather than relying on their own behaviour to prevent infection. In the case of women who get recurrent infections, it could also translate to solely using antibiotics rather than behavioural measures to prevent UTIs. Lastly, this part of the research also shows that participants indicated low self-efficacy in terms of how AMR could be tackled through public effort and instead attributed this

responsibility to healthcare professionals. This low self-efficacy stemmed from uncertainty onhow they could contribute as opposed to apathy towards AMR, indicating that there is a needfor better awareness of how the public can respond to AMR through focus on infection prevention.

8.2.2. Prescribers' perspectives

The research on the practice and perceptions of healthcare professionals also reveals several factors that have implications for AMR. The empirical prescribing of the broad spectrum second-line antibiotics (amoxicillin, cefalexin), as seen in the audit, contributes to the problem of AMR as they target a wide range of microorganisms. This can lead to AMR because indiscriminate eradication by broad spectrum antibiotics also impacts beneficial microbes which creates an advantage for resistant bacteria to multiply and cause further infections (Om et al., 2016; Paharik et al., 2017). The audit study also shows that the advice on self-care and prevention of UTIs is not routinely provided which can increase reliance on antibiotics and result in their overuse thus contributing to AMR. Interview results with the prescribers indicatethat their perceptions are reflected in a biomedical model in the context of UTIs. This can perpetuate the view that UTIs during pregnancy are unaffected by the personal behaviours of women and this phenomenon can be seen in the research with women who attributed pregnancy as the cause of UTIs. The unrestrictive and liberal prescribing practice during pregnancy, as alluded to in the interviews, can also lead to overuse of antibiotics and thus contribute to increased AMR.

The perceptions of both patients and healthcare professionals described above can lead to behaviours that contribute towards AMR through overconsumption of antibiotics. This phenomenon can be seen in the context of UTIs during pregnancy in studies that report

overuse of antibiotics in pregnant women (Moradi et al., 2021; Mosedale et al., 2013; Sekikuboet al., 2017). There is therefore a need to intervene and work with patients and healthcare professionals to encourage preventative behaviours which can minimise the use of antibiotics for UTIs during pregnancy. The following section uses the insights provided from the research presented in this thesis to make recommendations for future work which can affect change inantibiotic use and prescribing during pregnancy.

8.3. Implications for research and practice

The key finding from the research presented in this thesis highlights the need for behaviour change, in both patients and healthcare professionals, regarding UTIs in pregnancy. This thesisemployed behavioural science theories to develop deeper understanding of the findings. One of the main theories discussed is the COM-B model, which is described in chapter one (section1.4.5.). The COM-B model refers to the capability, opportunity, and motivation of an individualto perform specific behaviours. The perceptions and behaviours of patients and healthcare professionals can be targeted through health interventions that are linked with the components of the COM-B model.

Pregnancy has been seen as a ‘teachable moment’ for health behaviour change (Olander et al., 2016; Phelan, 2010) as women are more receptive to health information and adopting healthier lifestyles for the benefit of their baby. Pregnancy is therefore itself a useful social opportunity for health workers to increase public awareness about AMR. The collection of research in this thesis highlights how women experienced their pregnancy as a unique state that was different from the norm in terms of how they achieved or maintained health. Pregnant women have regular antenatal appointments with a midwife or doctor during the course of their pregnancy. The first appointment is

called the booking appointment in which women are given health information relevant to staying healthy during pregnancy. The information given includes details about infections during pregnancy that can affect the baby. The NICE CG62 guideline (2017) recommends screening for asymptomatic bacteriuria which is usually done early in pregnancy and involves taking a urine sample for culture. The booking appointment therefore provides a useful physical opportunity to situate an intervention where UTI prevention advice is provided to women by their midwife or GP. Requesting a urine sample for analysis also provides the healthcare professional a natural prompt to discuss infection prevention behaviours to minimise UTIs and avoid antibiotic use in response to AMR.

According to the behaviour change wheel framework (see Chapter One section 1.4.5.), education and training are intervention functions that are linked with improving the psychological and physical capability to perform desired behaviours (Michie et al., 2011). Pre-natal attachment causes women to focus on the short-term risks of a UTI and overlook the risks from using antibiotics (Ghouri et al., 2019). The intervention will therefore need to focus on increasing awareness and education of the risk of AMR from using antibiotics. This would mean educating and providing information on how AMR affects not just the individual but society and particularly the future health of their baby. There may also be a need to remove any potential uncertainty about finishing antibiotic courses for patients.

Perceptions reflected in a biomedical model demonstrate that women did not consider prevention and relied on antibiotics. The intervention will therefore need to address a change in perceptions to reflect a behavioural model and increase self-efficacy in

preventing infection. This would target the automatic motivation process that encourages reliance on antibiotics by directing attention towards preventative behaviours. The advice would also need to be persuasive and educative in nature to target women's reflective motivation. The research with women shows that pre-natal attachment causes them to focus on the risks of a UTI, but it could be directed to frame preventative behaviours as actions that they take to ensure the future health of their baby as well as a personal response to AMR. Emphasis would need to be placed on the importance and effectiveness of measures, such as drinking adequate fluids and not delaying urination, as specific behaviours that can prevent UTIs.

The preliminary research with prescribers also highlights several factors that contribute to inappropriate use of antibiotics for UTIs during pregnancy. Prescribers are motivated by their concern for the safety of women and the baby to prescribe antibiotics and base their decision to prescribe on the presenting symptoms. They referred to the inaccuracy of diagnostic tests such as the dip test and therefore prescribed empirical antibiotics. This reveals a physical capability issue with regards to the need for accurate diagnostic tests, a finding that agrees with research that explored the challenges of managing UTIs (Brookes-Howell et al., 2019). Interventions that provide enablement are linked to improving physical capability. Future work is therefore needed in diagnostics to enable healthcare professionals in their decision making with prescribing antibiotics to ensure patients receive them only when they have an active infection.

There is also scope for further clinical research on the necessity of antibiotic use for the treatment of asymptomatic bacteriuria in pregnancy as the current approach is based on out-dated and low-quality evidence (Kazemier et al., 2015). Conducting high quality

clinical trials might provide the evidence to change antimicrobial guidelines to recommend treatment only for symptomatic infections which would also enable the reduction of antibiotic prescribing during pregnancy. At the same time, healthcare professionals' motivation to limit inappropriate prescribing of antibiotic during pregnancy also needs to be addressed. The existence of an evidence-based leaflet provides a really useful resource and its use by prescribers can be promoted to encourage provision of self-care advice in consultations (Lecky et al., 2020). Case studies and scenarios that present the challenges of treating resistant infections during pregnancy and in babies could also be used to improve prescribers' automatic and reflective motivation to minimise inappropriate prescribing of antibiotics in this population.

8.4. Strengths and limitations

The collection of research presented in this thesis has strengths and limitations which are discussed in depth in the relevant chapters. The main strength of the thesis is its exploration ofa healthcare problem that is highly topical in a subset of population with distinct health needs.It is research in a niche context and yet has high relevance to public health. This is because it draws and combines the public health agendas of tackling AMR and improving health during pregnancy to safeguard a healthy start for children from birth. Another key strength of this research is that it voices the patient perspective by exploring theirviews and experiences. This is directly beneficial for practice and research from an epistemological and consequentialist point of view (Boote et al., 2015). The epistemological ppendiargument suggests that the patient voice supports rigour in research by offering their insight and the consequentialist argument supports their

involvement as it improves the delivery of healthcare (Denegri, 2014). The research also has the advantage that it attempts toprovide a comprehensive review of the problem by reporting both the public and healthcare professionals' perspectives. It is also based on a pragmatic approach to study the problem of AMR and UTIs during pregnancy which meant that the methods chosen were selected using a flexible approach and after evaluation of their practical advantage.

The overall research design also has limitations which affect the generalisability and transferability of the findings. Most of the participants in this research were of a similar demographic background. They were women that were of white ethnicity, age group between 30-40 and an education that includes a degree level qualification. Most of the women also had no relevant clinical history and had uncomplicated pregnancies. Therefore, the findings need tobe interpreted within this context and it may not be appropriate to generalise results to other subsets such as women from Black, Asian and Minority ethnic (BAME) groups or specific clinicalconditions like diabetes. Another limitation of the research relates to the conduct of the research which was impacted by the COVID-19 pandemic and affected the recruitment of healthcare professionals. The findings on the perspectives of the healthcare professionals are therefore preliminary and need further exploration, although the current initial data still provides valuable insight.

8.5. Conclusion

This research explored the role of behaviour in tackling AMR and managing UTIs during pregnancy. The perceptions and behaviours of people were studied within the context of UTIsduring pregnancy and their implications for AMR were evaluated. The findings

present behavioural measures as the safest and most effective approach of minimising UTIs during pregnancy. This infection prevention approach helps to minimise antibiotic use which is a highlydesirable outcome for tackling AMR. The research highlights the importance of pre-natal attachment in women's decision-making and shows that their perceptions are reflective of a biomedical model. This results in low self-efficacy and perceived control over how to manage their own health using preventative behaviours. Healthcare professionals on the other hand also demonstrate perceptions reflected through a biomedical model. This results in them exercising an overtly cautious approach and prescribing antibiotics when they might not be necessary. The thesis proposes that a shift in perceptions that reflect a more behavioural modelcan encourage adoption of preventative behaviours. It would mean interventions delivered by healthcare professionals should focus on the role of personal behaviours for infection prevention and presenting the risks of AMR in relation to antibiotic use. For healthcare professionals themselves, it would also mean following the guidelines to prescribe antibiotics safely and effectively. Ultimately, behaviour change from both women and healthcare professionals in the context of UTIs during pregnancy can help to prevent overuse of antibioticsand provide a solution to the global health threat of AMR.

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Appendix 1: Study One - Search strategy for systematic review

APPENDIX 1: Study One - Search strategy for systematic review

Additional file – search strategy

Database	Search terms	Records Retrieved
EMBASE	1 "urinary tract infection" or UTI or bacteriuria or cystitis	18,529
	2 prevention or control or management	1,041,064
	3 pregnan*	266,954
	1 AND 2 AND 3 Limits: English language	**744**
AMED	1 "urinary tract infection" OR UTI OR bacteriuria OR cystitis	199
	2 prevention OR control OR management	37,458
	3 pregnan*	1,316
	1 AND 2 AND 3 Limits: English language	**0**
BNI	1 "urinary tract infection" OR UTI OR bacteriuria OR cystitis	910
	2 prevention OR control OR management	101, 002
	3 pregnan*	18, 193
	1 AND 2 AND 3	**10**
CINAHL	1 "urinary tract infection" OR UTI OR bacteriuria OR cystitis	3,945
	2 prevention OR control OR management	443,963
	3 pregnan*	57,199
	1 AND 2 AND 3 Limits: English language	**66**
MEDLINE	1 "urinary tract infection" OR UTI OR bacteriuria OR cystitis	34, 570
	2 prevention OR control OR management	3,251,851
	3 pregnan*	424,799
	1 AND 2 AND 3 Limits: English language	**397**
PUBMED	1 "urinary tract infection" OR UTI OR bacteriuria OR cystitis	40,685

	2 prevention OR control OR management	5,532,953
	3 pregnan*	902,380
	1 AND 2 AND 3	**942**
PsycINFO	1 "urinary tract infection" OR UTI OR bacteriuria OR cystitis	574
	2 prevention OR control OR management	608,142
	3 pregnan*	39,650
	1 AND 2 AND 3 Limits: English language	**4**
Cochrane	1 "urinary tract infection" OR UTI OR bacteriuria OR cystitis	6892
	2 prevention OR control OR management	372680
	3 pregnan*	
	1 AND 2 AND 3 (Trials)	**102**
Scopus	(TITLE-ABS-KEY ("urinary tract infection" OR UTI OR bacteriuria OR cystitis) AND TITLE-ABS-KEY (prevention or control or management) AND TITLE-ABS-KEY (pregnan*) AND NOT TITLE-ABS-KEY (catheter OR catheter AND associated) AND NOT TITLE-ABS-KEY (antibacterial* OR antibiotic* OR antimicrobial*) Note: additional terms searched using 'NOT' due to too many results	**1008**
ScienceDirect (searching abstract +title + keyword gave 7,234 results)	KEYWORDS ("urinary tract infection" OR uti OR bacteriuria OR cystitis) and KEYWORDS (prevention OR control OR management).	**3**
Manual search		**0**

The authors of two systematic reviews were contacted to locate full text articles which they had included in their work but which were not available on open access:

- Ruth Jepson for conference abstract of study by Essadi et al (2010).
    - Jepson RG, Williams G, Craig JC. Cranberries for preventing urinary tract infections. Cochrane Database Syst Rev. 2012;10. doi: 10.1002/14651858.CD001321.pub5.
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Appendix 2: Study Two and Three - Ethics approval UREC Ref 17/30

Dr Amelia Hollywood
Lecturer in Health Services Research
School of Chemistry, Food and Pharmacy
University of Reading
Whiteknights
Reading
RG6 6AD

28 June 2017

Dear Amelia

UREC 17/30: Women's views on antimicrobial resistance and management of urinary tract infections in pregnancy. *Favourable opinion*

Thank you for the response (your email, dated 16 June 2017, refers) addressing the issues raised by the UREC Sub-committee at its June 2016 meeting (*my Favourable Opinion with Conditions email of 16 June 2017 including attachments refers*). On the basis of these responses, I can confirm that the Chair is pleased to confirm a favourable ethical opinion.

Please note that the Committee will monitor the progress of projects to which it has given favourable ethical opinion approximately one year after such agreement, and then on a regular basis until its completion.

Please also find attached Safety Note 59: Incident Reporting in Human Interventional Studies at the University of Reading, to be followed should there be an incident arising from the conduct of this research.

The University Board for Research and Innovation has also asked that recipients of favourable ethical opinions from UREC be reminded of the provisions of the University Code of Good Practice in Research. A copy is attached and further information may be obtained here:

http://www.reading.ac.uk/internal/res/QualityAssuranceInResearch/reas-RSqar.aspx.

Yours sincerely

Dr M J Proven
Coordinator for Quality Assurance in Research (UREC Secretary)
cc: Dr John Wright (Chair); Dr Becky Green (Head of Pharmacy); Barbara Parr (Research Secretary);

Appendix 3: Study Two - Permission to collect data from www.mumsnet.com

Flavia Ghouri

From: MN Report Post <hs_report_post@mumsnet.com>
Sent: 27 March 2017 16:13
To: Flavia Yousaf
Subject: Re: Permission to use views for research

Follow Up Flag: Follow up
Flag Status: Flagged

Hi there Flavia,

Thanks for contacting us about this - and for thinking of Mumsnet with regard to your research, which sounds really interesting.

We're sure there are Mumsnetters out there who would consider helping so you are very welcome to start a thread asking for volunteers.

Please acknowledge Mumsnet in the sources and keep the posters' identity anonymous (ie please don't use identifying details or their real life or usernames).

Please put your request in our Surveys/Students/Nonprofits topic:
www.mumsnet.com/Talk/surveys_students_non_profits_and_start_ups

We don't allow research to be conducted anywhere else on our site, though as long as you didn't start a thread, you're free to quote our site as long as Mumsnet is credited. What this means is that if mums are already discussing something relevant to your needs on our site, you can quote from their threads, but not start one yourself with the purpose of eliciting responses.

We wish you the very best of luck with it.

Best wishes,
Lorna
MNHQ

On Mon, Mar 27, 2017 at 4:01 PM BST, Flavia Yousaf <f.ghouri@reading.ac.uk> wrote:

> Dear Mumsnet team,
>
> I am emailing to request permission to use the views of your members as part of a study for my PhD project. I am a PhD researcher at the University of Reading and my study aims to establish the current views and beliefs of pregnant women with regards to using antibiotics for urinary tract infections in light of emerging antimicrobial resistance.
>
> As part of the study, I will extract information from the threads posted by members and analyse them for common themes and experiences. The results will be written up as a report and all information will remain anonymous as I only wish to use the views and do not require any other data about the members.
>
> Please may I have your kind permission to use this information? It will be really useful for my project and I would be really grateful. Please let me know if you would like any other information.
>
> Thank you for your assistance and I look forward to your response.
>
> Kind Regards,

Flavia Yousaf MPharm MRPharmS
Graduate Teaching Assistant
School of Pharmacy, University of Reading
Tel:

Appendix 4: Study Three - Participant Information Sheet

APPENDIX 4: Study Three - Participant Information Sheet

Supervisor
Dr Amelia Hollywood
Lecturer in Health Services Research

University of Reading, Room 1.05b,
Food Biosciences Building,
PO Box 226, Whiteknights, Reading,
Berkshire. RG6 6AP

Reading School of Pharmacy
Food Biosciences Building
Whiteknights, PO Box 226
Reading RG6 6AP
UK

PhD student
Flavia Ghouri

Information sheet Version 3: 27-04-2018

Title of the project: Women's views on antimicrobial resistance and management of urinary tract infections in pregnancy

UREC Approval number: 17/30

We would like to invite you to take part in our research study. Before you decide to take part we would like you to understand why the research is being carried out and what it would involve. If you need any clarification after reading this Information Sheet, we can call you and go through the information sheet with you in order to answer any questions you have. It should only take about 5 to 10 minutes to read this information sheet.

What is the purpose of the study?

The aim of this study is to explore women's views on antimicrobial resistance and the management of urinary tract infections (UTIs) with antibiotics during pregnancy. Women will be interviewed via telephone to explore their views on the treatment options for UTIs.

Why have you been invited?

You are being invited to take part in the project because you have either subscribed to a pregnancy forum such as www.mumsnet.com, www.pregnancyforum.co.uk or responded to our post on Twitter and Facebook. We would like to interview you to find out more about your views on antimicrobial resistance and using antibiotics for the management of UTIs in pregnancy.

Do you have to take part?

No. Taking part in the study is voluntary and entirely your decision. We can arrange to contact you to describe the study further and go through this information sheet. If you would like to discuss any information, please email us to arrange this (f.ghouri@pgr.reading.ac.uk). You are free to withdraw at any time without giving any reason. This would not affect your participation or use of www.mumsnet.com, www.pregnancyforum.co.uk, Twitter or Facebook or any other website you subscribed to.

What will happen to you if you take part?

If you choose to participate, you will take part in an interview about your views over the telephone. The interview will take around 30-40 minutes and will be recorded for transcription purposes to aid analysis. The interview recordings will be deleted after they have been transcribed and all quotations used in the reports will be anonymised.

What will you have to do?

If you have experienced a UTI during pregnancy, are not currently pregnant, over 18 years old and live in the UK and would like to take part in this study, we would like to ask you to fill out the consent form attached. Please print your name and sign the consent form. Kindly return the signed form by post to: Dr Amelia Hollywood, University of Reading, Room 1.05B. Food Biosciences Building, PO Box 226, Whiteknights, Reading, Berkshire, RG6 6AP.

Alternatively, you can email us (f.ghouri@pgr.reading.ac.uk) to request the study materials by post. We will send you the study materials with a stamped addressed envelope enclosed to return the consent form. We will contact you to arrange a time to conduct an interview over the phone once we have received the signed consent form and contact details.

What are the possible disadvantages and risks of taking part?

This study is designed with minimal potential risks to all participants. However the time taken to be involved will be approximately 30-40 minutes which may be a disadvantage. Also you have the right not to answer any questions that may result in some form of unease. In the unlikely event that you get upset while conducting the telephone interview you can stop answering the questions at any time without giving a reason why. The contact details of the supervisor are provided at the top of this sheet and they will be available to talk to you if you require additional support (a.hollywood@reading.ac.uk).

What are the possible benefits of taking part?

Taking part in this study will give participants the opportunity to reflect on their views on antimicrobial resistance and management of urinary tract infections during pregnancy. The

study may not help you in any specific way but the information you provide will help healthcare professionals' understanding of women's beliefs with regards to antimicrobial resistance and management of UTIs in pregnancy which may inform how they provide healthcare services.

What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer can be addressed by contacting the responsible research supervisor, Dr Amelia Hollywood (a.hollywood@reading.ac.uk) or the Quality Assurance in Research group at the University of Reading (qar@reading.ac.uk)

Will taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. Confidentiality will be ensured for all participants, and all data collected from the interview will be used only for scientific research purposes.

Your contact details are required to arrange the telephone interview but only the researcher and supervisors will have access to this information and it will be stored on a secure, password protected server. Once the study is completed, your contact details will be destroyed unless you have indicated that you would like to receive a summary of the results or would like to be notified of future research.

The telephone interviews will be recorded with your consent using an audio recording device which will be stored in a locked filing cabinet in a secure office. The digital recordings of the interviews will be downloaded to a password protected secure server for transcription and will be retained for 3 years as per University of Reading's Research Data Management Policy. Transcriptions of the recordings will be conducted using a Microsoft Word® document which will be stored on a password protected secure server. Hard copies of the transcripts may be required for analysis and these will be stored in a locked filing cabinet in a secure office and destroyed once analysis is complete.

Interview transcripts will be anonymized using pseudonyms to conduct the analysis, which is critical to ensure your anonymity and confidentiality throughout the write up of the results. All the information provided in the interview will be accessible only by the researcher and supervisors. At the conclusion of the study the recordings and any identifiable information will be completely destroyed and none of the identifiable information that you give will be disclosed to a third party.

What will happen if you don't carry on with the study?

If you do not wish to carry on with this study you can withdraw at any time without giving any reason. This would not affect your participation or use of www.mumsnet.com,

www.pregnancyforum.co.uk, Twitter or Facebook or any other website that you have subscribed to.

What will happen to the result of the study?

The results of the study will be used in the PhD thesis of the main researcher (Flavia Ghouri). The outcomes may be presented at academic and professional conferences and in academic journals. The details of all participants will be kept confidential and you will not be identifiable from any research papers or other publications. You can request a summary of the results on the consent form.

Who is organising and funding the research?

This study is being conducted with the University of Reading acting as the academic institution for the student thesis.

Who has reviewed the study?

This study has been subject to ethical review, according to the procedures specified by the University of Reading Research Ethics Committee, and has been allowed to proceed (Ref no. 17/30).

Appendix 5: Study Three - Consent Form

Dr Amelia Hollywood
Lecturer in Health Services Research

School of Chemistry, Food & Nutritional Sciences and Pharmacy

Whiteknights
PO Box 266,
Reading RG6 6AP, UK
phone

Consent Form for "Women's views on antimicrobial resistance and management of urinary tract infections in pregnancy"

UREC Approval Number: 17/30 Version 3: 27-04-2018

Please initial boxes

1. I confirm that I have read and understand the Participant Information Sheet dated 27-04-2018 for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason. ☐
3. I agree to the telephone interviews being audio-recorded and understand any direct quotes from the interviews will be anonymised. ☐
4. I agree to take part in the above study, which has been subject to ethical review according to the procedures specified by the University of Reading Research Ethics Committee and has been allowed to proceed. ☐
5. I have received a copy of this Consent Form and of the accompanying Participant Information Sheet. ☐
6. I wish to receive a summary of the overall results once the study is complete and analysed (OPTIONAL). ☐

Participant details

Name of Participant: Date of birth:

Address: Telephone:

Email: Signature & Date:

Name of researcher taking consent: Flavia Ghouri Date:

Appendix 6: Study Three - Interview schedule

APPENDIX 6: Study Three - Interview schedule

1. Please tell me about your experience of getting a urinary tract infection during pregnancy.
   Prompts for discussion:
   How did you get diagnosed with a UTI?
   What were your symptoms (if any)?
   What information were you given about your diagnosis?
   What treatment(s) were you given?
   Was the treatment in line with your expectations?
   How did you get along with the treatment? Did it work?
2. How do you think UTIs impact pregnancy?
   Prompts for discussion:
   What do you think causes UTIs during pregnancy?
   How do they affect the health of the woman or baby?
   How can UTIs be prevented in pregnancy?
3. What do you think about using antibiotics to treat UTIs during pregnancy?
   Prompts for discussion:
   What do you think are the risks and benefits to the woman or the baby?
   What do you about long term effects?
   What challenges, if any, do prescribers face when choosing to treat with antibiotics?
4. What do you think about antimicrobial resistance?
   Prompts for discussion:
   Where did you hear about antimicrobial resistance?
   Do you think antimicrobial resistance could impact you/your children/family and how?
   Is there a need to minimise antibiotic use and why?
   Do you think there are any ethical implications of using or withholding antibiotics in pregnancy?
5. What do you think about using alternatives to antibiotics to treat or prevent UTIs in pregnancy?
   What do you think about using alternative treatments such as herbal or nutritional supplements to prevent or treat UTIs?
   Prompts for discussion:
   How do they compare with antibiotics in terms of safety or effectiveness?
   Have you or would you ever use them and what would be your reason(s)?
6. Do you have any additional comments on the treatment of UTIs with antibiotics or antimicrobial resistance?

General prompts:
Could you say a bit more about that?
What makes you say that?
Could you give me an example?

Appendix 7: Study Four - Ethics approval SCFP Research Ethics Committee Ref 12/19

Flavia Ghouri

From: Julie Lovegrove
Sent: 19 July 2019 14:00
To: Amelia Hollywood; Flavia Ghouri; Kath Ryan
Cc: Barbara Parr
Subject: Ethics Approval - Amendment to Study Number 12/19

Follow Up Flag: Follow up
Flag Status: Flagged

Dear Amelia, Kath and Flavia

I am pleased to inform you that favourable opinion has been approved for the amendment to your study number 12/19 "An audit of treatment for urinary tract infections (UTIs) in pregnancy" via the in-School exceptions route. This email constitutes your permission to proceed with the studies as described in your application. The following study number has been assigned to your study and you should quote this number in any correspondence you undertake about your studies.

STUDY Number - 12/19 (as amended 18.07.19)

If you feel that you need to make changes to the way your studies are run, please let us know at the earliest opportunity and we can advise you of whether a formal amendment to your proposal is required or not.

I wish you the best of luck with the projects and finish by reminding you of the need for safe custody of project data at all times (a service that Barbara Parr, copied in, can provide if you require it).

Kind regards
Julie Lovegrove

Professor of Human Nutrition
Chair of the SCFP Research Ethics Committee

Appendix 8: Study Four - Data collection form to assess prescribing of antibiotics for UTIs in pregnancy

APPENDIX 8: Study Four - Data collection form to assess prescribing of antibiotics for UTIs in pregnancy

Data collection form to assess prescribing of antibiotics for UTIs in pregnancy (to be stored in clinic)

		Demographic data			**Clinical Data**					**Treatment Data**					Prescriber Type	Comment
	NHS no.	Age	Ethnicity	Trimester	Allergy	Symptoms (Y/N)	WBC (+/-)	Protein (+/-)	MSSU (Y/N)	Antibiotic	Dose	Duration	Self-care advice	Review? (Y/N)		
1																
2																
3																
4																
5																
6																
7																
8																
9																
10																
11																
12																
13																
14																
15																

WBC – White blood cells

MSSU – Mid-stream sample of urine

Appendix 9: Fifth Study - Ethics approval HRA & HRCW

Ref. 20/HRA/0163

Ms Flavia Ghouri
Harry Nursten 1.05
Whiteknights campus
University of Reading
RG6 6UR

Email: hra.approval@nhs.net
HCRW.approvals@wales.nhs.uk

21 January 2020

Dear Ms Ghouri

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**Exploring antimicrobial prescribing for urinary tract infections (UTIs) in pregnancy – a qualitative interview study**
IRAS project ID:	**266251**
Protocol number:	**N/A**
REC reference:	**20/HRA/0163**
Sponsor	**University of Reading**

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?

HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) have been sent to the coordinating centre of each participating nation. The relevant national coordinating function/s will contact you as appropriate.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?
HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?

The *"After HRA Approval – guidance for sponsors and investigators"* document on the HRA website gives detailed guidance on reporting expectations for studies with HRA and HCRW Approval, including:

- Registration of Research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics and is updated in the light of changes in reporting expectations or procedures.

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **266251**. Please quote this on all correspondence.

Yours sincerely,

Lauren Allen

Email: hra.approval@nhs.net

Copy to: *Dr Mike Proven*

List of Documents

The final document set assessed and approved by HRA and HCRW Approval is listed below.

Document	*Version*	*Date*
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Liability insurance certificate]		24 May 2019
Interview schedules or topic guides for participants [Interview schedule]	Version 1	02 October 2019
IRAS Application Form [IRAS Form 07012020]	266251/1396428/37/893	07 January 2020
Letter from sponsor [Sponsor Letter]	Version 1	07 January 2020
Letters of invitation to participant [Invitation email]	Version 2	17 January 2020
Organisation Information Document [Organised Information Document]	Version 2	17 January 2020
Other [FG Insurance confirmation]	Version 1	07 January 2020
Participant consent form [Consent form]	Version 2	17 January 2020
Participant information sheet (PIS) [Participant Information Sheet]	Version 2	17 January 2020
Research protocol or project proposal [Study Protocol]	Version 1	02 October 2019
Schedule of Events or SoECAT [Schedule of events]	Version 2	17 January 2020
Summary CV for Chief Investigator (CI) [Flavia Ghouri CV]		02 October 2019
Summary CV for student [Flavia Ghouri CV]		02 October 2019
Summary CV for supervisor (student research) [Amelia Hollywood CV]		21 August 2019
Summary CV for supervisor (student research) [Al Edwards CV]	Version 1	02 October 2019

Information to support study set up

The below provides all parties with information to support the arranging and confirming of capacity and capability with participating NHS organisations in England and Wales. This is intended to be an accurate reflection of the study at the time of issue of this letter.

Types of participating NHS organisation	Expectations related to confirmation of capacity and capability	Agreement to be used	Funding arrangements	Oversight expectations	HR Good Practice Resource Pack expectations
There is one participating site type. Local contacts at participating organisations will send study information to potential participants. Interviews will be conducted by the external research team either at the participating organisation or by telephone.	Organisations will not be required to formally confirm capacity and capability, and research procedures may begin after provision of the local information pack, provided the following conditions are met. • You have contacted participating NHS organisations (see below for details) • HRA and HCRW Approval has been issued • The NHS organisation has not	A Organisation Information Document has been submitted and the sponsor is not requesting and does not expect any other site agreement to be used.	There is no external funding for the research and no funding will be provided to participating organisations.	A Local Collaborator will be in place at participating organisations.	The research activity will involve interviewing staff participants only, therefore access arrangements are only applicable if the research activity is undertaken in patient care areas of the participating GP practices. As this study is taking place in GP practices you are advised to contact the primary care management function to follow local processes.

	provided a reason as to why they cannot participate • The NHS organisation has not requested additional time to confirm. You may start the research prior to the above deadline if HRA and HCRW Approval has been issued and the site positively confirms that the research may proceed. You should now provide the local information pack for your study to your participating NHS organisations. A current list of R&D contacts is accessible at the NHS RD Forum website and these contacts MUST be used for this purpose. The password to access the R&D contact list is				

	Redhouse1.				

Other information to aid study set-up and delivery

This details any other information that may be helpful to sponsors and participating NHS organisations in England and Wales in study set-up.
There will be 5 participating organisations as listed in IRAS Part C.

Appendix 10: Fifth Study - Ethics approval UREC Ref 20/06

APPENDIX 10: Fifth Study - Ethics approval UREC Ref 20/06

Dr Amelia Hollywood,
Reading School of Pharmacy
University of Reading
Whiteknights
PO Box 226
RG6 6AP

31 January 2020

Dear Amelia,

UREC 20/06: Exploring antimicrobial prescribing for urinary tract infections (UTIs) in pregnancy – a qualitative interview study
Favourable opinion with conditions

Thank you for the application (email dated 23 January 2020 and including attachments refers). On the basis of these documents I can confirm that the Chair is pleased to confirm a favourable ethical opinion subject to the following conditions:

(i) The Committee asked that the Participant Information Sheet be amended to include the statement that the project had been reviewed by the University Research Ethics Committee and given a Favourable Opinion for conduct.
(ii) The Committee asked that the Consent Form be amended to capture the date of birth of the consenting participant.

I would be grateful for your response to these points in due course – ***and in any case before the practical work of the study commences.***

Mindful of the HRA approval that had already been granted, the Committee were keen to point out that the amendments required by these Conditions would be considered by the Sponsor (i.e. the University) to be *minor*. As a consequence, the requirement would be only to *notify* the HRA of the changes in due course *rather than* seek further HRA approval.

Please note that the Committee will monitor the progress of projects to which it has given favourable ethical opinion approximately one year after such agreement, and then on a regular basis until its completion.

Please also find attached Safety Note 59: Incident Reporting in Human Interventional Studies at the University of Reading, to be followed should there be an incident arising from the conduct of this research.

The University Board for Research and Innovation has also asked that recipients of favourable ethical opinions from UREC be reminded of the provisions of the University Code of Good Practice in Research. A copy is attached and further information may be obtained here:

http://www.reading.ac.uk/internal/res/QualityAssuranceInResearch/reas-RSqar.aspx

Yours sincerely

Dr M J Proven
Coordinator for Quality Assurance in Research (UREC Secretary)
cc: Professor Julie Lovegrove (UREC Chair); Barbara Parr (SREC Administrator); Dr Katrina Bicknell (Pharmacy SREC Chair)

Flavia Ghouri

From: Mike Proven
Sent: 03 February 2020 11:27
To: Amelia Hollywood; UREC; Barbara Parr
Cc: Flavia Ghouri
Subject: RE: UREC 20/06: Exploring antimicrobial prescribing for urinary tract infections (UTIs) in pregnancy – a qualitative interview study Favourable opinion with conditions

Hi Amelia

Thanks for that – and, yes, I believe that you may commence the practical work.

Cheers

Mike

Dr M J Proven | Coordinator for QAR (UREC Secretary); Specialist Adviser to the Establishment Licence Holder; Warden – Childs Hall | The University of Reading, Whiteknights, Reading, RG6 6AH | Tel | www.reading.ac.uk/qar/index.htm

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From: Amelia Hollywood
Sent: 03 February 2020 11:26
To: Mike Proven

Subject: FW: UREC 20/06: Exploring antimicrobial prescribing for urinary tract infections (UTIs) in pregnancy – a qualitative interview study Favourable opinion with conditions

Dear Mike,
Thank you for confirming that the Chair is pleased to confirm a favourable ethical opinion subject to the minor changes. Please find attached a response letter to UREC and the updated documents with the changes requested by the committee.

In summary, the changes made include:
(i) The Participant Information Sheet has been amended to include the statement that the project had been reviewed by the University Research Ethics Committee and given a Favourable Opinion for conduct.
(ii) The Consent Form has been amended to capture the date of birth of the consenting participant.

We have notified the HRA of the minor changes.

Please could you confirm we can now commence the practical work of the study?
Kind regards
Amelia

Dr Amelia Hollywood PhD, CPsychol, FHEA
Health Psychologist, Lecturer in Health Services Research
School of Pharmacy, University of Reading
1.05b Harry Nursten Building, Whiteknights, Reading, RG6 6AP
Tel: Email: Twitter: @AmeliaHollywood

Website: http://www.reading.ac.uk/pharmacy/about/staff/a-hollywood.aspx

If using Satellite Navigation to find the University, please enter RG6 6UR which should lead you directly to our campus.

Please note I do not work on Fridays.

From: UREC
Sent: 31 January 2020 12:00
To: Amelia Hollywood
Cc: Julie Lovegrove ; Katrina Bicknell >; Barbara Parr

Subject: UREC 20/06: Exploring antimicrobial prescribing for urinary tract infections (UTIs) in pregnancy – a qualitative interview study Favourable opinion with conditions

Hi Amelia

Attached (and with apologies for the delay), please find confirmation of the Favourable Opinion (with a couple of minor conditions) for your recent application: UREC 20/06: Exploring antimicrobial prescribing for urinary tract infections (UTIs) in pregnancy – a qualitative interview study.

With kind regards

Cheers

Mike

Dr Mike Proven | Coordinator for Quality Assurance in Research (**UREC Secretary**) | Academic and Governance Services | The University of Reading, Whiteknights, Reading, RG6 6AH | |

Sinead Latham | Executive Administration Officer | Academic and Governance Services | The University of Reading, Whiteknights, Reading, RG6 6AH | |

http://www.reading.ac.uk/internal/res/ResearchEthics/reas-REethicshomepage.aspx

Appendix 11: Fifth Study - Participant Information Sheet

Supervisors

Dr Amelia Hollywood

Lecturer in Health Services Research

Dr Alexander Edwards

Associate Professor in Biomedical Technology

Reading School of Pharmacy

Food Biosciences Building

Whiteknights, PO Box 226

Reading RG6 6AP

UK

PhD Researcher

Flavia Ghouri

Version 3

Date: 02-02-2020

IRAS Project ID: 266251

Title: Exploring antimicrobial prescribing for urinary tract infections in pregnancy – a qualitative interview study

We would like to invite you to take part in our research study. Before you decide to take part, we would like you to understand why the research is being carried out and what it would involve. If you need any clarification after reading this Information Sheet, we can call you and go through the information sheet in order to answer any questions you have. It should only take about 5 to 10 minutes to read this information sheet.

What is the purpose of the study?

The aim of the study is to explore the prescribing practice of GPs and non-medical prescribers for UTIs in pregnancy. Prescribers will be interviewed, face to face or via telephone, about their prescribing practice.

Why have you been invited?

You are being invited to take part in the project because you are a prescriber working in primary care. We would like to interview you to find out more about your decision making in relation to prescribing antibiotics for the management of UTIs in pregnancy.

Do you have to take part?

No. Taking part in the study is voluntary and entirely your decision. We can arrange to contact you to describe the study further, go through this information sheet and answer any questions you may have. If you would like to discuss any information, please email us to arrange this (f.ghouri@reading.ac.uk). You are free to withdraw at any time without giving any reason.

What will happen to you if you take part?

If you choose to participate, you will take part in an interview face to face or over the telephone, according to your preference. The interview will take around 45 minutes and will be recorded using an audio recorder for transcription purposes to aid analysis. The interview recordings will be deleted from the recorder after they have been transcribed and all quotations used in any subsequent reports will be anonymised.

What will you have to do?

If you are a registered prescriber who has experience of prescribing antibiotics in pregnancy and would like to take part in this study, we will ask you to fill out a consent form. Please print your name and sign the consent form. Kindly return the signed form by email to f.ghouri@reading.ac.uk or by post to: Flavia Ghouri, University of Reading, Room 1.05. Harry Nursten Building, PO Box 226, Whiteknights, Reading, Berkshire, RG6 6AP. We will contact you to arrange a time to conduct the interview over the phone once we have received the signed consent form and contact details.

What are the possible disadvantages and risks of taking part?

This study is designed with minimal potential risks to all participants. However, the time taken to be involved will be approximately 45 minutes which may be a disadvantage. Also, you have the right not to answer any questions that may result in some form of unease. In the unlikely event that you get upset while conducting the telephone interview you can stop answering the questions at any time without giving a reason why. You can contact Dr. Amelia Hollywood, the research supervisor, whose contact details are provided at the top of this sheet who will be available to talk to you if you wish (a.hollywood@reading.ac.uk).

What are the possible benefits of taking part?

Taking part in this study will give you an opportunity to reflect on your views about antimicrobial resistance and the management of UTIs during pregnancy. The study may not help you in any

specific way but the information you provide can help optimise the prescribing of antibiotics in pregnancy. We would also like to offer you a £10 Amazon voucher to thank you for your participation.

How will we use information about you?

We will need to use information from you for this research project.

This information will include your

- Name and Date of birth
- Contact details (work address, telephone and email).

People will use this information to do the research or to check your records to make sure that the research is being done properly. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you safe and secure. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

Where can you find out more about how your information is used?

You can find out more about how we use your information

- by asking one of the research team
- by sending an email Quality Assurance in Research at University of Reading qar@reading.ac.uk, or
- by ringing us on 0118 378 6069.

What if there is a problem?

Any complaint about the way you have been dealt with during the study can be addressed by contacting the responsible research supervisor, Dr Amelia Hollywood (a.hollywood@reading.ac.uk) or the Quality Assurance in Research group at the University of Reading (qar@reading.ac.uk)

Will taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. Confidentiality will be ensured for all participants, and all data collected from the interview will be used only for scientific research purposes. Your contact details are required to arrange the telephone interview but only the researcher and supervisors will have access to this information, and it will be stored on a secure, password protected server.

The telephone interviews will be recorded with your consent using an audio recording device which will be stored in a locked filing cabinet in a secure office. The digital recordings of the interviews will be downloaded to a password protected secure server for transcription and will be retained for three years as per University of Reading's Research Data Management Policy. Transcriptions will be stored as a Microsoft Word® document on a password protected secure server. Interview transcripts will be anonymized using pseudonyms to conduct the analysis, which is critical to ensure your anonymity and confidentiality throughout the write up of the results. All the information provided in the interview will be accessible only by the researcher and supervisors. At the conclusion of the study the recordings will be destroyed and none of the identifiable information that you provide will be disclosed to a third party.

What will happen if you don't carry on with the study?

If you do not wish to carry on with this study, you can withdraw at any time without giving any reason.

What will happen to the results of the study?

The results of the study will be used in the PhD thesis of the main researcher (Flavia Ghouri). The outcomes may be presented at academic and professional conferences and in academic journals. The details of all participants will be kept confidential and you will not be identifiable from any research papers or other publications. You can request a summary of the results on the consent form.

Who is organising and funding the research?

This study is being conducted with the University of Reading acting as the academic institution for the student thesis.

Who has reviewed the study?

The study has been reviewed and granted approval by NHS Health Research Authority and Health and Care Research Wales (HCRW) (Ref 20/HRA/0163). It has also been reviewed and granted favourable opinion for conduct by the University of Reading Research Ethics Committee (UREC 20/06).

Appendix 12: Fifth study - Consent Form

APPENDIX 12: Fifth Study - Consent Form

Dr Amelia Hollywood
Lecturer in Health Services Research

School of Chemistry, Food & Nutritional Sciences and Pharmacy

Whiteknights
PO Box 266,
Reading RG6 6AP, UK
phone
fax

CONSENT FORM
Version 3
Date: 02-02-2020
IRAS ID: 266251
Participant Identification Number for this study:

Title of Project: Exploring antimicrobial prescribing for urinary tract infections in pregnancy – a qualitative interview study

Name of Researcher: Flavia Ghouri

Please initial box

1. I confirm that I have read the information sheet dated..... (version.....) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
3. I agree to the interviews being audio recorded and understand any direct quotes from the interviews will be anonymised ☐
4. I agree to take part in the above study which has been subject to ethical review and has been allowed to proceed. ☐
5. I wish to receive a summary of the overall results once the study is complete and analysed (OPTIONAL). ☐

Name of Participant	Date of birth	Signature & Date
Name of Person taking consent	Signature & Date	

Appendix 13: Fifth Study - Interview schedule

Interview Schedule

Version 1

Date: 02-10-2019

IRAS Project ID: 266251

1. Please describe, in detail, how you would diagnose a UTI in a pregnant woman?

2. How do you decide on the treatment plan?

3. Do you consider AMR when prescribing antibiotics?

4. Do you give any non-pharmacological advice on treatment or prevention of UTIs in pregnancy? (self-care/behavioural counselling)

5. Do you have any concerns with treating UTIs in pregnancy?

6. Do pregnant women share any concerns with you on this issue?

7. What are your thoughts about a new technological test, that was quicker or gave more useful information, to aid diagnosis?

Appendix 14: Book Chapter - Pregnancy, urinary tract infections and antibiotics: pre-natal attachment and competing health priorities.

Chapter Five in *Living Pharmaceutical Lives* (In press).

Living Pharmaceutical Lives

Chapter: Pregnancy, Urinary Tract Infections and Antibiotics: Pre-natal Attachment and Competing Health Priorities

Flavia Ghouri, Dr. Amelia Hollywood, Prof. Kath Ryan

Introduction

Pregnancy is the period in which a foetus grows and develops inside a woman's body. The normal duration of a pregnancy is usually over nine months or about 40 weeks. It is a physiological state in which women go through a number of physical and emotional changes. The physical changes can be accompanied by uncomfortable symptoms such as nausea or vomiting and cause women to seek medical support and advice. Among the many different types of health problems experienced during pregnancy, one common condition that can affect women is an infection of the urinary tract. A urinary tract infection (UTI) is normally caused by transfer of bacteria from the gut into the genitourinary tract where they can multiply and cause an infection (Flores-Mireles, Walker, Caparon, & Hultgren, 2015). Behaviours such as not drinking adequate water or wiping the genitals from back to front after urination are associated with developing urinary infections (Ghouri, Hollywood, & Ryan, 2018). UTIs are amongst the most frequently occurring infections in pregnancy and cause symptoms such as increased frequency of urination and burning pain when passing urine (Delzell & Lefevre, 2000). Infections can also be asymptomatic, however, meaning that bacteria can infect the urinary tract without any outward signs or symptoms.

Asymptomatic infections are estimated to affect 2-12 % of pregnant women (UK National Screening Committee, 2017) and are normally diagnosed through routine screening in the first trimester of pregnancy. Previous studies have shown that UTIs, both symptomatic and asymptomatic, are associated with a number of negative outcomes in pregnancy. For example, there are studies which associate UTIs with pre-term birth, restricted foetal growth and even miscarriage (Matuszkiewicz-Rowińska, Małyszko, & Wieliczko, 2015). Due to these risks, routine screening for UTIs in pregnant women is a standard practice in many countries. Treatment is essential upon a positive diagnosis and a short course of a suitable antibiotic is prescribed to clear the infection. Although women and health professionals can sometimes be concerned about using medicines in pregnancy, due to a risk of teratogenicity

(i.e. harm to the developing foetus), most antibiotics used to treat UTIs are effective and have a good safety profile (Crider et al., 2009).

Despite their value in avoiding complications arising from UTIs, antibiotic use is not without risks. One major issue with antibiotics, regardless of the state of pregnancy, is the problem of antimicrobial resistance (AMR). Antimicrobial resistance is a naturally occurring phenomenon by which micro-organisms such as bacteria undergo spontaneous changes in their genetic make-up to develop resilience against antibiotic medicines. The genetic changes allow bacteria to resist antibiotic treatment and cause infections that can eventually progress to life-threatening conditions if no effective antibiotic is available. Antimicrobial resistance is fuelled by antibiotic use therefore a conservative approach to using antibiotics is vital and discouraging excessive use has been the focus of attention in multiple health campaigns (Mcnulty & Johnson, 2008; McNulty, Nichols, Boyle, Woodhead, & Davey, 2010). Considered within the context of pregnancy, it is also evident that antimicrobial resistant infections can be a particular challenge for women. This is because suitable antibiotics to treat infections in pregnancy are those that are not only effective at treating the infection but also do not cause any negative impact on foetal development. The requirement to ensure foetal safety can thus limit antibiotic treatment options which might otherwise be available to non-pregnant women (Rizvi, Khan, Shukla, Malik, & Shaheen, 2011).

We conducted two qualitative research studies with pregnant women to explore their experience of developing a UTI in pregnancy (Study One), and their perceptions of AMR (Study Two). The first study analysed the views of women as expressed through their posts on an online pregnancy forum (Ghouri, Hollywood, & Ryan, 2019). The online forum serves as a digital space, predominantly for women, where people can share their experiences on different topics or 'conversational threads'. Topics discussed on the forum vary and can range from health issues to political and social agendas. The conversation threads were searched using the search function on the website under the topic of UTIs in pregnancy. The search results were then downloaded and analysed using inductive thematic analysis. Although the exact demographics is difficult to ascertain, a census described subscribers to this website as predominantly White, British, women in their 30s or 40s with a degree qualification (Mumsnet Census, 2009). The second study was conducted by interviewing 15

women about their views on AMR. The demographic details of the women in the interview study were similar to the women in the first study. Women were invited to participate in this research study through online advertisements on social media. A single telephone interview was then conducted with women who lived in the UK and had experienced a UTI during pregnancy. The interviews were recorded for the purpose of transcription and then analysed using inductive thematic analysis. Both studies revealed multiple concerns within the context of UTIs in pregnancy. The benefits and risks to the women, the foetus, and society are weighed and assigned priority. This chapter collates and presents the research using excerpts from participants in the two research studies with a focus on women's perspectives of experiencing a UTI during pregnancy, in an era where AMR is a growing and pressing health threat.

Illness perceptions

Illness perceptions is a term used to describe people's knowledge and beliefs about their illness (Boltz et al., 2013). It can be defined as 'a patient's common-sense beliefs about their illness' (Leventhal, Meyer, & Nerenz, 1980) which determines how they behave in response to becoming ill. UTIs are the most frequent type of infection affecting women during their pregnancy and this was a common perception held by the majority of women in both studies. As well as viewing UTIs as being common in pregnancy, however, women also attributed the pregnancy as the cause of the UTI. Many women had the perception that they had a lowered state of immunity while they were pregnant which when combined with hormonal changes in the body, puts them at a greater risk of developing a UTI compared to when not pregnant.

> You're so susceptible when you're pregnant because your immune system seems to be so uhm… compromised when you're pregnant. (Study Two, Participant 1, 31 years)

Most women thought that the physiological changes due to pregnancy meant that diagnosis through a dipstick test was trickier compared to when not pregnant. A dipstick test refers to a diagnostic test in which a chemically treated strip of material is dipped into a urine sample to indicate the presence of an infection. Similarity between the symptoms of a UTI, and the

uncomfortable symptoms that women might experience in the normal course of pregnancy, such as increased frequency of urination and back or abdominal pain, were also thought to contribute to this diagnostic difficulty. The problem with differentiating the symptoms also led to women's feelings of uncertainty about the need for antibiotics.

> I also had trouble getting diagnosed when pregnant and was told by the midwife that it's because there are so many things present in your pee and altering what's in your pee when pregnant that it can be hard to get a dip result indicating a UTI. (Study One, Bella)

Women who had a history of UTIs, however, felt more confident that they had an infection when they experienced UTI-like symptoms. Knowing their own bodies, and having experienced UTI symptoms in the past, meant that they felt certain about when they had a UTI as opposed to a symptom of their pregnancy. In such cases, women felt that they were right in seeking medical assistance and demanding the care that they needed.

> I suffer cystitis awfully regularly and really painfully when I'm not pregnant and knew exactly what was wrong with me but for whatever reason, there was not enough bacteria to show in my pee. I had to fight for antibiotics to put it right and it was only due to my medical history that I was prescribed anything! (Study One, Brenda)

There was also a perception that the development of a UTI during pregnancy was a greater cause for concern than when not pregnant. The reason behind this perception was the association of UTIs with negative pregnancy outcomes such as pre-term birth or miscarriage. Most women's views are reflected in the following two quotes that demonstrate the fear and anxiety felt due to a UTI in pregnancy.

> I'm really worried as I'm aware UTIs, if left untreated, can cause miscarriage. I feel like a sitting duck! I'm obviously glugging away at the water and cranberry juice, but the pains are worrying me. (Study One, Rachel)

> I decided that I would take the antibiotics because normally when I had UTIs outside of pregnancy I would just take lots of water and let it ride it out but because I was pregnant I knew there was a risk of early birth so I was happy to take the antibiotics at that point (Study Two, Participant 3, 31 years).

In contrast, there were a small number of women who did not think that UTIs were anything to be overly concerned about as they are fairly common and easily treatable with antibiotics.

> I had the same around 20 weeks pregnant and I've had 4 more since (I'm now 36 week) the antibiotics should clear it up pretty quick and they are forever testing your urine... I wouldn't worry (Study One, Nicole).

The majority of women expressed concern and a keenness to obtain prompt antibiotic treatment to clear the infection. The uncertainty about the cause of the symptoms, either pregnancy or an infection, combined with an awareness that UTIs can negatively affect pregnancy caused increased expectation to use antibiotics as an insurance option 'to be on the safe side' and 'just in case' of an infection. Most women did not consider preventative behaviours, such as maintaining adequate fluid intake, to be effective at avoiding UTIs and indicated an automatic reliance on antibiotics if symptoms of a UTI were experienced. Furthermore, combined with the previously mentioned risks that UTIs pose to pregnancy, most women felt obliged to use antibiotics even when some might have preferred alternative management options.

> Um well, you know, normal hygiene that everyone knows. Sort of wiping from front to back and general cleanliness – although I mean I suppose that doesn't make much difference (Study Two, Participant 12, 43 years).

> If you weren't pregnant you could maybe take your friend's advice to drink water and cranberry juice and wait it out but given that you are pregnant it's irresponsible advice to be honest (Study One, Nikita).

The preference to use antibiotics was demonstrably clear in the descriptions surrounding antibiotic use. Understandably however, a few women were concerned about using antibiotics whilst they were pregnant because of uncertainty and a fear relating to how the medication might affect their baby as seen in the following quote.

> They gave me antibiotics for what they suspect is a UTI… just worried now after seeing the heartbeat that taking the antibiotics will do something to baba?? (Study One, Sally).

Despite the concerns, most women felt that antibiotics were safe in comparison to the risks of a UTI. They used their doctor's prescription as evidence of the safety of the antibiotics because they trusted their doctor not to prescribe something that might cause harm to their baby.

> Doc wouldn't prescribe if dangerous. It's more dangerous to leave a UTI, as at its worst it can cause kidney issues and miscarriage (Study One, Carey).

The illness perceptions of women experiencing a UTI indicate that they thought they had reduced 'self-efficacy' for maintaining their own health in pregnancy. Self-efficacy is a theoretical construct developed by Bandura in his Social Cognition Theory (Bandura, 1986). It refers to the belief a person has in their own ability to perform an action to bring about a desired change. Self-efficacy is linked with personal agency, which is the sense of control and power a person feels, about performing a task or behaviour. A review by Luszczynska and Schwarzer (2015) described how an individual's expectancy about a behaviour and their self-efficacy determines their performance of that behaviour. Women's illness perceptions showed that, on the whole, they expected UTIs to have highly negative outcomes and therefore relied on pharmaceuticals i.e. antibiotics in this case. Similarly, they expected prevention measures to be ineffective and therefore did not consider them to be an important part of their personal health routine thus demonstrating low self-efficacy in managing their health in pregnancy.

Ogden *et al.* have described health models where the cause of an illness and its resolution could be attributed to internal individual or external uncontrollable factors (Ogden et al., 1999; Ogden et al., 2001). Women's illness perceptions, described above, are reflected in a 'biomedical model'. The biomedical model, as defined by Ogden (2012) refers to associating the cause of an illness as external and beyond the control of the self. In the biomedical model, an ill person assigns the cause of an illness to involuntary factors beyond their direct influence, for example germs or their genetic make-up. The biomedical model encourages medical solutions to problems and unsurprisingly pharmaceuticals, in these cases antibiotics, were seen as the main solution for UTIs according to women and their accounts of the healthcare professionals they consulted.

As previously mentioned, a number of women attributed lowered immunity due to pregnancy as the cause of the infection. As a result, the solution to disease and illness was

also viewed to be external from the self, provided by healthcare professionals through interventions such as antibiotics. Since the biomedical model focuses on external factors as the cause and solution of an illness, it overlooks internal factors, such as one's own health behaviours, which can play a key part in causing and solving health issues. Most women in the two studies attributed the cause of their UTI to lowered immunity in pregnancy that resulted in increased pharmaceuticalization in their lives. This led them to rely on antibiotics for a quick, albeit efficient, cure. The reliance on antibiotics was strongly indicated by the following quote, 'How will I ever get rid of this without antibiotics [is the] question that really dragged me down' (Study One, Lynn)

Conceptualisation of antimicrobial resistance

Women's conceptualisation of antimicrobial resistance (AMR) in the two studies was not considerably different from what has previously been described in the literature on public perceptions of AMR (Brookes-Howell et al., 2012; Brooks, Shaw, Sharp, & Hay, 2008; Norris et al., 2013) . The majority of women had heard about AMR and described it as a health threat due to antibiotics losing their effectiveness. Despite this awareness, however, uncertainty about the problem still existed. The main area where women expressed uncertainty was with regards to how AMR affects society versus an individual who is prescribed and uses antibiotics. Most women were unclear about how resistant bacteria transfer among people in close contact and spread across the social community to cause a rise in antimicrobial resistant infections.

> Well I assumed that it was an individual that built up resistance because they were given a lot of antibiotics and that eventually it stops working on that person. I'm not sure how it works if you've never taken antibiotics and then you need them. (Study Two, Participant 1, 31 years)

AMR was often referred to as a hypothetical problem that had the potential to be a significant health issue in the future if antibiotics were to 'eventually stop working'. It was not described as a current health threat that affects people in the present.

> I think I've heard in the media that they've [antibiotics] been overprescribed in the past and – and, we might end up at a point where some of us are resistant to uh, like, they won't help us. (Study Two, Participant 11, 29 years)

Despite viewing it as a future problem, AMR was acknowledged as a health risk that needed to be tackled. A few women suggested focusing on improving diagnostic support and increasing efforts to educate the public, however, most women were unsure about how they should respond to this issue. In this vein, they considered AMR as a problem affecting the healthcare sector that could therefore be best addressed through the increased awareness and efforts of healthcare professionals rather than members of the public.

> I would say there is a bit of an issue with GPs over prescribing antibiotics and there needs to be more awareness at the healthcare professional level. (Study Two, Participant 7, 32 years)

The uncertainty surrounding antibiotic use and how individuals could respond to AMR was often referred to in relation to the beneficial effects of antibiotics. As these medicines are valuable in treating infections, AMR posed a dilemma around how they could be used appropriately. As one interview participant (Study Two, Participant 8, 38 years) mentioned, antibiotics caused problems but they 'also save lives'.

Uncertainty surrounding AMR was also particularly apparent when women expressed confusion due to 'conflicting messages' about the consumption of antibiotics. Treatment with antibiotics normally occurs over a defined period of days, which is termed as the 'antibiotic course'. Traditional health advice encourages people to finish the treatment course, even if they feel they have recovered, to prevent re-infections with resistant bacteria. A small number of women, however, reported feeling a conflict with regards to whether they should finish the antibiotic course after being exposed to a different message in the news. For example,

> You get the odd media report saying that, you know, you shouldn't finish the course and your doctor's telling you to finish the course, so I think there is a lot of misinformation about resistance. (Study Two, Participant 3, 31 years)

The way women conceptualised AMR demonstrated a picture of uncertainty about their own role in tackling this health issue. They recognised AMR as a threat but one that affected

the health of the individual taking antibiotics rather than society as a whole. It was seen as a risk that might become problematic in the future, in contrast to a current and pressing issue. This way of conceptualising AMR reduces 'self-efficacy', that is their belief that they can do anything to reduce the rise of AMR, a construct that was introduced earlier. The uncertainty surrounding AMR coupled with anxiety over the risk of a UTI in pregnancy meant that most women delegated responsibility to health care professionals. They felt disempowered about the decision-making affecting their health, even though they recognised AMR as a health threat. In a small number of cases, because the short-term worry about UTIs upstaged the longer-term concerns about using antibiotics, women felt like they had to argue their case to ensure they were treated.

> The walk-in centre doctor tried to turn me away too with a negative dip result, but I argued the toss with her because I'd had so many that I knew what it was and she gave me the antibiotics. (Study One, Bella)

Overall, women's illness perceptions about UTIs in pregnancy and their conceptualisation of the effects of AMR on personal and societal health contributes to pharmaceuticalization in pregnancy. The uncertainties and risks associated with experiencing an infection, which can affect both their own and their baby's health, resulted in women considering antibiotics as a safe necessity while the health risks of AMR become overshadowed.

Pregnancy as deviation from the norm

Previous research into women's experiences have shown that UTIs can cause painful symptoms that might lead to a significant disruption to women's daily lives (Butler, Hawking, Quigley, & McNulty, 2015; Flower, Bishop, & Lewith, 2014; Malterud & Bærheim, 1999). The research studies discussed in this chapter also correspond with the previous research, as women frequently expressed their pain and discomfort if they had a symptomatic UTI. In addition to the unpleasant symptoms, however, women's concern for their child was clearly evident in their frustration and anxiety. Feelings of guilt due to developing an infection which put their unborn baby at risk was a significant difference between experiencing a UTI in pregnancy compared to when not pregnant. Descriptions of

the infection in relation to the pregnancy were therefore highly emotive and highlighted the pregnancy as a unique physiological state.

> I don't know why but it makes me feel like such a failure each time the results come back with an infection still present. I get angry with myself that I can't get my body to do its job to fight it and I'm putting my baby at risk. Stupid I know but I can't help it. (Study One, Nadia)

The increased anxiety due to the infection, because of the risks of the UTI in pregnancy, also affected how women considered the management of the infection. For example, a number of women described themselves as people who do not like taking antibiotics because of the side effects or because they had concerns about AMR. During pregnancy, however, they felt that it was their only option even if they had concerns about using medicines in pregnancy. The following quote demonstrates the reluctance of a woman to take antibiotics but changed her mind after communicating with a healthcare professional who convinced her to take them .

> Um, I – I think this is where she [pharmacist] just said, if – you know, if the infection goes from your urinary tract into the womb [sic] that it, it could be very very serious, that it could…it could go wrong very quickly. (Study Two, Participant 9, 43 years)

The distinctiveness of pregnancy also highlighted the issue with using any new alternative treatment to antibiotics. Although it might be useful in response to AMR, new treatments might not be an option for pregnant women because of concerns about how it might impact the foetus.

> It's a very good idea, anything that reduces the need for antibiotics. It depends what they are in some respects so if you're talking about probiotics or food supplements or something like that, that's one thing, but if it's a novel drug then you're always concerned about new drugs in pregnancy. (Study Two, Participant 3, 31 years)

Women's references to their pregnancy demonstrated that they had a strong maternal attachment that drove them to be concerned about the safe development of their baby. This 'pre-natal attachment' to the foetus before its birth has been described in literature and was derived from John Bowlby's Theory of Human Attachment (Bowlby, 1958). Pre-natal attachment can be described as 'the extent to which women engage in behaviours

that represent an affiliation and interaction with their unborn child'(Cranley, 1981). Research has shown the value of pre-natal attachment in promoting health behaviours, as women with higher levels of attachment are more receptive to adopting health protective behaviours (Lindgren, 2001; Magee et al., 2014). Almost all women strongly perceived UTIs to threaten the normal progression of their pregnancy and feared that developing an infection would hinder the normal growth of the foetus and also increase the risk of pre-term birth. Their main concern, therefore, arose not from experiencing debilitating symptoms but a fear for the safety of their child, particularly evident by women expressing worry even when they had asymptomatic infections. Pre-natal attachment to the baby also led some women to question the use of antibiotics during pregnancy. It was this same attachment and concern for their child, however, that meant they were convinced by healthcare professionals to use the antibiotics because it was in the best interests of their baby. In essence, the research studies highlighted feelings that are deeply emotive, as seen through women's illness perceptions, and conveyed a clear sense of maternal concern for their baby and less focus on the impact of the UTI on their own health. Pregnancy is therefore a state that deviates from the norm in terms of the immediate concerns that a non-pregnant individual, affected by ill health, might face.

Pre-natal attachment in competing health priorities

The nature of UTIs in pregnancy is a situation where a relatively common and easy to treat infection affects an individual whose health directly affects the health of another, the developing foetus. Pregnancy, therefore, presents multiple challenges for women as they seek to weigh the risks and benefits to their own health and the developmental health of their baby.

Both studies report women's distress when they develop a UTI during pregnancy because of debilitating symptoms that significantly affect their quality of life. Experiencing symptoms of a UTI at a time when women are already going through potentially uncomfortable physical changes be an emotional experience and cause feelings of frustration. At the same time, risks of a UTI such as pre-term birth or even miscarriage can be particularly frightening. This is especially true in circumstances where the pregnancy can be classed as 'precious', for example in cases where women struggled with infertility or a history of miscarriage. The use

of pharmaceuticals during pregnancy adds an additional layer of distress for some women. Research on the perceived risks of harm to the foetus has shown that women consider antibiotics to be moderately harmful in pregnancy (Petersen, McCrea, Lupattelli, & Nordeng, 2015). Although most women who participated in our research were quite optimistic about the safety of antibiotics, there was still a small proportion of women who experienced side effects or for whom using an antibiotic whilst pregnant was a source of anxiety. This was evident in some of the quotes in earlier sections and in the following quote, 'I'm petrified that taking amoxicillin will harm baby!' (Study One, Liza). The well-established risk of AMR that is associated with the use of antibiotics adds further complexity to this mix of issues. Health campaigns on AMR have been targeting the public with the message of conserving antibiotics to ensure they are effective when their need is essential. Faced with these issues, it would appear that women's behaviour is determined through a process of assigning priority to these problems.

The findings from the two studies presented in this chapter, show the crucial role of pre-natal attachment in women's decision-making about the management of UTIs during pregnancy. In the presence of multiple issues, it is the attachment to the foetus and the desire to protect and ensure its safety that primarily determines women's perceptions and behaviour. Therefore, while maintaining concerns about using antibiotics in pregnancy, women opt to use them to minimise the risks to their pregnancy from UTIs as these are the risks that they are more aware of and consider to be severe. Similarly, while recognising AMR as a risk to societal health, pre-natal attachment to the foetus remains the determining factor for mothers' reliance on antibiotics to achieve and maintain health.

Conclusion

This chapter summarises the research from two qualitative studies that explored women's experiences of UTIs during pregnancy and their perceptions of AMR. Women attributed pregnancy as the cause of their UTIs, due to lowered immunity that increased the risk of developing infections. Most considered it harder to get diagnosed and be treated for UTIs in pregnancy compared to when not pregnant. Similarly, they also viewed UTIs to be more serious in pregnancy because of risks such as pre-term birth and miscarriage. For these reasons, the majority of women expected and relied on antibiotics when they had

symptoms suggestive of a UTI, such as increased frequency of urination, even though these might be normal symptoms of pregnancy. Illness perceptions reflected in a biomedical model reduced self-efficacy and increased pharmaceuticalization in pregnancy. The women sought medical solutions (external) in favour of behaviour change (internal) that could ease symptoms and prevent infections.

AMR was conceptualised similarly to previous studies and many women were uncertain about how it affects society when it is an individual who is given antibiotics. Most also viewed AMR to be a future threat, with short-term worries about developing UTIs transcending their concern about resistant infections. Some women also expressed confusion about conflicting messages with regards to AMR that resulted in feelings of uncertainty about how this health issue could be tackled by them. The perceptions surrounding AMR also show reduced self-efficacy as women looked towards healthcare professionals for solutions and were uncertain about how they could be involved with tackling AMR.

Both the studies highlighted pregnancy as a unique state and a deviation from the non-pregnant norm in terms of how UTIs affect health. Pre-natal attachment to their baby was pivotal in shaping women's decision-making and behaviour. As the UTI not only affected their own health but also the development of the foetus, women had strong maternal feelings and, in some cases, expressed guilt about developing an infection. Since UTIs could result in negative outcomes for the pregnancy, women considered antibiotics to be a better and safer option than avoiding antibiotics, even when they had concerns about using pharmaceuticals during pregnancy. In this way, pregnancy was pharmaceuticalized in response to the high risks associated with a UTI in this population.

The research presented in this chapter demonstrates the complexity of issues that arise when women experience UTIs in pregnancy. Women have to consider their own health as well as the effects of the infection and treatment on their baby. At the same time the rising risk of AMR requires careful evaluation of antibiotics, which has been the focus of multiple public health campaigns discouraging excessive use. Faced with these competing priorities, women base their decisions on the best interest of their baby because of pre-natal attachment. Ultimately, this results in increased pharmaceuticalization through reliance on antibiotics, as the risks of AMR become eclipsed by the risks of a UTI.

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Appendix 15: COVID-19 Impact Statement

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To: **The Examiners and Doctoral Examinations Officer**

Subject: **COVID 19 impact statement**

The purpose of this statement is to highlight the impact of the COVID-19 pandemic on the research activities related to the completion of the doctoral thesis entitled, 'Behavioural Insights into Tackling Antimicrobial Resistance and Urinary Tract Infections during Pregnancy'.

In March 2020, the research plan was to focus on completing the analysis and write up of the fourth audit study for publication (achieved), and recruit and interview participants for the fifth interview study with prescribers (pending). The goal for the fifth study had been to interview 10-20 healthcare professionals and write up the results for publication in a peer-reviewed journal. The final thesis would then have comprised a set of five published research articles to provide a comprehensive overview of antibiotic use and prescribing for UTIs in pregnancy.

The fifth study had been designed and obtained ethical approval for conduct, however the progress of the study was affected by the COVID-1 pandemic. The lockdown affected the availability of GPs and allied healthcare professionals to participate in research activity as they had to restructure and prioritise their workload in response to the health threat from COVID-19. This had a direct effect on recruitment for the final study and a decision was therefore made to hold off recruitment until clinical and research activities returned to normality. Upon further reflection with the way that the pandemic outcomes enfolded, and subsequent lockdown measures enforced, the difficult decision was eventually made to allow ongoing recruitment but analyse and include data that had been collected to date. The rationale for this decision was the valuable insight provided by the initial data whilst still subject to further analysis and interpretation. The preliminary analysis is therefore included in chapter seven in the form of a thesis chapter and has also been noted in the discussion chapter as a limitation of the research.

With sincere gratitude for your time and consideration,

Flavia Ghouri