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The Medication Dilemma in Pregnancy: Balancing Efficacy and Safety

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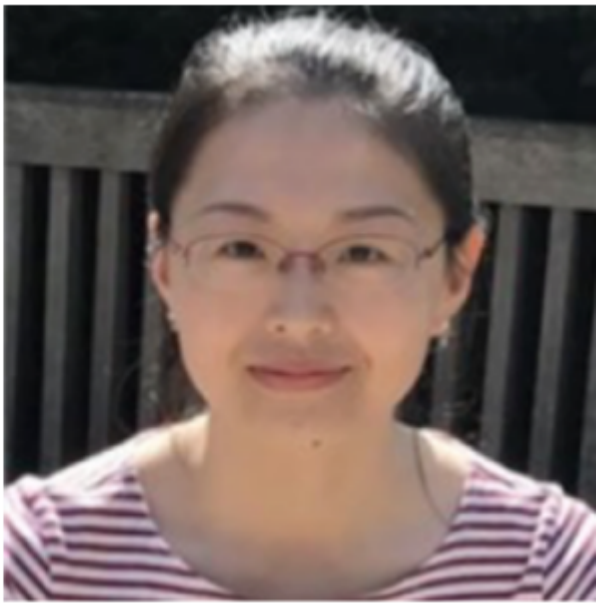

By Dr Megha Singh, MuM-PreDiCT programme manager, and Dr Jingya Wang, epidemiologist, University of Birmingham

Introduction

Pregnancy represents a unique physiological state that necessitates careful consideration of both maternal well-being and fetal development. A particularly complex challenge in this context is the use of medications. On the one hand, untreated maternal health conditions can result in serious complications for both the pregnant person and the developing baby; on the other, certain medications may cross the placental barrier and affect the baby. Because pregnancy is a unique physiological state, the short- and long-term effects of drug use on both maternal and child health remain incompletely understood. This article discusses the core components of this dilemma, the clinical scenarios in which it commonly arises, the frameworks available to support clinical decision-making, and future directions for improving care.

1. Why is medication use in pregnancy so complex?

Medication use in pregnancy is particularly complex because of several overlapping factors. Pregnancy induces major physiological changes that alter the way medicines are absorbed, distributed, metabolised, and eliminated, including increased blood volume, enhanced renal clearance, and changes in liver enzyme

activity, which may necessitate dose adjustments. Yet most medicines are not tested in pregnant populations, making it difficult to predict the pharmacokinetics[1] in this setting. At the same time, polypharmacy[2] is increasingly common among women of reproductive age, driven in part by chronic illness, older maternal age, and multimorbidity (having two or more co-existing medical conditions), and to some extent by the medicalisation of conditions that, rightly or wrongly, were previously framed as part of the human condition.[3] This raises important questions about whether specific medicines are linked to adverse maternal or infant health outcomes.[4] Research is further constrained by ethical and legal considerations: pregnant women have historically been excluded from clinical trials due to concerns about fetal safety, leaving clinicians reliant on observational studies, case reports, and post-marketing surveillance to guide prescribing decisions.[5, 6]

Another layer of complexity arises from the potential risks to fetal development. Medications can cross the placenta, and exposure during the first trimester, when organs are forming, can be especially harmful. Some drugs are well-recognised teratogens (drugs that can cause congenital anomalies[7]), while others may affect fetal growth, neurodevelopment, or increase the risk of miscarriage or stillbirth. However, not treating maternal illness may carry equal or greater risks.[8, 9]

These challenges play out in several common clinical scenarios. Mental health disorders such as depression and anxiety are common during pregnancy, and selective serotonin reuptake inhibitors (SSRIs - a class of antidepressants) like fluoxetine are associated with a number of potential risks, including neonatal adaptation syndrome[10] and, rarely, persistent pulmonary hypertension of the newborn.[11] However, untreated maternal depression increases risks of poor antenatal care, substance misuse, preterm birth, and maternal suicide. Fluoxetine is one of the most extensively studied SSRIs, with overall evidence supporting its use when benefits outweigh risks.[12, 13] Hypertension, including chronic hypertension and pre-eclampsia, is a leading cause of maternal and perinatal complications. Antihypertensives such as labetalol and methyldopa are generally considered safe, whereas angiotensin-converting enzyme inhibitors and angiotensin receptor blockers are contraindicated due to links with fetal renal and skeletal abnormalities. Early adjustment of therapy, ideally before conception, is recommended.[14]

Epilepsy poses another dilemma: seizures increase risks of trauma, hypoxia, and miscarriage, but some antiepileptic drugs, particularly valproate, are strongly linked to neural tube defects and impaired cognitive outcomes. Using safer options, such as lamotrigine, at the lowest effective dose and supplementing with high-dose folic acid is the preferred strategy.[15, 16]

Autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis, and inflammatory bowel disease often require ongoing treatment. While teratogenic immunosuppressants such as methotrexate and mycophenolate should be avoided, other agents like hydroxychloroquine, azathioprine, and low-dose corticosteroids are considered safe under medical supervision. Disease control before and during pregnancy is crucial, as active disease itself increases risks of pre-eclampsia and preterm birth.[17] Infections are also common, as pregnancy alters immune function. Here, careful drug choice is essential: tetracyclines (a class of antibiotics) are avoided due to adverse effects on fetal

bone and teeth development, whereas penicillins and cephalosporins (both types of antibiotics) are widely considered safe.[18]

Clinical decisions regarding the prescribing of medication in pregnancy must therefore be guided by a thorough assessment of the potential benefits to the mother against possible risks to the fetus, in discussion with the mother, who will make the final decision on its use.[19]

2. Improving information on medication in pregnancy

Over the past decade, several initiatives have sought to improve the safety of medication use in pregnancy. In the US, the FDA[20] (Food and Drug Administration), replaced the outdated pregnancy letter categories with the Pregnancy and Lactation Labeling Rule (PLLR), which provides structured risk summaries and clinical guidance.[21] In Europe and the UK, regulators introduced stricter risk minimisation for teratogens, such as valproate, through pregnancy prevention programmes.[22] Open-access teratology information services, including UKTIS/Best Use of Medicines in Pregnancy (BUMPS) and MotherToBaby, now provide evidence-based safety summaries for both clinicians and patients.[23, 24] Professional societies such as the American College of Obstetricians and Gynecologists (ACOG) have issued condition-specific guidelines, for example on perinatal mental health, emphasising the importance of balancing medication risks with the consequences of untreated illness.[25] At the research level, international methodological standards have been established for pharmacoepidemiology[26] in pregnancy,[27] and large population-based studies have clarified risks of commonly used medicines, such as the association between late-pregnancy SSRI exposure and persistent pulmonary hypertension of the newborn.[28] Public health programmes like CDC's *Treating for Two* further integrate research, policy, and communication to support safer prescribing.[29]

3. MuM-PreDiCT's contribution

The MuM-PreDiCT team studied medicine use in pregnancy to understand how common it is for women to take several medicines at once (polypharmacy), what factors make this more likely, and whether certain medicines are linked to pregnancy or baby health problems.

A review of previous studies found that between 5% and 62% of pregnant women are prescribed two or more medicines, but little is known about how this affects women with multiple health conditions or their babies.[30] A qualitative study revealed women with multiple health conditions in pregnancy often received conflicting or inconsistent medication advice, leading to mistrust, fear, and the need to search for information themselves. Healthcare professionals acknowledged that clearer preconception counselling and better-coordinated, team-based care could reduce confusion and improve women's confidence in medication decisions.[31]

Using GP records from over 800,000 UK pregnancies (2000–2019), researchers found that about 1 in 4 women took two or more medicines in the first trimester, rising to over 1 in 2 across the whole pregnancy. The most common prescriptions were antibiotics, painkillers, and treatments for infections, as well as combinations for long-term conditions like asthma and depression. Women were more likely to

be prescribed multiple medicines if they were younger or older, had a high BMI, smoked, had multiple health problems, came from ethnic minority backgrounds, had several previous pregnancies, or lived in more deprived areas.[32]

A separate study (not yet published) has used records from over 1.5 million pregnancies (2000–2022) to systematically examine links between over 600 medicines and 36 health outcomes for mothers and babies during pregnancy (e.g. miscarriage, pre-eclampsia), the perinatal period (e.g. preterm birth, small for gestational age), and the postpartum period (e.g. postnatal mental illness, neonatal congenital anomalies). Out of over 88,000 comparisons, about 2,800 possible signals were found — meaning a medicine and outcome occurred together more often than expected. These findings don't prove cause and effect but point to medicines that need more safety research.

In short: taking multiple medicines during pregnancy is common and increasing, especially among women with health problems or certain social factors. While many medicines are necessary and safe, more research is needed to fully understand the risks and benefits for mothers and babies

4. Further work needed

Clinical decision-making around medication use in pregnancy must be guided by a careful risk–benefit analysis, weighing maternal health needs against possible fetal risks, while also recognising that not treating maternal illness can lead to more serious adverse outcomes.[33] Ensuring pregnant individuals receive balanced, comprehensible information and that their preferences are central to treatment choices is critical.[34] In practice, this requires clear communication and patient-centred counselling rather than reliance on rigid categorisation systems.

In more complex cases, a multidisciplinary approach is essential. Collaboration between general practitioners, obstetricians, maternal medicine specialists, psychiatrists, neurologists, and pharmacists helps optimise care where both maternal and fetal outcomes are at stake—for example, in epilepsy, severe mental illness, or autoimmune conditions.[35] Looking ahead, progress will depend on ethically including pregnant individuals in research, strengthening real-world evidence from linked datasets[36], and embedding structured communication tools[37] into clinical care. Ultimately, a patient-centred, evidence-informed, and team-based approach remains key to navigating the medication dilemma in pregnancy.[38]

Conclusion

The safe use of medications during pregnancy is a complex but essential aspect of maternal healthcare. Clinicians must weigh the potential risks of pharmacological treatment against the dangers of untreated illness, often in the context of limited evidence. Ethical inclusion of pregnant individuals in research, better data collection, and enhanced communication between clinicians and patients are essential steps toward improving decision-making in this area. A patient-centred, multidisciplinary, and evidence-informed approach remains key to navigating the medication dilemma in pregnancy.

Author Bios:

Dr Megha Singh is a Research Fellow at the Institute of Applied Health Sciences, University of Birmingham. She trained as a medical doctor and completed a Master's in Public Health, gaining extensive experience in maternal and reproductive health research across the UK, India, and South Africa.Megha has contributed to projects supporting the development of healthcare professionals and the translation of research into practice. In her current role, she works with colleagues to deliver research that improves understanding of maternal long term health conditions and their influence on pregnancy pathways and care trajectories.

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Readers may also want to look at these AIMS information pages:

- Medications in pregnancy
- Medications and breastfeeding

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1 Pharmacokinetics is the process by which (or the study of how) the body interacts with administered substances for the entire duration of exposure

2 Editor's note: Polypharmacy is the regular use of multiple medications by a single person, often due to having several health conditions.

3 Martínez, M. D. L. L. C. (2023) The medicalization of life: An interdisciplinary approach. Heliyon Volume 9, Issue 6. https://www.sciencedirect.com/science/article/pii/S2405844023038446

4 Adam, M.P., J.E. Polifka, and J.M. Friedman, *Evolving knowledge of the teratogenicity of medications in human pregnancy*. Am J Med Genet C Semin Med Genet, 2011. **157c**(3): p. 175-82. https://2024.sci-hub.st/6201/20f861192ea90a734b7d499c58ece09c/adam2011.pdf

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6 Blehar, M.C., et al., *Enrolling pregnant women: issues in clinical research*. Women's Health Issues, 2013. **23** (1): p. E39-45.

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7 Editor's note: Congenital anomalies are unusual conditions that a baby is born with.

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10 Editor's note: Neonatal adaptation syndrome, also known as poor neonatal adaptation (PNA), is a withdrawal-like reaction in newborns whose mothers took certain medications during pregnancy, especially SSRIs.

MGH (2015) SSRIs and Poor Neonatal Adaptation: How Long Do the Symptoms Last?

https://womensmentalhealth.org/posts/ssris-and-poor-neonatal-adaptation-how-long-do-the-symptoms-last/

NHS Wales (2019) Guidance for Newborn Assessment Exposed to Psychotropic Medication In-Utero

https://share.google/54J1BZ7Z6atAmuAQH

11 Marchocki Z, Russell NE, Donoghue KO. Selective serotonin reuptake inhibitors and pregnancy: A review of maternal, fetal and neonatal risks and benefits. Obstet Med. 2013 Dec;6(4):155-8. doi: 10.1177/1753495X13495194. Epub 2013 Aug 8. PMID: 27656248; PMCID: PMC5004326. https://pmc.ncbi.nlm.nih.gov/articles/PMC5004326/#sec2-1753495X13495194

12 Howard, L.M., et al., *Non-psychotic mental disorders in the perinatal period.* Lancet, 2014. **384**(9956): p. 1775-88.

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14 Cooper, W.O., et al., *Major congenital malformations after first-trimester exposure to ACE inhibitors.* N Engl J Med, 2006. **354**(23): p. 2443-51. https://www.nejm.org/doi/full/10.1056/NEJMoa055202

15 Inoyama, K. and K.J. Meador, *Cognitive outcomes of prenatal antiepileptic drug exposure.* Epilepsy Res, 2015. **114**: p. 89-97. https://pmc.ncbi.nlm.nih.gov/articles/PMC4475275/

16 Meador, K.J., et al., *Effects of periconceptional folate on cognition in children of women with epilepsy: NEAD study*. Neurology, 2020. **94**(7): p. E729-e740. https://pmc.ncbi.nlm.nih.gov/articles/PMC7176294/

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18 Stock, S.J. and J.E. Norman, *Medicines in pregnancy*. F1000Res, 2019. **8**. https://f1000research.com/articles/8-911

19 Lynch, M.M., et al., *Making Decisions About Medication Use During Pregnancy: Implications for Communication Strategies.* Matern Child Health J, 2018. **22**(1): p. 92-100. https://europepmc.org/backend/ptpmcrender.fcgi?accid=PMC5764786&blobtype=pdf

20 Editors' note: The FDA is a federal agency responsible for protecting public health by ensuring the safety of foods, drugs and other products.

21 *FDA. Pregnancy and Lactation Labeling Final Rule (PLLR). 2021https://www.fda.gov/drugs/labeling-information-drug-products/pregnancy-and-lactation-labeling-resources#:~:text=The%20PLLR%20requires%20changes%20to,need%20to%20take%20medication%2C%20thus.*

22 Eriksson, S., P. Tittensor, and S. Sisodiya, *National compliance with UK wide guidelines for usage of valproate in women of childbearing potential.* Seizure, 2022. **98**: p. 8-12. https://www.sciencedirect.com/science/article/pii/S105913112200070X

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26 Pharmacoepidemiology is a "bridge science" that applies the methods of epidemiology (the study of disease in populations) to pharmacology (the study of drugs), focusing on the uses, benefits, risks, and effectiveness of medical products in large human populations.

27 *European Network of Centres for Pharmacoepidemiology and Pharmacovigilance https://encepp.europa.eu/encepp-toolkit/methodological-guide_en*

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32 Subramanian, A., et al., *Polypharmacy during pregnancy and associated risk factors: a retrospective analysis of 577 medication exposures among 1.5 million pregnancies in the UK, 2000-2019.* BMC Medicine, 2023. **21**(1): p. 21. https://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-022-02722-5

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34 Barry, M.J. and S. Edgman-Levitan, *Shared decision making--pinnacle of patient-centered care.* N Engl J Med, 2012. **366**(9): p. 780-1.

35 Harris, R.C., et al., *Multidisciplinary management of pregnancy in complex congenital heart disease: a model for coordination of care.*

Congenit Heart Dis, 2014. **9**(6): p. E204-11.

36 Editor's note: Real-world evidence is clinical evidence about the benefits or risks of a medical product, derived from analyzing data collected from routine patient care, not controlled clinical trials.

37 Editor's notes: Structured communication tools in clinical care, like SBAR (Situation, Background, Assessment, Recommendation), provide a standardised framework for healthcare teams to share information efficiently, improving patient safety and care quality.

38 Sinclair, S.M., et al., *Medication Safety During Pregnancy: Improving Evidence-Based Practice.* J Midwifery Womens Health, 2016. **61**(1): p. 52-67.