Evidence for the use of RT in Pregnancy

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Pharmacological management of acute disturbance
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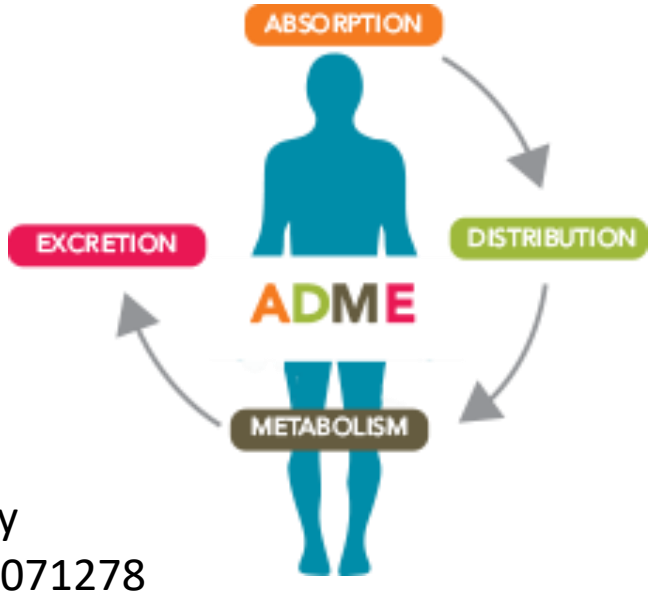
Prescribing RT in Pregnancy

- Prescribing for women
  - Prescribing for pregnant women[1]
    - Prescribing for acute mental illness in pregnancy
      - **Prescribing RT for pregnant women**

QTc prolongation
% body fat
% body water
Gut motility
Metabolism
Renal blood flow & GFR



1. Facilitating participation in clinical trials during pregnancy
Vousden *BMJ* 2023;380:e071278 | doi: 10.1136/bmj-2022-071278

Psychopharm

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SAGE

British Association for Psychopharmacology consensus guidance on the use of psychotropic medication preconception, in pregnancy and postpartum 2017

R Hamish McAllister-Williams[1,2], David S Baldwin[3,4], Roch Cantwell[5], Abby Easter[6], Eilish Gilvarry[2,7], Vivette Glover[8], Lucian Green[9], Alain Gregoire[3,10], Louise M Howard[11,12], Ian Jones[13], Hind Khalifeh[11,12], Anne Lingford-Hughes[14], Elizabeth McDonald[15,16,17], Nadia Micali[18], Carmine M Pariante[12,19], Lesley Peters[20], Ann Roberts[20,21,22], Natalie C Smith[23], David Taylor[12,24], Angelika Wieck[25,26], Laura M Yates[27,28] and Allan H Young[12,19]; endorsed by the British Association for Psychopharmacology

Abstract

Decisions about the use of psychotropic medication in pregnancy are an ongoing challenge for clinicians and women with mental health problems, owing to the uncertainties around risks of the illness itself to mother and fetus/infant, effectiveness of medications in pregnancy and risks to the fetus/infant from in utero exposure or via breast milk. These consensus guidelines aim to provide pragmatic advice regarding these issues. They are divided into sections on risks of untreated illness in pregnancy; general principles of using drugs in the perinatal period; benefits and harms associated with individual drugs; and recommendations for the management of specific disorders.

Prescribing in Pregnancy

- **Pharmacological and pharmacokinetic changes**
  - variations in clearance between trimesters;
  - increased glomerular filtration rate;
  - expansion of plasma volume
    - which subsequently returns to pre-pregnancy states soon after delivery
  - Avoiding drugs that may accumulate in both maternal and foetal tissues is an advisable precautionary measure; for example by not prescribing oral diazepam and selecting medication with a short half-life

(McAllister-Williams et al., 2017).

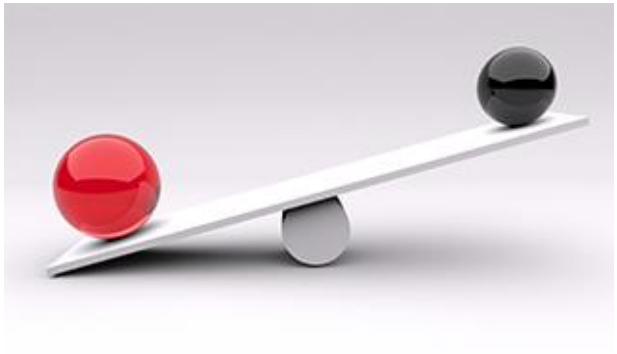
Prescribing in Pregnancy – Weighing it up

Treating

- Medication risks to the foetus relate to *ongoing use*, not single doses
- May ↑ baseline risk of structural malformations (1st trimester)
- May affect foetal development, growth defects
- May lead to complications at birth (3rd trimester)
  - floppy baby syndrome with benzodiazepines
  - EPS with antipsychotics
- ↑ risk of teratogenicity if multiple medicines
- In 2nd & 3rd trimesters developing organs are susceptible to damage
- Teratogenicity usually dose-dependent, dose response curve is steep
- Direct effects of RT on the neonate are likely to be minimal
- The risks associated with use of restraint and any ongoing treatment

Not treating

- Risks to the foetus/ neonate if the mother's mental illness relapses due to no treatment

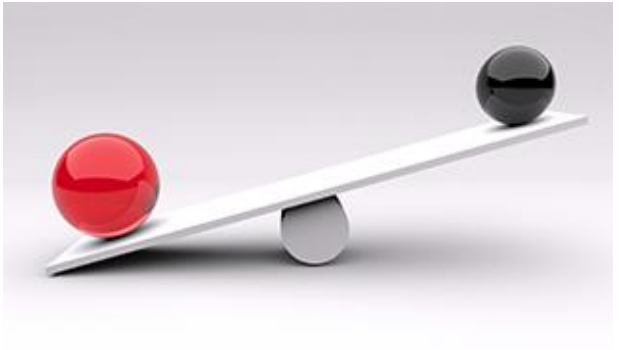


Prescribing in Pregnancy – Weighing it up

How do you decide on the risk?

Individual

- What happens when she becomes unwell?
- How serious is her illness?
- What has been tried in the past?
  - Medications & non-drug options
- What is her current treatment?
- What are the treatment options?



Prescribing RT in Pregnancy – The evidence

- A retrospective case series (n=80), 39% of pregnant women received oral (pre-RT) or IM (RT) medication for agitation in the USA emergency department; the authors did not make any active recommendations as to what to use (Ladavac et al., 2007).

Prescribing RT in Pregnancy – Recommended medicines

- IM **lorazepam**, **haloperidol** & **promethazine***
- Minimal efficacy evidence in this population
  - NO tx isn't better, extrapolate in data absence
- No evidence to suggest these should not be used in a pregnant woman
- Absence of specific efficacy data in this population, so it is recommended that these agents are used
  - as per recommendations for non-pregnant women
- No license contraindications
- Regular dosing has more impact on the neonate than stat RT doses

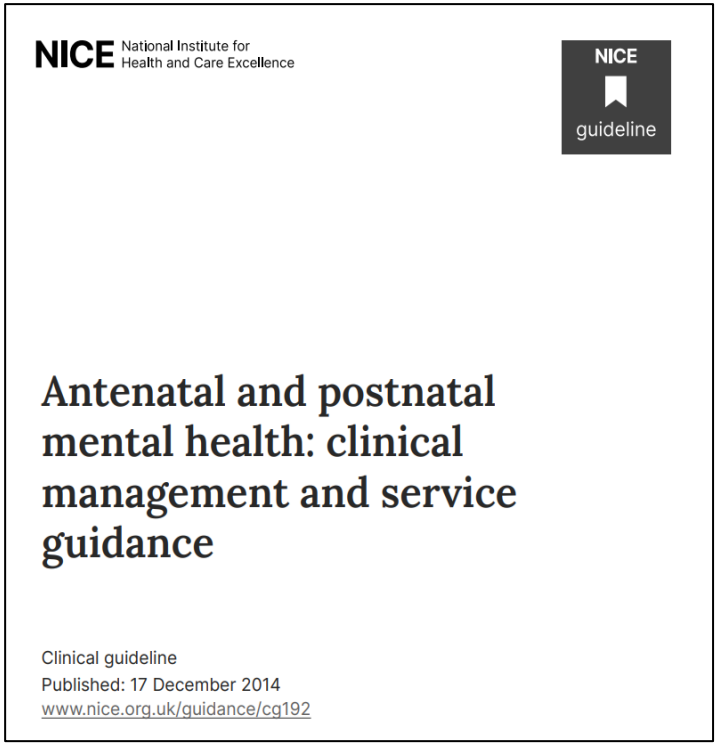
* Several meta-analyses and guidelines have concluded that promethazine is safe in pregnancy for the ongoing management of nausea and hyperemesis gravidarum, and recommend it.

Prescribing in Pregnancy – Benzodiazepines

- **Teratogenicity** - studies are conflicting about a possible association with increased risk of congenital malformation, specifically of orofacial clefts
  - Older studies suggest possible increased risks of congenital malformation, including orofacial clefts and cardiac malformations.
  - More recent, better designed studies, have failed to identify such associations

Prescribing in Pregnancy – Antipsychotics

- Overall the data for the majority of antipsychotics do not suggest increased risk of major malformations or adverse foetal outcomes
- Consider side effects, particularly metabolic

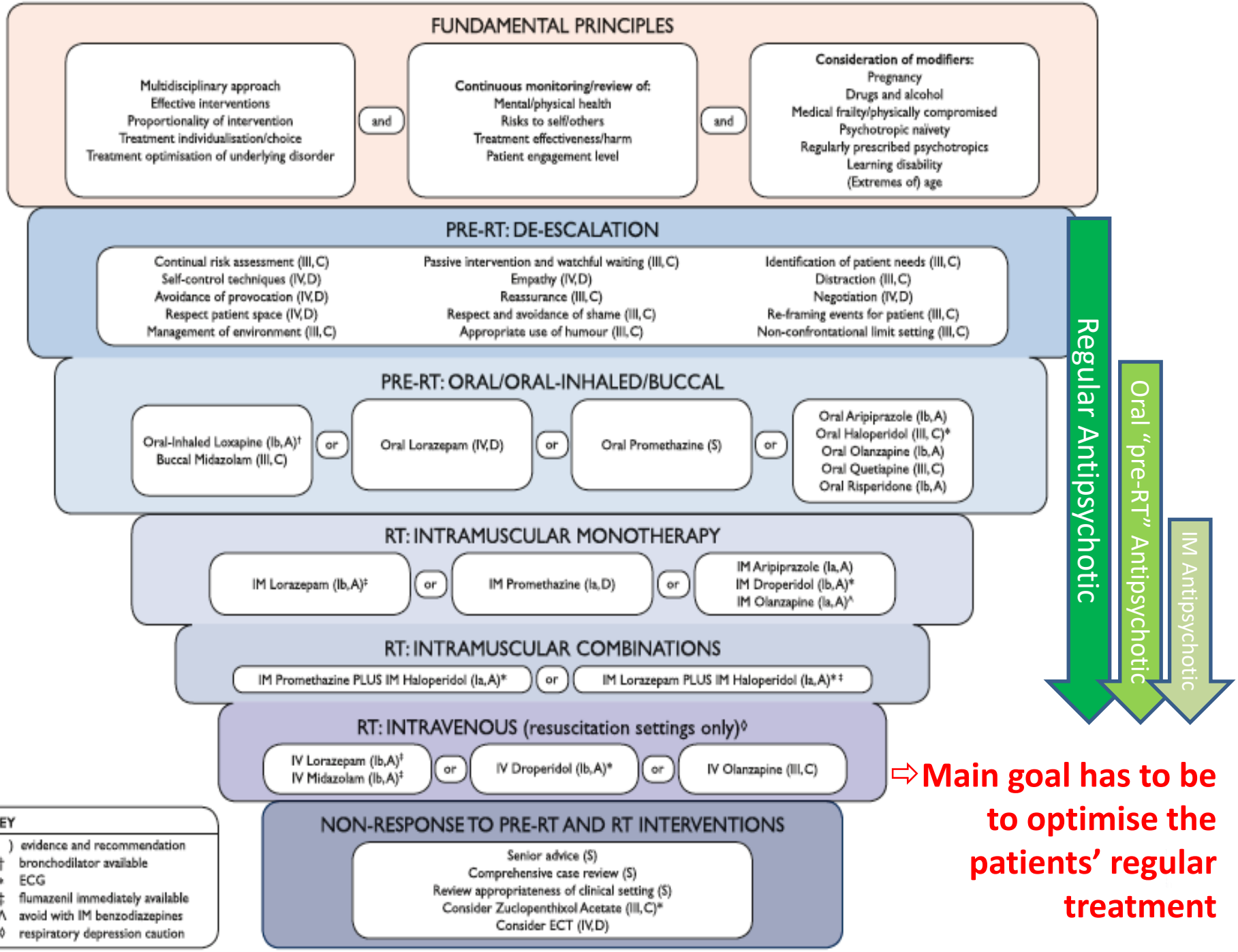


Antenatal and postnatal mental health: clinical management and service guidance (nice.org.uk)

Prescribing in Pregnancy – Promethazine

- Several recent meta-analyses and guidelines have concluded that promethazine is safe to use pregnancy in the ongoing management of nausea and hyperemesis gravidarum and recommend it.
- *"A number of dopamine antagonists may be used to treat NVP: phenothiazines (eg, chlorpromazine, perphenazine, prochlorperazine, promethazine, and trifluoperazine), domperidone, droperidol, metoclopramide, and trimethobenzamide. Anecdotal case reports have associated first trimester phenothiazine use with major malformations. However,* ***the bulk of evidence suggests that phenothiazines show no evidence of teratogenicity…..****"*

Magee LA, Mazzotta P, Koren G. Evidence-based view of safety and effectiveness of pharmacologic therapy for nausea and vomiting of pregnancy (NVP). Am J Obstet Gynecol 2002;186 Suppl 2:S256–61.
http://download.xuebalib.com/xuebalib.com.24865.pdf
The Management of Nausea and Vomiting of Pregnancy and Hyperemesis Gravidarum"
2016. https://www.rcog.org.uk/globalassets/documents/guidelines/green-top-guidelines/gtg69-hyperemesis.pdf
Full NICE guideline CG62 "Antenatal care routine care for the healthy pregnant woman"


FUNDAMENTAL PRINCIPLES
Multidisciplinary approach
Effective interventions
Proportionality of intervention
Treatment individualisation/choice
Treatment optimisation of underlying disorder
and
Continuous monitoring/review of:
Mental/physical health
Risks to self/others
Treatment effectiveness/harm
Patient engagement level
and
Consideration of modifiers:
Pregnancy
Drugs and alcohol
Medical frailty/physically compromised
Psychotropic naïvety
Regularly prescribed psychotropics
Learning disability
(Extremes of) age
PRE-RT: DE-ESCALATION
Continual risk assessment (III, C)
Self-control techniques (IV, D)
Avoidance of provocation (IV, D)
Respect patient space (IV, D)
Management of environment (III, C)
Passive intervention and watchful waiting (III, C)
Empathy (IV, D)
Reassurance (III, C)
Respect and avoidance of shame (III, C)
Appropriate use of humour (III, C)
Identification of patient needs (III, C)
Distraction (III, C)
Negotiation (IV, D)
Re-framing events for patient (III, C)
Non-confrontational limit setting (III, C)
PRE-RT: ORAL/ORAL-INHALED/BUCCAL
Oral-Inhaled Loxapine (Ib, A)†
Buccal Midazolam (III, C)
or
Oral Lorazepam (IV, D)
or
Oral Promethazine (5)
or
Oral Aripiprazole (Ib, A)
Oral Haloperidol (III, C)*
Oral Olanzapine (Ib, A)
Oral Quetiapine (III, C)
Oral Risperidone (Ib, A)
RT: INTRAMUSCULAR MONOTHERAPY
IM Lorazepam (Ib, A)‡
or
IM Promethazine (Ia, D)
or
IM Aripiprazole (Ia, A)
IM Droperidol (Ib, A)*
IM Olanzapine (Ia, A)^
RT: INTRAMUSCULAR COMBINATIONS
IM Promethazine PLUS IM Haloperidol (Ia, A)*
or
IM Lorazepam PLUS IM Haloperidol (Ia, A)*‡
RT: INTRAVENOUS (resuscitation settings only)◊
IV Lorazepam (Ib, A)†
IV Midazolam (Ib, A)‡
or
IV Droperidol (Ib, A)*
or
IV Olanzapine (III, C)
NON-RESPONSE TO PRE-RT AND RT INTERVENTIONS
Senior advice (5)
Comprehensive case review (5)
Review appropriateness of clinical setting (5)
Consider Zuclopenthixol Acetate (III, C)*
Consider ECT (IV, D)
KEY
( ) evidence and recommendation
† bronchodilator available
* ECG
‡ flumazenil immediately available
^ avoid with IM benzodiazepines
◊ respiratory depression caution
Regular Antipsychotic
Oral "pre-RT" Antipsychotic
IM Antipsychotic
⇨Main goal has to be to optimise the patients' regular treatment