The hypertensive disorders of pregnancy (HDPs) – best practices

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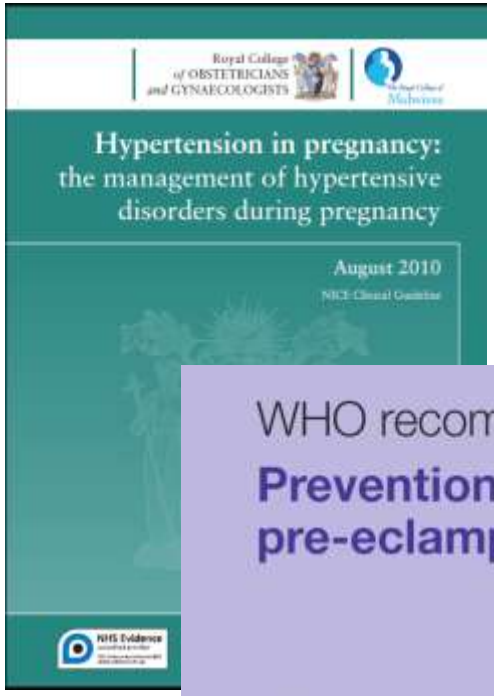
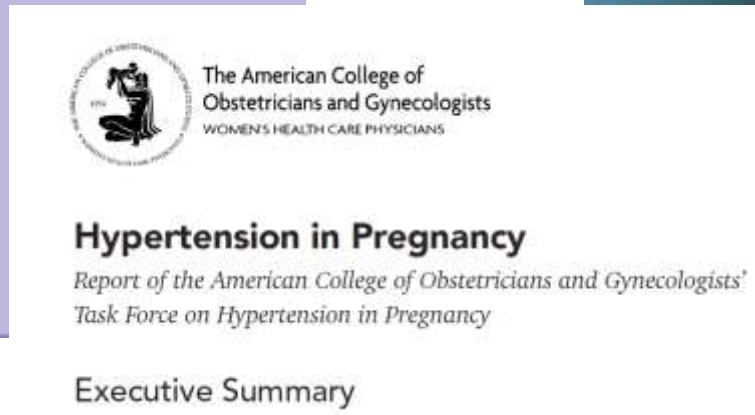
Women Deliver

16 May 2016

Guidelines for the hypertensive disorders of pregnancy (HDP)

2010-2014





Review of the clinical practice guidelines (CPGs), 2014

PLOS ONE

RESEARCH ARTICLE

Hypertensive Disorders of Pregnancy: A Systematic Review of International Clinical Practice Guidelines

Tessa E. R. Gillon[1], Anouk Pels[2], Peter von Dadelszen[3,4], Karen MacDonell[5], Laura A. Magee[3,4,6,7*]

- Broad search, 2003-13, English, French, German, or Dutch
- 13 CPGs, 3 multinational (ISSHP, WHO, and ESC)
- Tough to summarise: 3-1188 pages in length, 8 different grading systems, no guideline scored ≥80% on every domain of AGREE II for assessment of guideline methodological quality

Consistency – potential for prioritisation and standardisation

- Definitions
  - Hypertension
  - Chronic hypertension, gestational hypertension
- Prevention of pre-eclampsia among women at increased risk
  - Low-dose aspirin
  - Calcium when baseline intake is low
  - NOT vitamins C&E or diuretic therapy
- Management
  - Antihypertensives for severe hypertension
  - $MgSO_4$ for eclampsia, 'severe' pre-eclampsia
  - Antenatal corticosteroids when delivery likely within 7d
  - Delivery for pre-eclampsia either before fetal viability or at term
  - Active management of third stage of labour with oxytocin

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  - Low-dose aspirin
  - Calcium when baseline intake is low
  - NOT vitamins C&E or diuretic therapy
- Management
  - Antihypertensives for severe hypertension
  - *Antihypertensive therapy for non-severe hypertension (target dBP)*
  - MgSO4 for eclampsia, 'severe' pre-eclampsia, *and fetal neuroprotection*
  - Antenatal corticosteroids when delivery likely within 7d
  - Delivery for pre-eclampsia either before fetal viability or at term
    - *Expectant care at 34-36 weeks*
  - Active management of third stage of labour with oxytocin

Diagnosing hypertension requires BP measurement

- Guidelines are based on the assumption that BP is measured and that we can find the 5-10% of pregnant women who are hypertensive
- Although BP measurement is one of the more commonly received components of ANC in under-resourced settings, many women still do not have their BP measured
- AND there is variability in rates of BP measurement from country to country, according to DHS results:
  - >90% of women in Cambodia and Ghana
  - ~85% in Nepal, Pakistan and Rwanda
  - Only 53% in Laos
  - Variable in many African countries, such as 75% in Malawi, 52.5% in Uganda, and 40% in Kenya

Ref: The FIGO textbook of pregnancy hypertension – an evidence-based guide to monitoring, prevention and management 2016 (in press)

Diagnosing hypertension

- **Low-cost devices and novel technologies for interpretation are being tested**

CRADLE device (BMGF)

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mHealth application – POM (Piers On the Move) (BMGF)

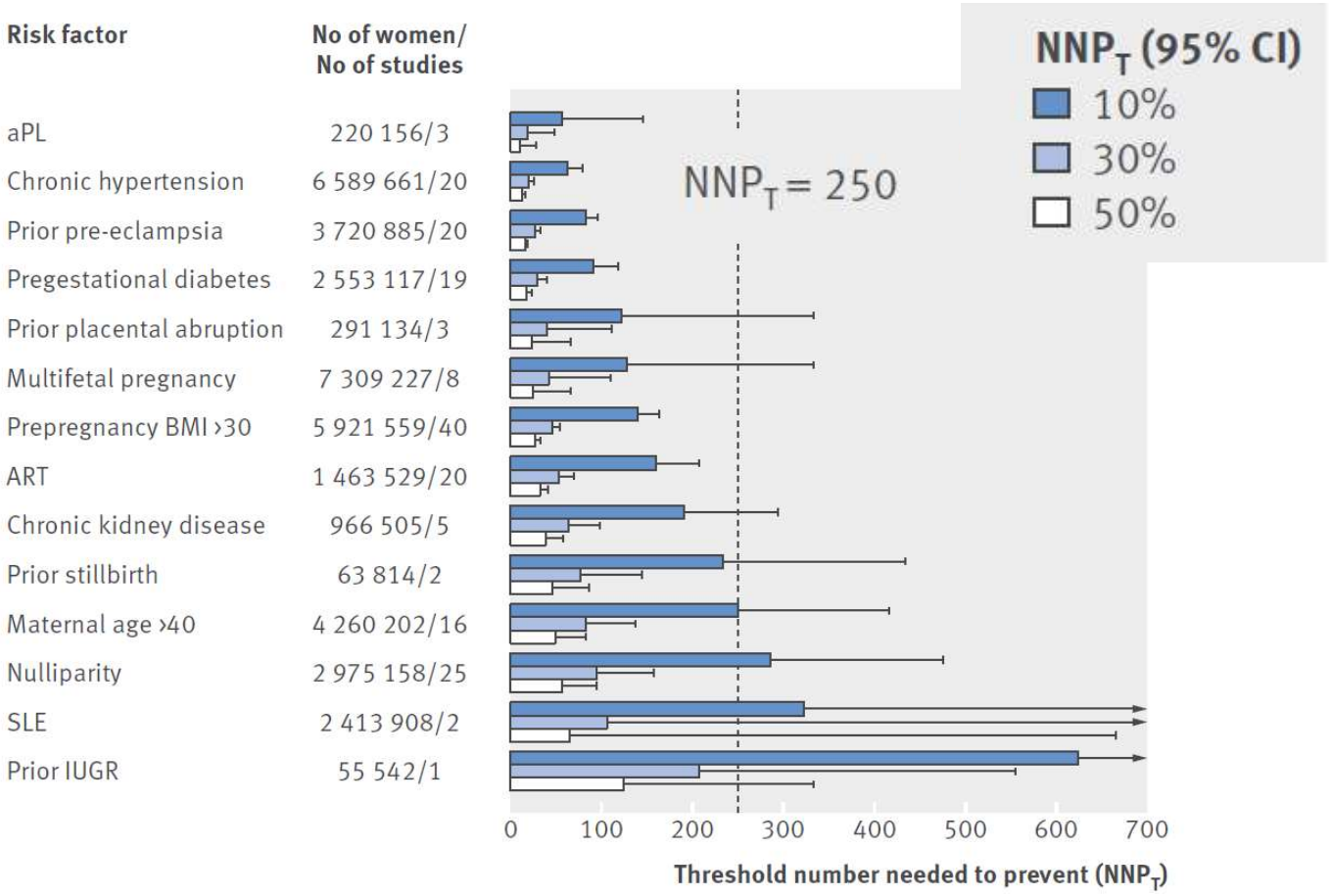
Prevention of pre-eclampsia

- Screening only by clinical risk markers is recommended with no guideline recommending routine use of biomarkers or ultrasound
- The actual risk markers were not reviewed, and the list is long…
- Among women at increased risk of pre-eclampsia
  - Low-dose aspirin (60–162 mg/d) [ACOG, AOM, NICE, SOGC, WHO]
    - From early pregnancy [ACOG, AOM, NICE, SOGC, WHO] until delivery [AOM, NICE, SOGC]
  - Calcium supplementation (1–2.5 g/d) if calcium intake is low [AOM, WHO, SOGC]

Clinical risk factors for pre-eclampsia determined in early pregnancy: systematic review and meta-analysis of large cohort studies

Emily Bartsch,[1] Karyn E Medcalf,[1] Alison L Park,[2] Joel G Ray[3] on behalf of the High Risk of Pre-eclampsia Identification Group

BMJ 2016;353:i1753 (http://dx.doi.org/10.1136/bmj.i1753)



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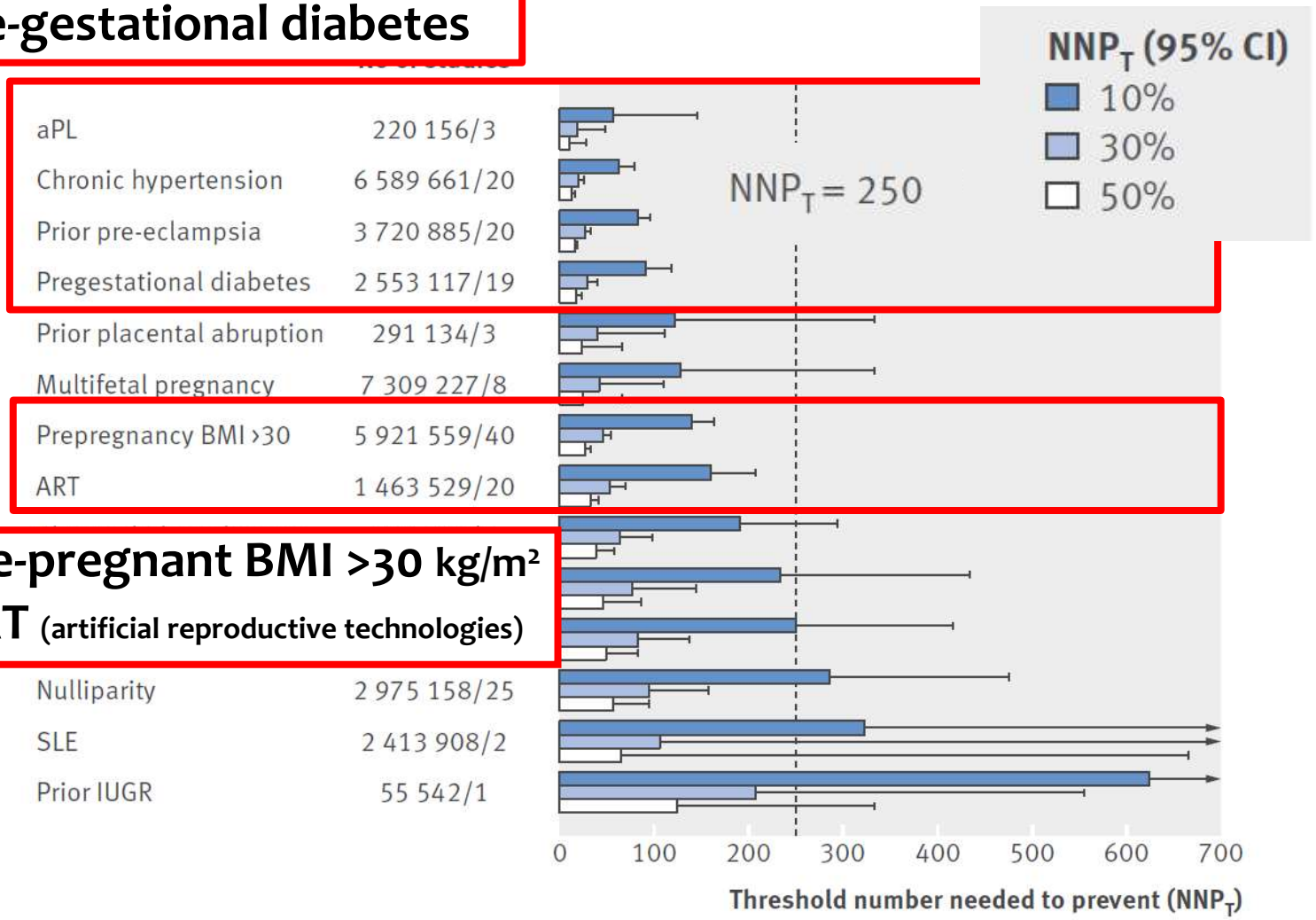
1. aPL
2. Chronic hypertension
3. Prior pre-eclampsia
4. Pre-gestational diabetes



5. Pre-pregnant BMI >30 kg/m²
6. ART (artificial reproductive technologies)

Population attributable fraction (PAF)

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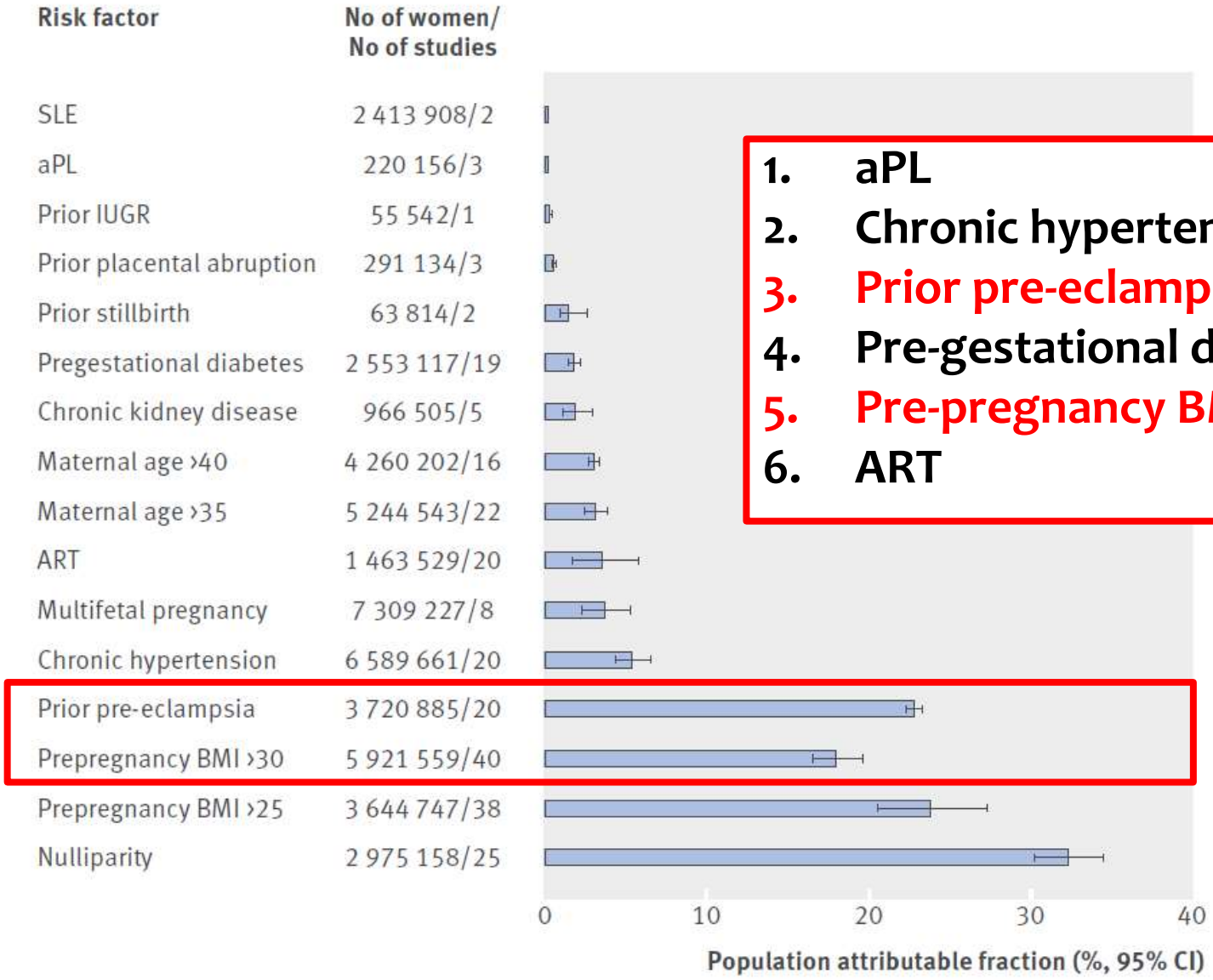

1. aPL
2. Chronic hypertension
3. Prior pre-eclampsia
4. Pre-gestational diabetes
5. Pre-pregnancy BMI >30
6. ART

CHIPS Trial results

(The Control of Hypertension In Pregnancy Study)
(ISRCTN 714169114)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 29, 2015 VOL. 372 NO. 5

Less-Tight versus Tight Control of Hypertension in Pregnancy

Laura A. Magee, M.D., Peter von Dadelszen, M.B., Ch.B., D.Phil., Evelyne Rey, M.D., Susan Ross, M.B.A., Ph.D., Elizabeth Asztalos, M.D., Kellie E. Murphy, M.D., Jennifer Menzies, M.Sc., Johanna Sanchez, M.I.P.H., Joel Singer, Ph.D., Amiram Gafni, D.Sc., Andrée Gruslin, M.D.,* Michaël Helewa, M.D., Eileen Hutton, Ph.D., Shoo K. Lee, M.D., Ph.D., Terry Lee, Ph.D., Alexander G. Logan, M.D., Wessel Ganzevoort, M.D., Ph.D., Ross Welch, M.B., B.S., D.A., M.D., Jim G. Thornton, M.B., Ch.B., M.D., and Jean-Marie Moutquin, M.D.

ABSTRACT

- 987 recruits, 94 sites in 15 countries
- Open, international, multicentre RCT of women
- At 14+0 weeks to 33+6 weeks gestation
- Non-proteinuric, non-severe pre-existing or gestational hypertension
- Live fetus
- Randomly assigned to ‘less tight’ control (target diastolic BP, 100mmHg) or ‘tight’ control (target diastolic BP, 85mmHg)

CHIPS – management of non-severe hypertension

- 987 women; 74.6% had pre-existing hypertension
- Mean diastolic BP was 4.6mmHg (95% CI 3.7, 5.4) higher in 'less tight' control
- Composite primary outcome (pregnancy loss or high-level neonatal care for >48hr) during the first 28 postnatal days
  - 31.4% ['less tight'] vs. 30.7% ['tight']; adjOR 1.02; 95% CI 0.77, 1.35
- Secondary outcome (serious maternal complications) up to 6wk post partum or until hospital discharge, whichever was later
  - 3.7% ['less tight'] vs. 2.0% ['tight']; adjOR 1.74; 95% CI 0.79, 3.84
- Severe hypertension (≥160/110mmHg)
  - 40.6% ['less tight'] vs. 27.5% ['tight']; p<0.001
- Platelets <100x10^9/L
  - 4.3% ['less tight'] vs. 1.6% ['tight']; p<0.05
- Elevated liver enzymes with symptoms
  - 4.3% ['less tight'] vs. 2.0% ['tight']; p<0.05

CHIPS - management of non-severe hypertension

- **'Less tight' control is not a sound investment because it offers no rewards (perinatal or maternal) in exchange for risk (maternal, at minimum severe hypertension)**

Province	'Less tight'	'Tight'	Difference in means	95% CI		p value
Ontario	$30,191.62	$24,469.06	CAD$5,723	-$296	$12,272	0.0725
BC	$30,593.69	$24,776.51	CAD$5,817	-$385	$12,349	0.0725
Alberta	$31,510.72	$25,510.49	CAD$6,000	-$154	$12,781	0.0637

Management of severe hypertension

WHO recommendations for

Prevention and treatment of pre-eclampsia and eclampsia

Recommendation	Quality of evidence	Strength of recommendation
In areas where dietary calcium intake is low, calcium supplementation during pregnancy (at doses of 1.5–2.0 g elemental calcium/day) is recommended for the prevention of pre-eclampsia in all women, but especially those at high risk of developing pre-eclampsia.	Moderate	Strong
Low-dose acetylsalicylic acid (aspirin, 75 mg) is recommended for the …npsia in women at high risk of developing the	Moderate	Strong
…ic acid (aspirin, 75 mg) for the prevention of pre-…ed complications should be initiated before ….	Low	Weak
…pertension during pregnancy should receive …rtensive drugs.	Very low	Strong
The choice and route of administration of an antihypertensive drug for severe hypertension during pregnancy, in preference to others, should be based primarily on the prescribing clinician's experience with that particular drug, its cost and local availability.	Very low	Weak
Magnesium sulfate is recommended for the prevention of eclampsia in women with severe pre-eclampsia in preference to other anticonvulsants.	High	Strong
Magnesium sulfate is recommended for the treatment of women with …	…	Strong
…	…	Strong
…	…	…
…	…	Weak
… 34 and 36 (plus 6 days) weeks of gestation, a policy of expectant management may be recommended, provided that uncontrolled maternal hypertension, increasing maternal organ dysfunction or fetal distress are absent and can be monitored.	Very low	Weak
In women with severe pre-eclampsia at term, early delivery is recommended.	Low	Strong
In women with mild pre-eclampsia or mild gestational hypertension at term, induction of labour is recommended.	Moderate	Weak
In women treated with antihypertensive drugs antenatally, continued antihypertensive treatment postpartum is recommended.	Very low	Strong
Treatment with antihypertensive drugs is recommended for severe postpartum hypertension.	Very low	Strong

Women with severe hypertension in pregnancy should receive treatment with antihypertensive drugs

Very low **Strong**

Management of severe hypertension

- Uncontrolled severe hypertension is the most widely regarded maternal indication for delivery (and treatment) [NICE, WHO, ACOG]
- Recognition that standardisation of treatment is necessary
  - Safe Motherhood Initiative, NY State
- Most commonly used agents that are endorsed internationally achieve treatment success in about 80% of women
  - Nifedipine (orally, tablets or capsules)
  - Labetalol (usually iv)
  - Hydralazine (usually iv)
- Interest in focussing on oral therapy [BJOG. 2014 Sep;121(10):1210-8]
  - Further explored in a RCT of oral nifedipine, oral labetalol, and oral methyldopa [*Gnyuity* oral antihypertensive trial]


Oral antihypertensive therapy for severe hypertension in pregnancy and postpartum: a systematic review

T Firoz,[a,b] LA Magee,[c,d] K MacDonell,[e] BA Payne,[b,c] R Gordon,[c] M Vidler,[b,c] P von Dadelszen,[b,c] for the Community Level Interventions for Pre-eclampsia (CLIP) Working Group

MATERNAL DEATH FROM PRE-ECLAMPSIA

by diagnosis – UK; 1952 – 2008

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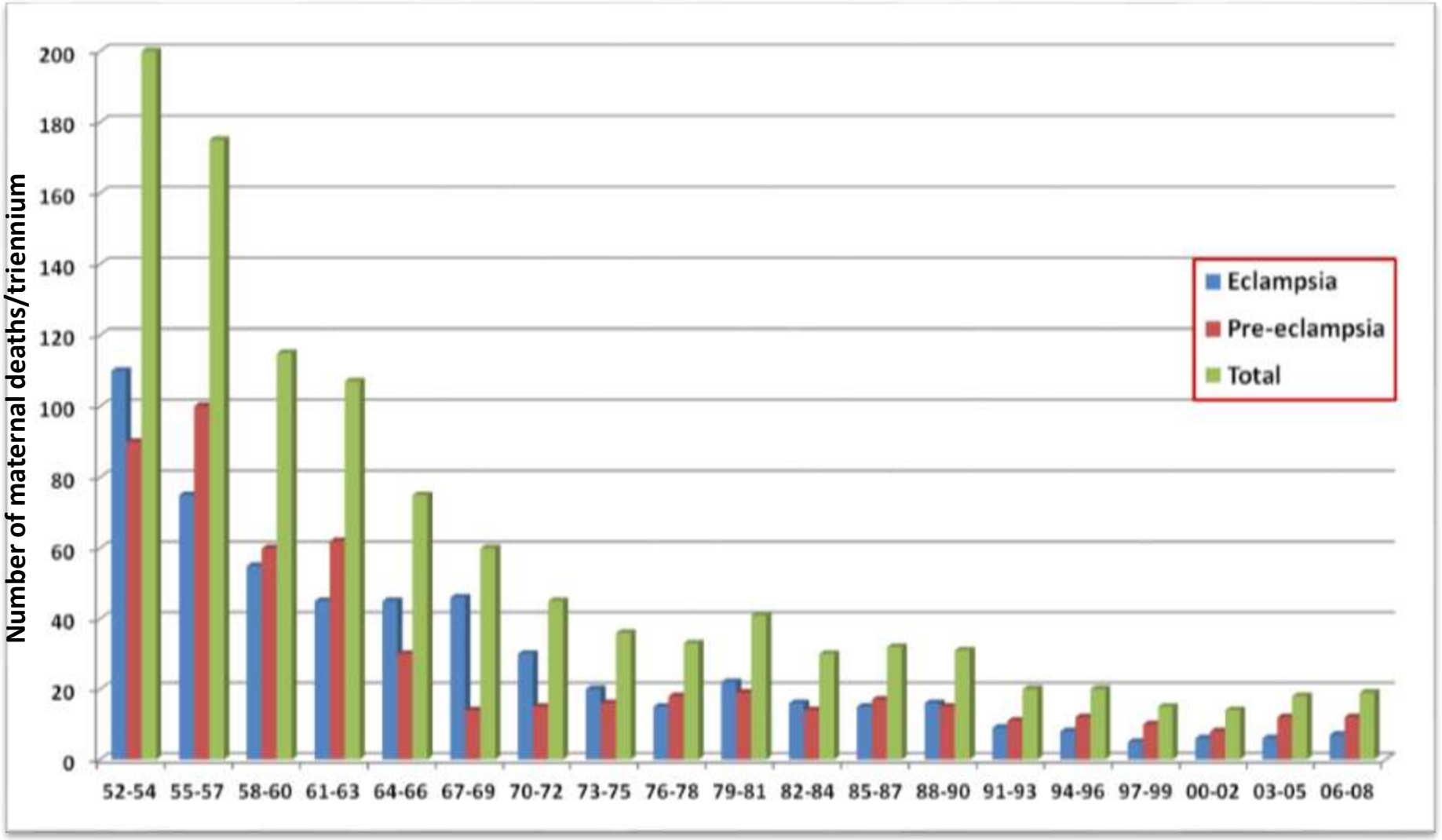

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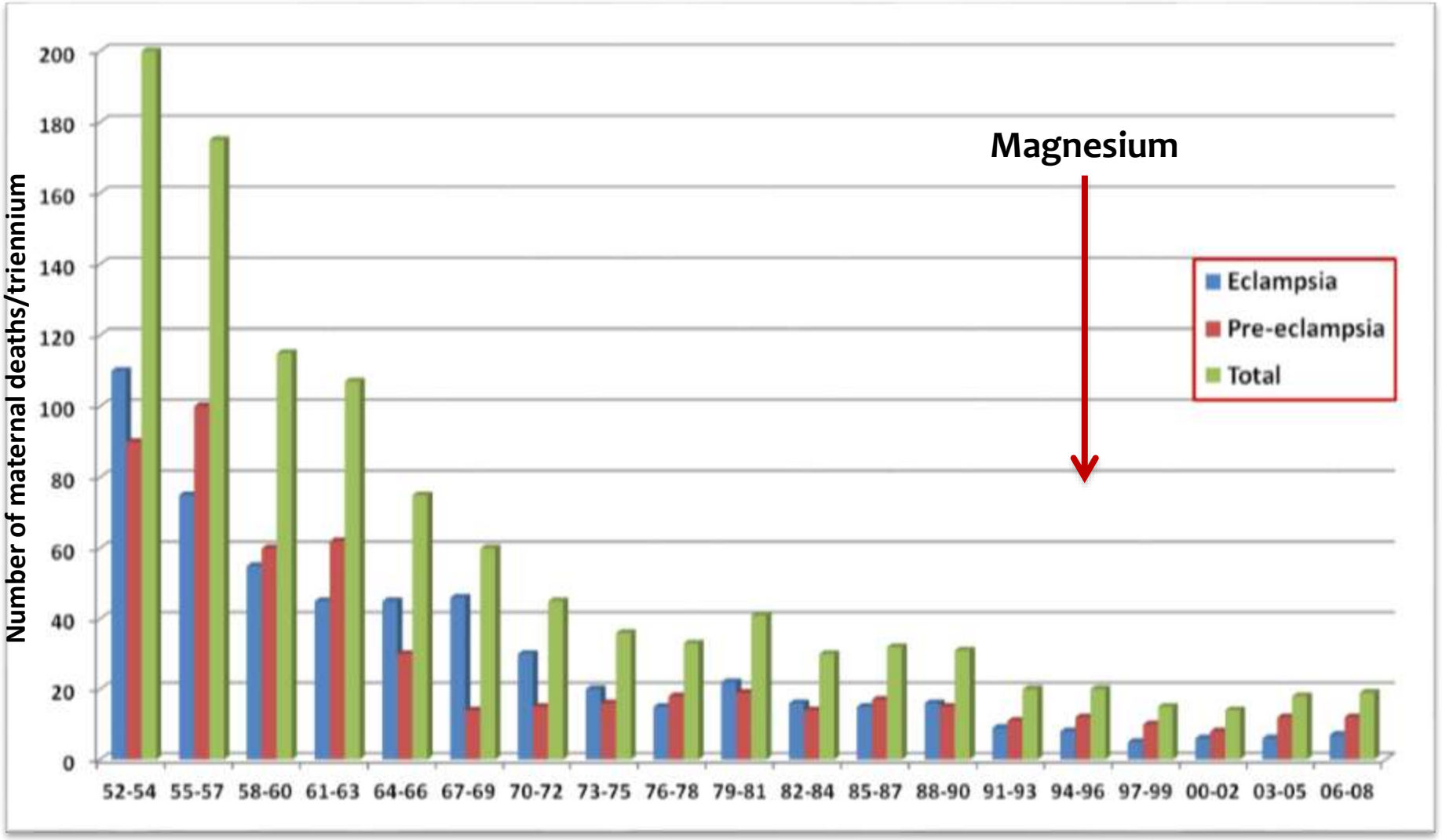

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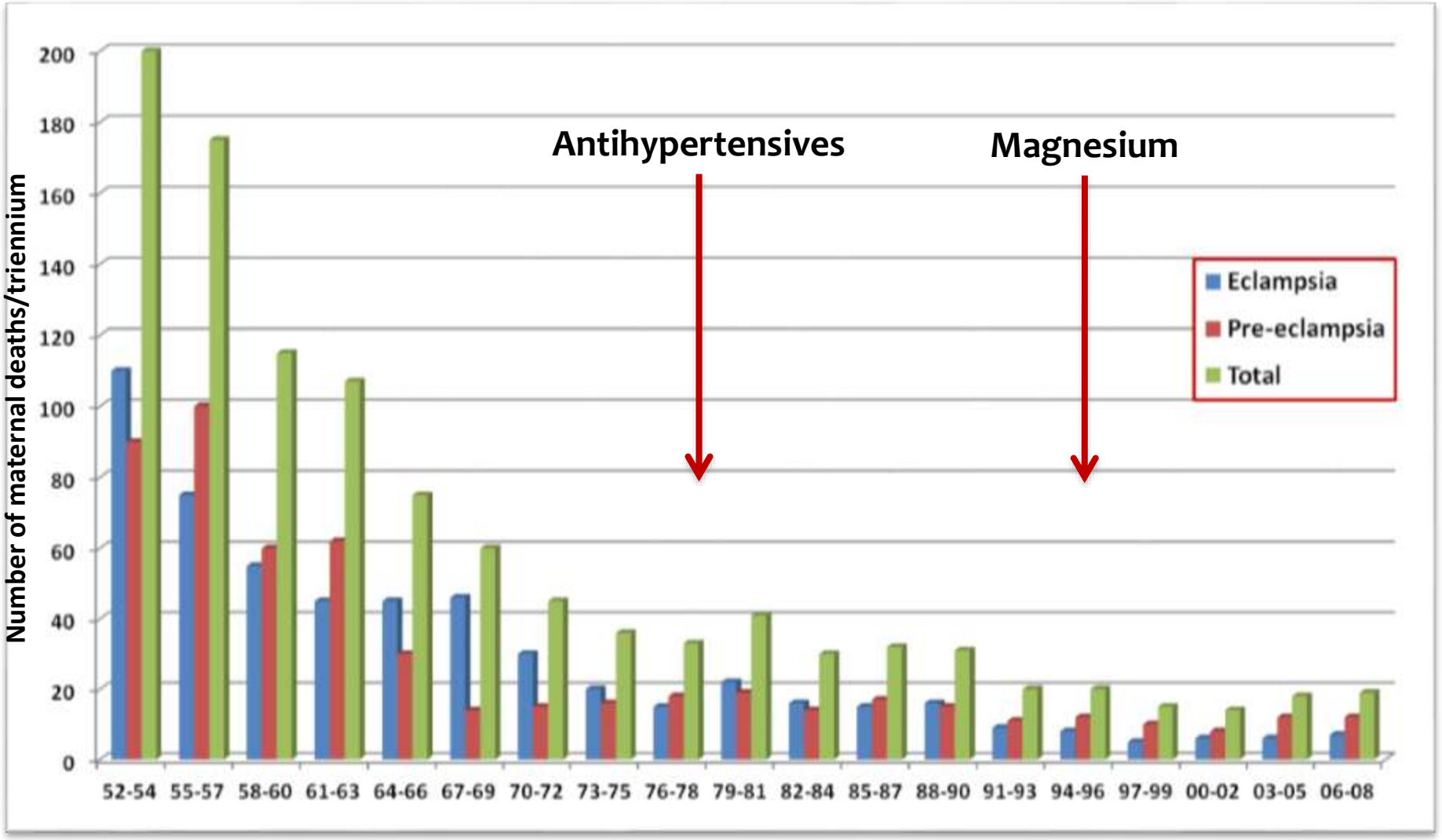

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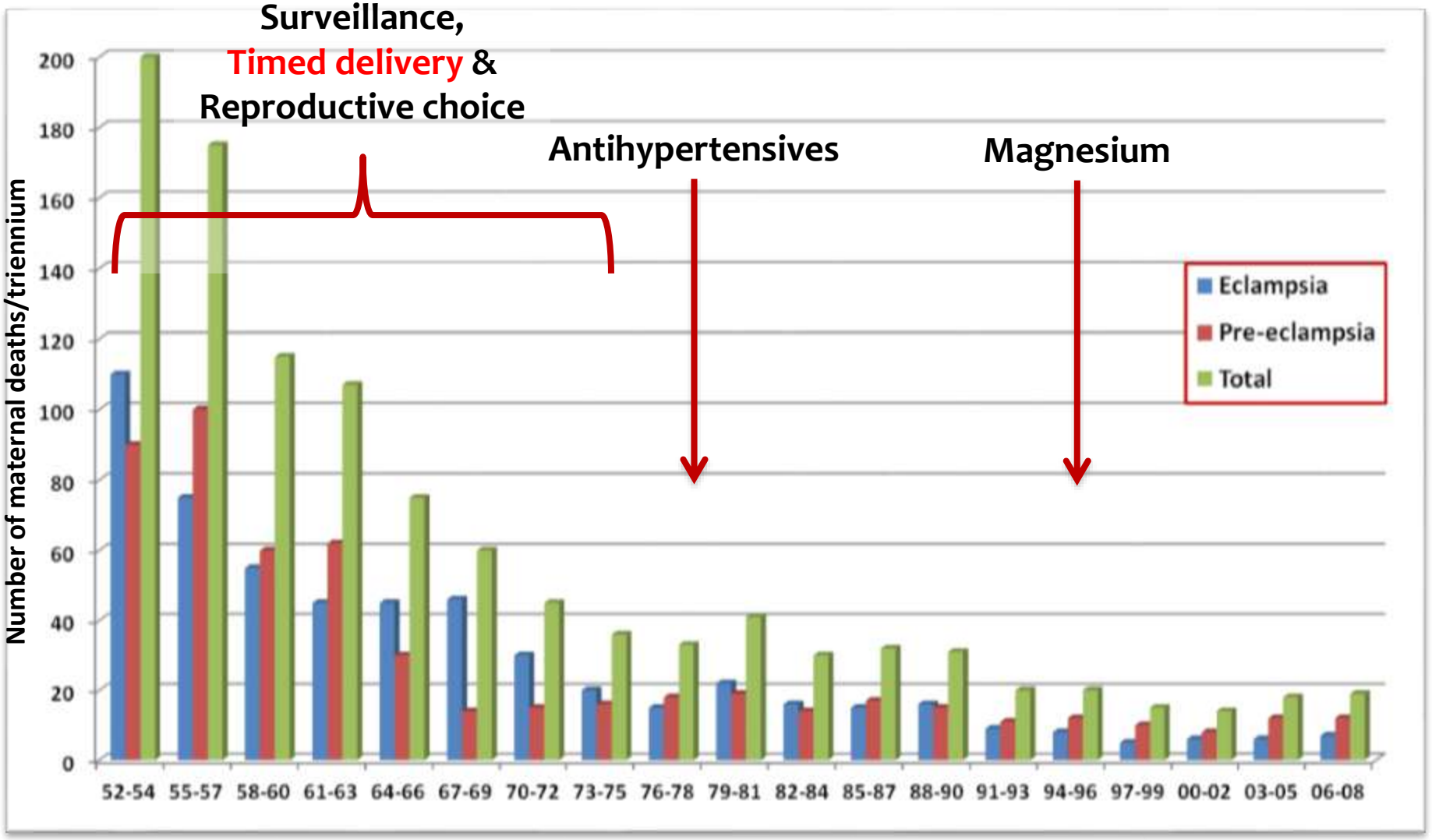

Data from CEMD ,UK

Management – timed delivery

- Recommendations focus on women with pre-eclampsia [ACOG, NICE, NVOG, SOGC, WHO]
  - Delivery at a pre-viable gestational age if the disease severe [WHO, ACOG, SOGC], and at term [NICE, WHO, ACOG, SOGC]
- Expectant management possible at viability at <34 wk [NICE, ACOG, SOGC] may decrease perinatal risk without increasing maternal risk
  - Only about 40% of women are eligible
- Expectant care at 34-36 wk is reasonable
  - HYPITAT II [Lancet 2015]
  - Adverse maternal outcomes: 4 (1.1%) vs. 11 (3.1%),p-0.069
  - Respiratory distress syndrome: 20 (5.7%) vs. 6 (1.7%), p=0.005
  - There were no maternal or perinatal deaths
- Gestational hypertension
  - Delivery at term - HYPITAT [WHO, ACOG, SOGC]
- Chronic hypertension - ??

Immediate delivery versus expectant monitoring for hypertensive disorders of pregnancy between 34 and 37 weeks of gestation (HYPITAT-II): an open-label, randomised controlled trial

Consistency – potential for standardisation

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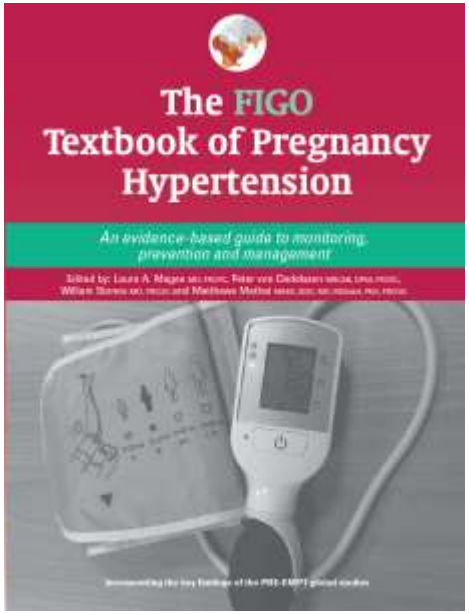
  - **Low-dose aspirin**
    - **Women with prior pre-eclampsia and pre-pregnancy BMI >30**
    - Calcium when baseline intake is low
  - NOT vitamins C&E or diuretic therapy
- Management
  - **Antihypertensives for severe hypertension – more oral therapy?**
    - **Antihypertensive therapy for non-severe hypertension to prevent maternal risk (at minimum, severe hypertension)**
  - $MgSO_4$ for eclampsia, 'severe' pre-eclampsia, and fetal neuroprotection
  - Antenatal corticosteroids when delivery likely within 7d
  - **Delivery for pre-eclampsia either before fetal viability (with severe disease) or at term**
    - **Expectant care can be undertaken at 34-36 weeks for neonatal reasons**
  - Active management of third stage of labour with oxytocin

"Women are not dying of diseases we can't treat... They are dying because societies have yet to make the decision that their lives are worth saving."

[M Fathalla]

"Safer motherhood will happen when evidence for best practice is integrated into systems of care for all patients."

[Martin JN Jr, Semin Perinatol 2016]



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Dhannvaad
Vielen Dank
Köszönjük
Thank you
Gracias
Dziękujemy
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tänan
merci
Obrigado