PERINATAL MENTAL ILLNESS

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Learning objectives

- Learning about the epidemiology of perinatal mental illness (from conception up to the 1st year post-delivery).
- Understanding the clinical impact of untreated perinatal mental illness
- Current evidence-based pharmacological interventions for the management of perinatal mental illness
- Overview of current perinatal mental health services in the North West London Sector

PERINATAL MENTAL ILLNESS OUTLINE OF THE LECTURE

- Introduction
- Epidemiology
- Consequences of untreated maternal mental illness
  - Maternal
  - Foetal, neonatal, infant and child
- Prescribing in pregnancy and lactation
- Referral pathways and packages of care

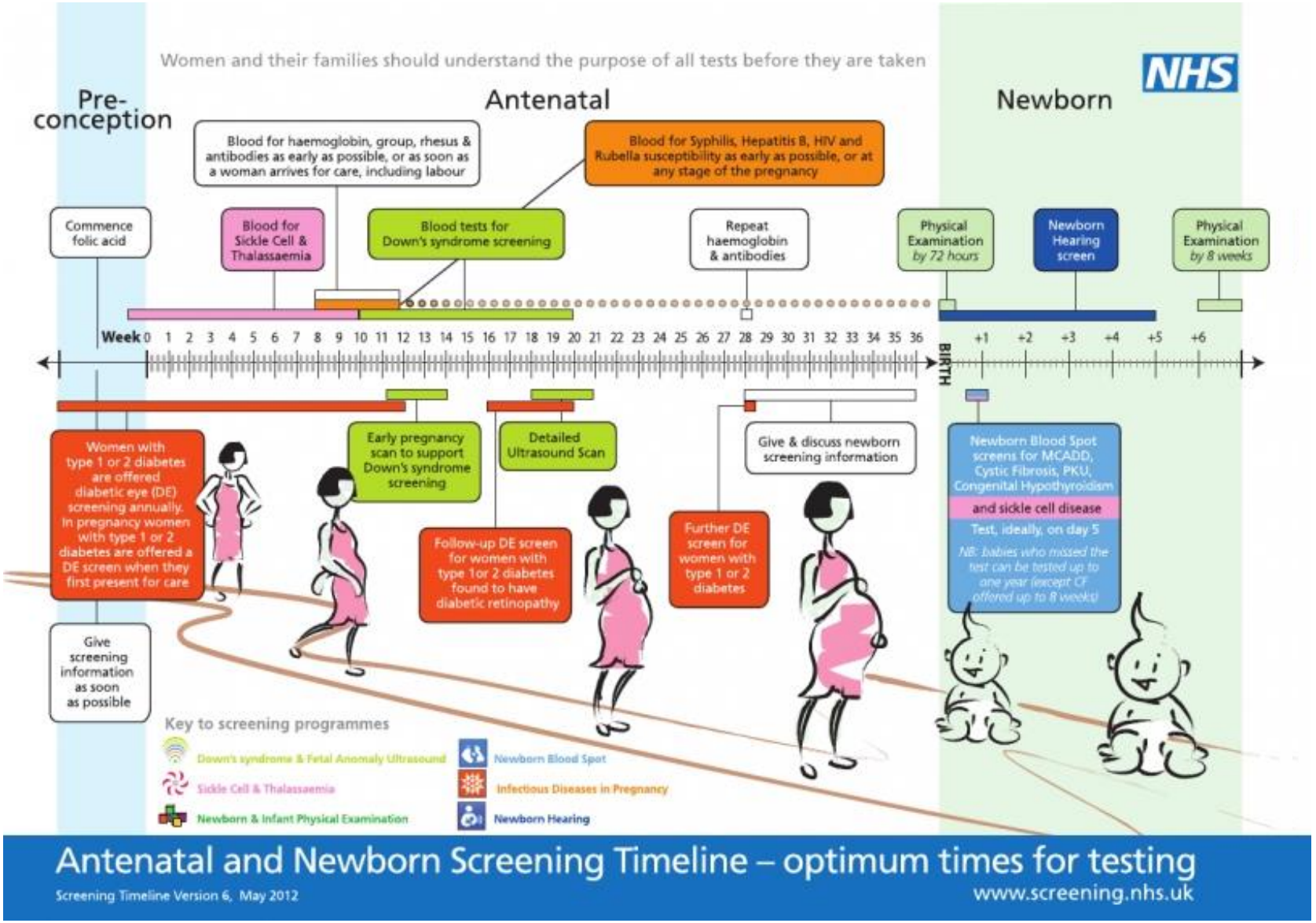
PREGNANCY: A FITNESS TEST FOR LIFE

- Gestational syndromes: *pre-eclampsia, post – partum thyroid disease*
- Subclinical autoimmune illnesses flare-up in pregnancy: *SLE*
- Pre-existing medical exacerbated by pregnancy: *diabetes*
- Maternal diseases identified by effects on the foetus: *thyroiditis*
- Pregnancy outcomes predict future maternal health (Smith et al, 2001 Lancet 357: 2002-6). Pre-eclampsia increases the risk of hypertension (RR3.70), IHD (RR 2.16), stroke (RR1.81), VTE (RR 1,79) (Bellamy L.et al. BMJ 2007, 335:974)

PREGNANCY: A MENTAL HEALTH FITNESS TEST FOR LIFE

- Postnatal depression, puerperal psychosis
- Pregnancy can unmask subclinical psychiatric symptoms e.g. eating disorders, obsessive compulsive disorders.
- Relapse of pre-existing mental illness in remission e.g. bipolar affective disorder
- Infant may present with disturbances indicative of the presence of a mental illness in mothers
- Perinatal mental illness increases the risk of future mental illness (Cooper and Murray 1995)

Antenatal and Newborn screening timeline does not consider mental health



Epidemiology of Perinatal Mental Illness

- Reported prevalence rate for **baby blues (**self-limiting mood changes are common after delivery) are in the range of 50% (Henshaw 2003).

Depressive Disorders	Antenatal	Postnatal	(Gavin, Gaynes et al. 2005)
Major depression	3.1- 4.9%	4.70%	Point prevalence
Minor depression	11%	13%	Point prevalence
All depression	18.40%	19.20%	Period prevalence

- **Perinatal depression** 33% begins in pregnancy and 27% pre-date pregnancy (Wisner at al. 2013)
- **Anxiety Disorders** A large US population-based study reported a prevalence of 13% (Vesga-Lopes 2008)
- **Maternal OCD:** 2.9-9% A meta-analysis reported a significant higher risk of obsessive compulsive disorders in the perinatal periods compared to other time of life (Russell et al.2013);
- 57% of *post-partum* women report obsessional thoughts of harm to their baby and most have checking compulsions i.e. highly repetitive night time checking to make sure the baby's breathing (Wisner et al., 1999)
- **Psychotic Disorders** Few studies have examined the incidence of severe mental illness and pregnancy. A US epidemiological study showed no difference in the prevalence of psychotic and broadly defined bipolar disorder in past year pregnant women compared with non-pregnant women reporting prevalence figures of 0.4% and 2.8% respectively (Vesga-Lopes 2008)
- **Eating Disorders** : 5% A retrospective questionnaire study reported a 11.5% prevalence of some type of eating disorders (Larsson et al.2003)

Pharmacological interventions: risk-benefit analysis

Risks of treating

- Teratogenicity
- Obstetric complications
- Neonatal toxicity and withdrawal symptoms
- Neonatal complications (nPPH)
- Risks mediated by incompatibility with breastfeeding
- Neuro-developmental disorders (autism)
- Child psychopathology

Risk of untreated maternal mental illness:

1. Maternal Outcomes
2. Foetal & Neonatal Outcomes
3. Infant & Child Outcomes

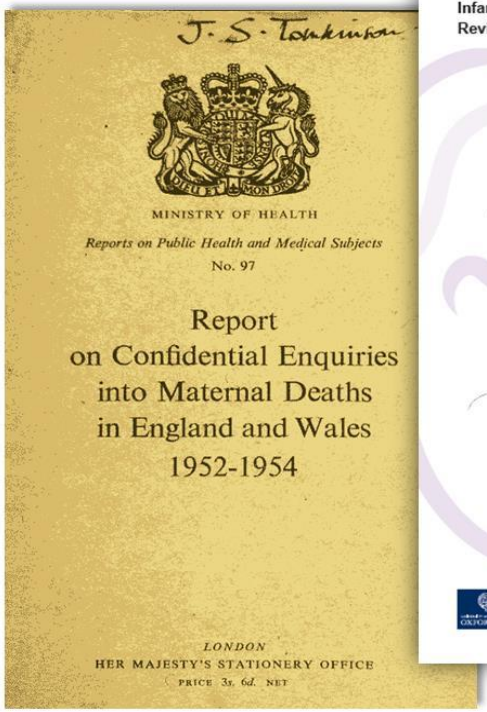
Effects of untreated maternal mental illness (I)

Maternal outcomes

- Increased risk of relapse (Viguera et al., 2007) (Cohen et al. 2006); (Wesseloo et al., 2016)
- Increase risk of hospitalisation (Kendell et al., 1987 Munk-Olsen et al., 2006)
- Worsening of long-term prognosis
- Suicide (MBBRACE Mother and Babies Reducing Risk through Audit and Confidential Enquiry) – (maternal mortality 10/100,000 2009-2012)

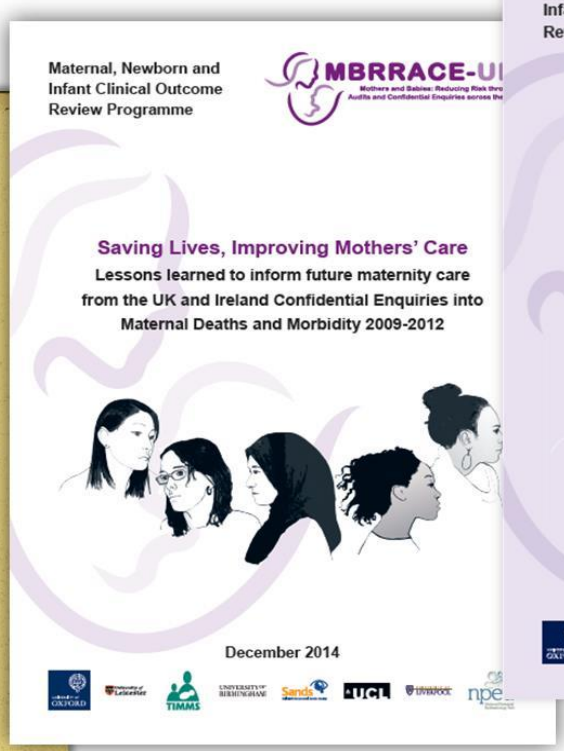
Maternal Mortality in the UK

1952-54



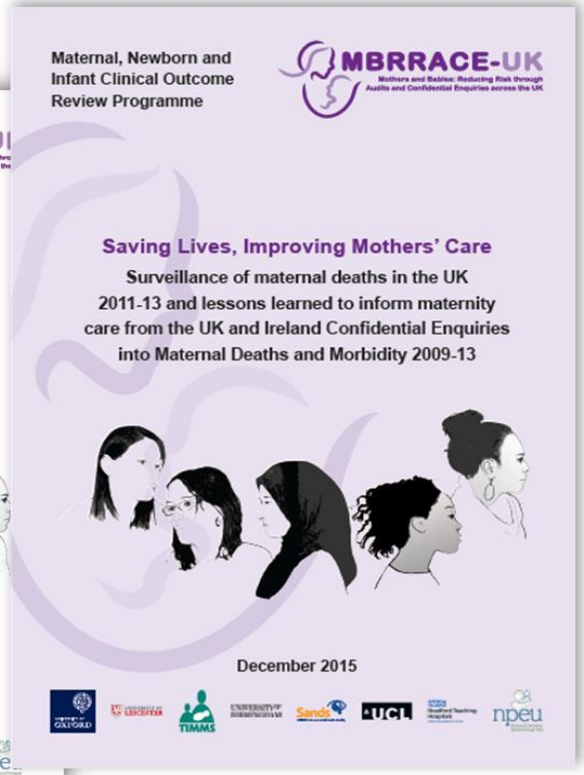
90 per 100,000 maternities

2010-12



10 per 100,000 maternities

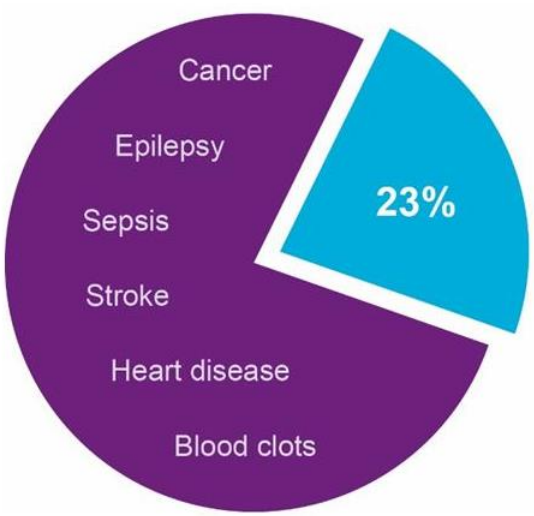
2011-13



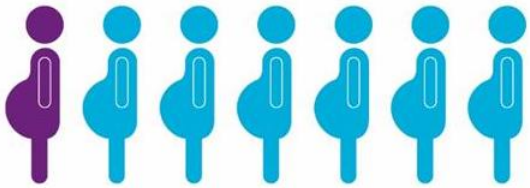
9 per 100,000 maternities

MBRRACE-UK
Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK

Mental health-related deaths



Almost **a quarter** of women who died between six weeks and one year after pregnancy died from **mental-health related causes**



1 in 7 women died by **Suicide**

Risks of untreated maternal mental illness (II)

FOETAL & NEONATAL OUTCOMES

- Antenatal depression is associated with an increased risk of premature delivery
- Evidence is inconsistent for the associations between anxiety and adverse foetal outcomes
- Maternal anorexia nervosa is associated with low birth weight (LBW)
- Schizophrenia has been associated with and increased risk of LBW, pre-term delivery, still birth, and infant death within 1 year after birth (but environmental factors associated with adversity are also important).

Risks of untreated maternal mental illness (II) Child outcomes [possible mediator poor quality of parenting]

South London Child Development Study (SLCDS) (1986-2013)

- Use of a prospective, longitudinal, community study from pregnancy through the next 26 years
- To trace the course of maternal depression throughout the child bearing and child rearing years
- To identify associations between maternal depression and child outcome
- To ascertain the optimal time for detecting maternal depression in order to offer treatment with possible beneficial consequences for the child
- Evidence indicate that exposure to maternal depression *in utero* increases the risk of child and adolescent psychopathology (Pawlby et al 2013)

The Avon Longitudinal Study of Parents and Children (ALSPAC)

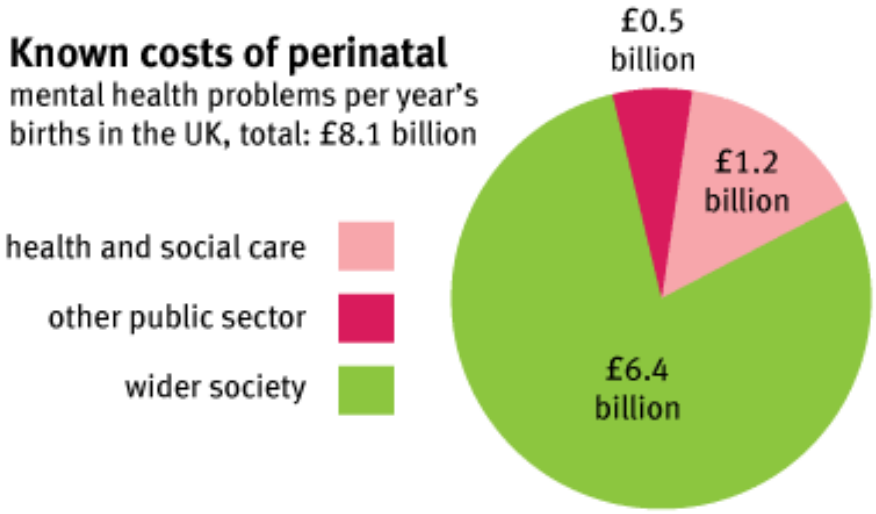
- Cohort study of children born in the former county of Avon between 1992-1993. There are comprehensive data on 10,000 children and their parents from early pregnancy to late childhood.
- Untreated maternal mental illness has long lasting effects on the psychological development of the child.
- Antenatal maternal anxiety predicted behavioural/emotional problems in boys (OR=2.14, 95% CI 1.48-3.10) and girls (OR=1.88, 95% CI 1.3-2.69) (Glover and O'Connor 2002).

THE LONDON SCHOOL OF ECONOMICS AND POLITICAL SCIENCE

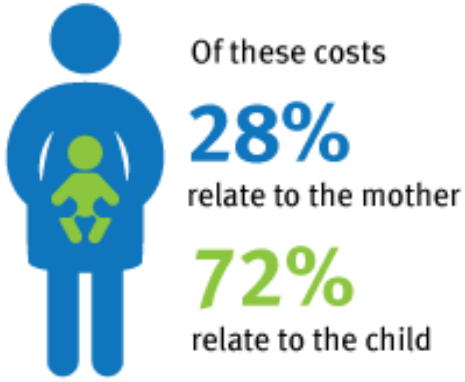
Centre for Mental Health

Economic costs

(LSE & Centre for Mental Health, 2014)



from The Costs of Perinatal Mental Health Problems, available at:
http://www.centreformentalhealth.org.uk/perinatal



from The Costs of Perinatal Mental Health Problems, available at:
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Selective Serotonin Reuptake Inhibitors

In utero exposure has been associated with birth defects, spontaneous abortion, pre-term birth and low birth weight, persistent pulmonary hypertension of the newborn, poor neonatal adaptation syndrome and autism spectrum disorders (ASDs).

Teratogenesis

Cardiac malformation

- Three studies reported an increased risk of cardiac malformations following exposure to paroxetine (Kallen et al.,2006; Cole et al., 2007; Kallan et al., 2007), but two studies have not confirmed the findings (Alwan et al.2007, Luiket et al., 2007).
- A large meta-analysis (>900,000 women) (Huybrechts et al., 2014) and a meta-analysis of prospective cohort studies (Wang et al. 2015) found no association between exposure to SSRIs and cardiac malformations

Major Birth defects

- Four meta-analysis (Addis et al., 2000; Eiharson et al., 2005; Rahimi et al.,2006; O'Brien et al., 2008) found no association between exposure to SSRIs and major birth defects.

The consensus is that the risks of major malformations deriving from exposure to SSRIs (mono-therapy), if it exists, is small (Yonkers et al. 2009)

Selective Serotonin Reuptake Inhibitors

Persistent Pulmonary Hypertension of the newborn

- Persistent pulmonary hypertension (PPHN) complicates the course of approximately 10% of infants with respiratory failure (prevalence 2%)
- Rare, 2:1000, but is a source of considerable mortality (10-20%) and morbidity
- First report: case control study (337 – control 836) OR 6.1 (Chambers et al., 2006)
- Three out of six additional studies (Kallen et al., 2008, Kieler et al., 2012; Huybrecths et al., 2015) confirmed the associations but when adjusted for confounders the OR was not significant 1.10 (0.94-1.29)

Poor Neonatal Adaptation Syndrome (PNAS)

First described in 1973, it is unclear if it is caused by withdrawal or toxicity.

Most cases are mild, self-limiting and not associated with long-lasting effects (Moses-Kolko 2005)

Autistic Spectrum Disorders (ADSs)

Case-control study (298 matched control 1507) - found a doubling of the risk of ADSs OR 2 (1.2-3.6)) (Cronen et al.2007)

Cohort study (626 875) found no association between SSRIs and increased risk ASDs (OR 1.2 [0.90-1.61] (Hviid et al., 2013)

ANTIPSYCHOTICS (First and Second Generation Antipsychotics)

Antipsychotics may exacerbate metabolic adaptation to pregnancy and are associated with an increased maternal BMI, increased infant birth weight and of increase risk of gestational diabetes (Seeman et al. 2013, Newport et al., 2007, Newham et al.,2008)

First generation antipsychotics (FGAs)

- FGAs have been available for 45 years and are considered having a better safety profile in pregnancy than SGAs. The consensus is that the risk of major congenital malformation is minimal (ACOG 2008)
- Association with transient neonatal extrapyramidal and withdrawal symptoms (Haberman et al., 2013)
- American Academy of Paediatrics recommends high potency FGAs to minimise maternal anticholinergic, hypotensive and anti-histaminergic effects of low potency FGAs (AAP, 2000)
- Depot antipsychotics not recommended

Second generation antipsychotics (SGAs)

- Similar safety profile of FGAs – best evidence is for Olanzapine (Brunner et al., 2013)

MOOD STABILIZERS

Lithium

Exposure to Lithium in the 1st trimester of the pregnancy was found to be associated to an increased risk of Ebstein's anomaly (1:1000 live births); pooled analysis of lithium exposed pregnancies found the defect only in 1/1000-1/2000 exposed children (Cohen et al., 1994)

Sodium Valproate

Valproate during pregnancy is associated with high rate of malformations (10%) and lower cognitive test scores in children (compared to children exposed to other anti-seizure medications during pregnancy) (Pearlstain et al., 2013)

Carbamazepine

Carbamazepine carries an increased risk of malformations, mainly spina bifida and neural tube defect (2.2-3.3%) (Pearlstain et al., 2013)

Lamotrigine

10.4 fold increase (4.3-24.9) of the risk of oral cleft defects (Holmes et al.2006) was not confirmed by a large (3.9 millions birth) population based case-control design and data from EUROCAT congenital malformation registries (Dolk et al. 2008)

Pharmacological interventions: risk-benefit analysis

Cost of treating maternal mental illness

- Teratogenicity
- Obstetric complications
- Neonatal toxicity and withdrawal symptoms
- Neonatal complications (nPPH)
- Risks mediated by incompatibility with breastfeeding*
- Neuro-developmental disorders (autism)

Cost of not-treating mental illness

- Increased risk of maternal relapse
- Increased risk of maternal hospitalisation
- Increased risk of adverse obstetric outcomes
- Increased risk of bonding and attachment disorders (contingent upon maternal mental illness)
- Increased risk of child cognitive deficits
- Increased risk of child psychopathology

Prescribing principles in lactation

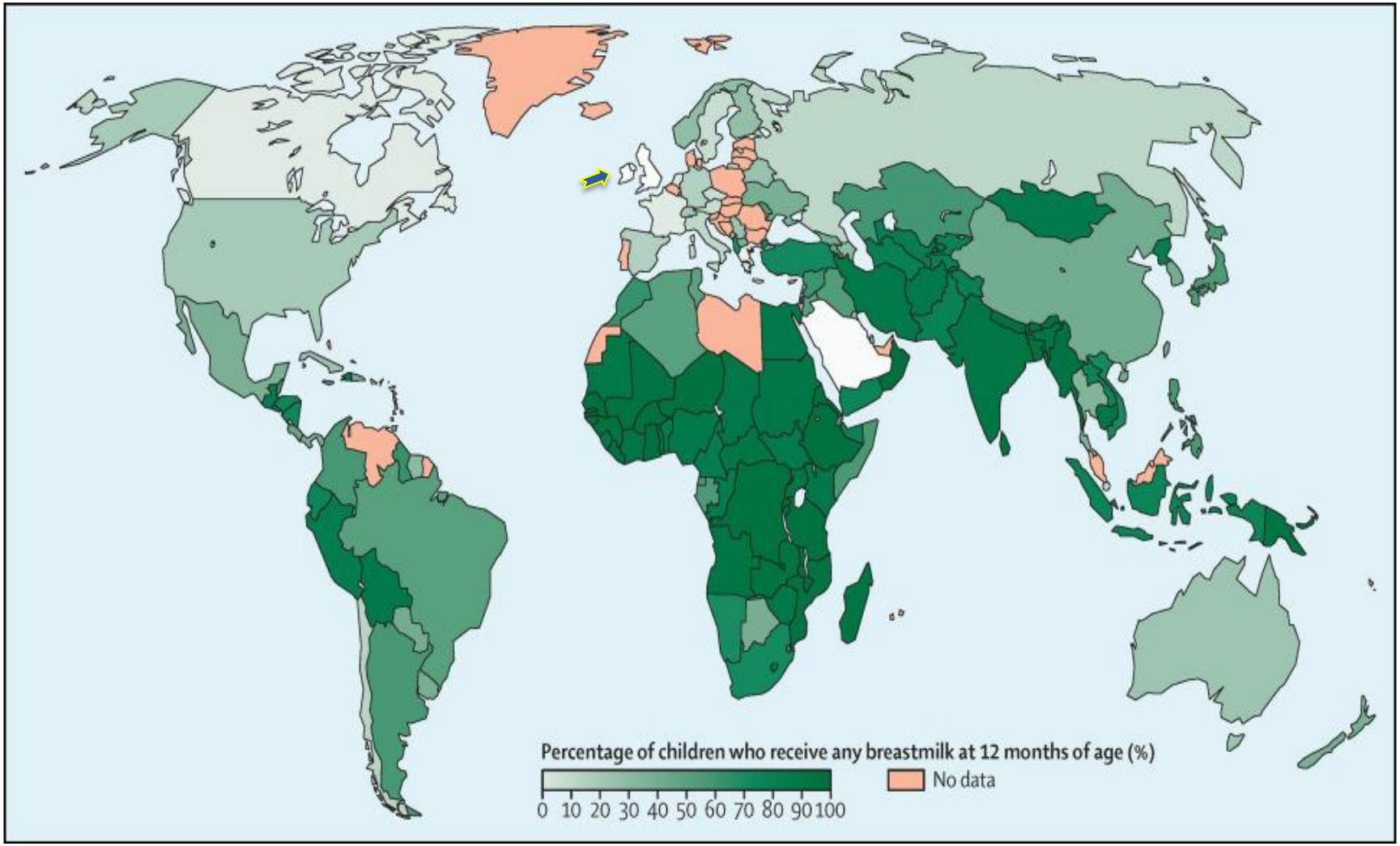
- All psychotropic drugs pass into the breast-milk; most pass by simple diffusion processes.
- Maternal drug concentration (controlled by maternal pharmacokinetics) and milk plasma ratio are major determinants of infant dose via milk (Rampono, 2006)
- Hind milk has a higher concentration of maternal (lipophilic) medication (higher lipids content) than fore-milk (Burt, 2001).

- Relative Infant Dose (RID)

$$\frac{\text{Infant dose/Kg bw}}{\text{Maternal dose/ Kg bw}}$$

- RID<10% regarded as relatively safe (Bennett et.al,1996)
- Most psychotropic drugs have a RID <10%

Global breastfeeding rates at age 1 year (Lancet 2016;387:475-90)



By 6 weeks only 21% and by 6 months only 1% of the infants are exclusively breastfed in the UK

CNWL FT Perinatal Mental Health Services (from pre-conception to 12 months post-delivery)

https://www.cnwl.nhs.uk/services/mental-health-services/perinatal-mental-health-services/

DIRECT CARE

BIO-PSYCHO-SOCIAL ASSESSMENT OF THE MOTHER AND THE INFANT

- Preconception advice **and promotion of positive mental health.**
- Advice on prescribing in pregnancy and lactation
- Assessment and management of mental health needs and the risk of relapse
- Management of the impact of obstetric complications in **the monthly joint obstetric-psychiatry liaison clinic.**
- **Screening for bonding and attachment related difficulties.**
- Pre-birth planning, including safeguarding and social care, for women with SMI
- Signposting or shared management planning with primary care for women with less severe mental illness
- **Assessment for suitability for psychological intervention, including parent-infant psychotherapy.**

ACCESS TO EVIDENCE BASED INTERVENTIONS

- Psycho-education (maternal and infant mental health)
- Peer-support group – facilitated by a member of the team
- Individual psychological therapy for complex presentation based on cognitive behavioural therapy, interpersonal therapy or out-reach model (Nancy Grote protocol).
- CBT for relapse prevention
- Post-natal depression groups CBT (Jeanette Milgrom method)
- Parent-Infant Psychotherapy
- Video-interactive Guidance and Positive Parenting (VIPP)
- Pharmacological treatment

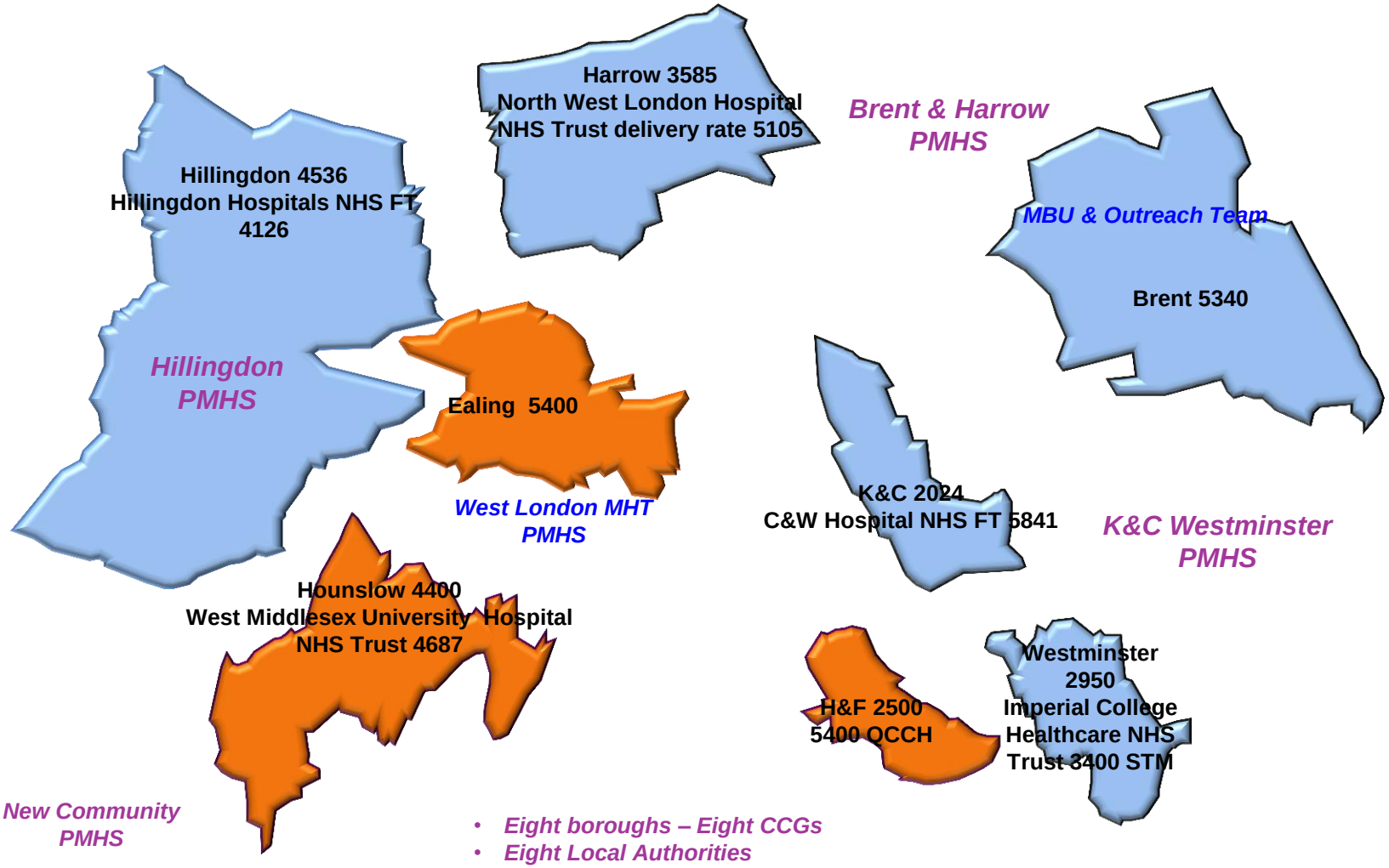
INDIRECT CARE

SUPPORT OF DIRECT CARE & SUPPLEMENITNG CARE PROVIDED BY OTHER PROFESSIONALS

- Education
- Teaching
- Training
- Supervision
- Clinical Placements
- Perinatal Champions

North West London Perinatal Mental Health Services

Imperial College Healthcare NHS Trust



New Community PMHS

CNWL-FT

WLMHT

*data source ONS 2016

- *Eight boroughs – Eight CCGs*
- *Eight Local Authorities*
- *Four Maternity Units – Four Acute Trusts*
- *Two Mental Health Trusts*

Perinatal Mental Health Packages of Care & Population Coverage

Imperial College Healthcare NHS Trust

FULL PACKAGE

- **Preconception advice.**
- **Antenatal care**: from pregnancy recognition and booking up to labour commencing.
- **Intra-partum care**: from labour until mother and baby are discharged from the maternity unit (i.e. emergency and routine reviews on the labour and postnatal wards and pre-discharge planning meeting). PMHS retains the responsibility to coordinate intra-partum care also for NWL residents delivering out-of-area.
- **Postnatal care**: from discharge from the maternity unity up to 6-12 months post-delivery (domiciliary and community reviews). *NB WLMHT currently to 6 months postnatal only.*

INTERMEDIATE PACKAGE

- **Antenatal care.**
- **Intra-partum care**.

MINIMUM PACKAGE

- **Intra-partum care** (until the woman and the baby are discharged from maternity).

Criteria	Full package	Full package	Full package	Intermediate package	Intermediate package	Minimum package
Live/Resident/Address	Yes	Yes	Yes	No	No	No
Registered GP in area	Yes	No	No	Yes	No	No
Maternity Care in NWL	Yes	Yes	No	Yes	Yes	Yes
PMHS out-of area	N/A	N/A	N/A	No	No	Yes
Eligible for NWL PMHS	Yes	Yes	Yes	Yes up to delivery	Yes up to delivery	Redirect to local PMHS

Perinatal Mental Illness: conclusions

- Psychiatric disorders are common in pregnancy and in the post-partum
- Untreated maternal mental illness is associated with adverse consequences for the mother, the foetus and the newborn.
- Longitudinal UK studies show that maternal mental disorders are associated with an increase in a range of psychological and developmental and psychiatric disturbances in children.
- Prescribing strategies should be guided by the risk benefit analysis of the in-utero exposure with the adverse outcomes associated with untreated maternal mental illness
- A proportion of perinatal psychiatric mortality and morbidity is avoidable by enhancing health care.