Pre-eclampsia: From prevention to diagnosis of high-risk pregnancies

Telle Ukonaho

Maternal-Fetal Health

Reproductive Health Business, Revvity

revvity

40 000 MOMS AND 500 000 BABIES LOSE THEIR LIVES EVERY YEAR

PRE-ECLAMPSIA **AFFECTS** BOTH MOTHER AND THE CHILD **ALSO LATER IN LIFE**

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Kuklina EV et al. Obstet Gynecol 2009; 113: 1299-306. All figures are approximates. Poon L et al. Obgyn 2021; 154(S1): 3-31.

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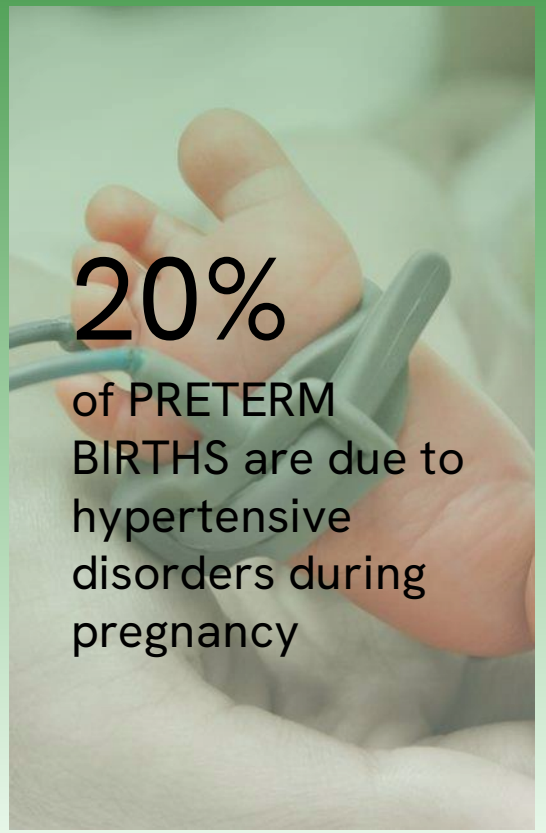


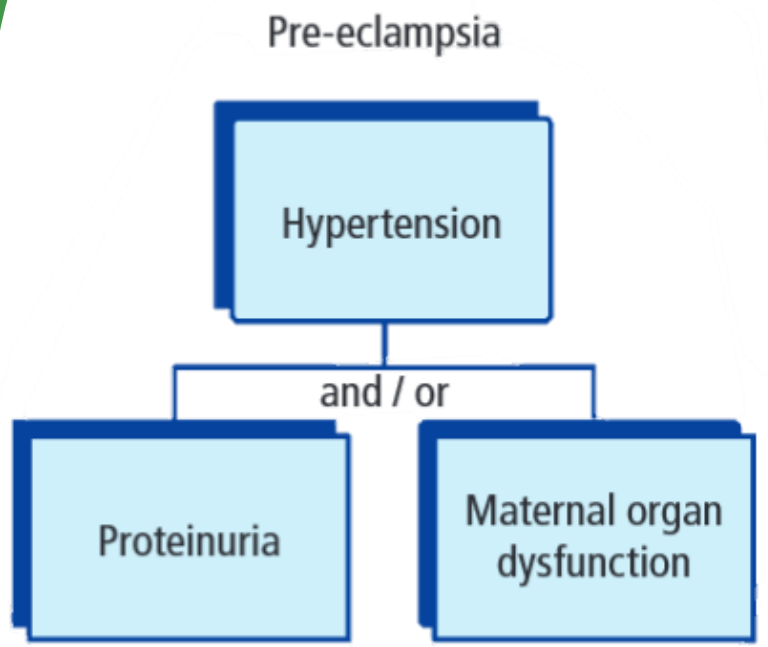
AVOIDING THIS CONDITION WOULD BRING SUBSTANTIAL IMPROVEMENTS TO MATERNAL AND FETAL HEALTH AND TO COSTS

Kuklina EV et al. Obstet Gynecol 2009; 113: 1299-306. All figures are approximates. Poon L et al. Obgyn 2021; 154(S1): 3-31. Revvity does not endorse or make recommendations with respect to research, medication, or treatments. All information presented is for informational purposes only and is not intended as medical advice. For country specific recommendations, please consult your local health care professionals.

Pre-eclampsia introduction

- Pre-eclampsia is one of the leading causes of maternal and perinatal morbidity and mortality
- Symptoms start after 20th week of gestation
- Pre-eclampsia is a multisystem disorder of pregnancy, clinically defined by hypertension and protein in the urine. In the absence of proteinuria, the finding of maternal organ dysfunction can serve as an indicator of pre-eclampsia
- As the only cure for pre-eclampsia after onset is delivery, pre-eclampsia often leads to premature delivery of the fetus
- Both the mother and her baby are at increased risk of serious health complications and even death

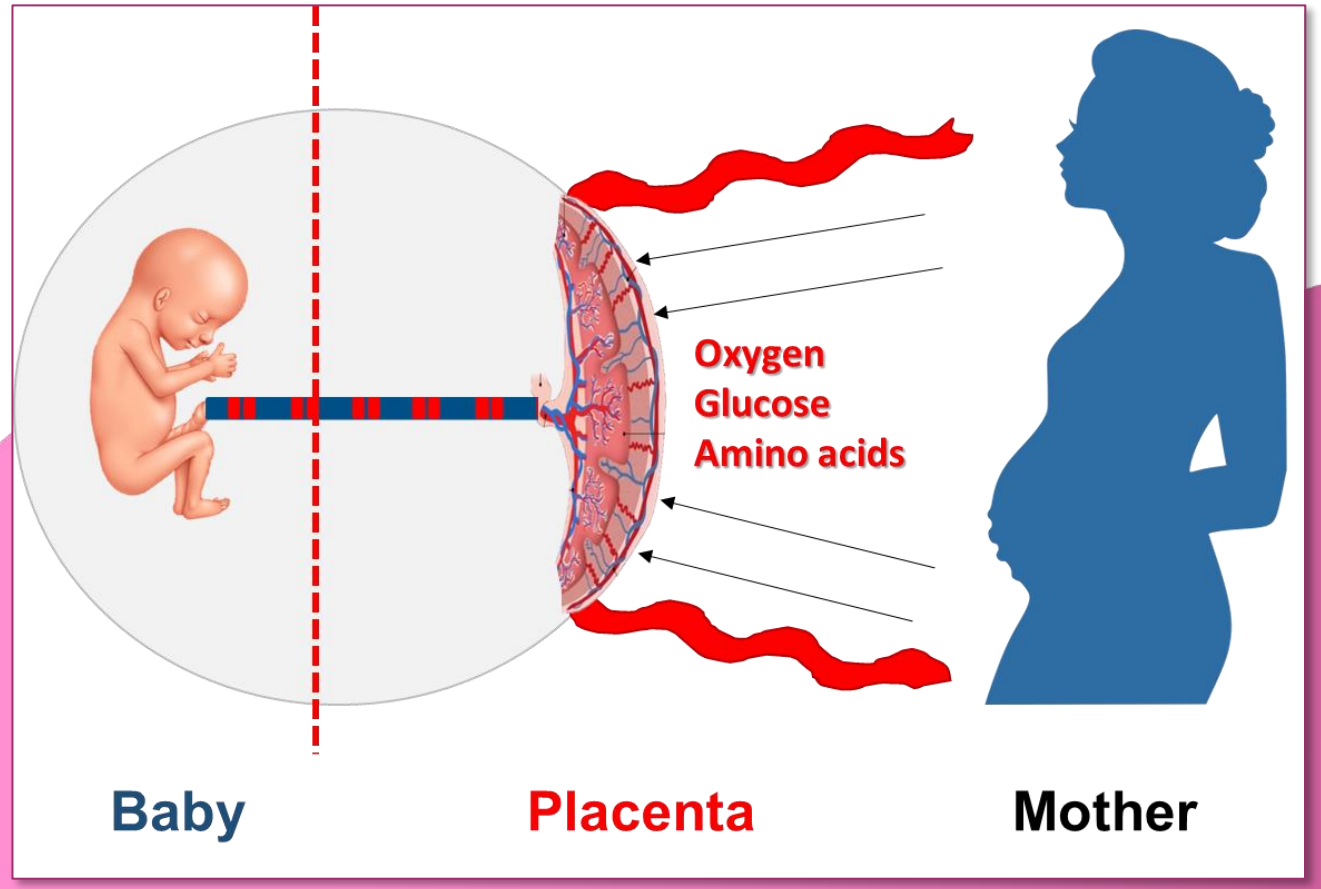
AVOIDING THIS CONDITION WOULD BRING SUBSTANTIAL IMPROVEMENTS TO MATERNAL AND FETAL HEALTH



40%of patients with new-onset hypertension or new-onset proteinuria will develop pre-eclampsia.

Barton & Sibai. Obstet Gynecol. 2008

MAKING A BIG DIFFERENCE IN PREGNANCY CARE



Professor Ranjit Akolekar,
Medway Maritime Hospital, UK.

"The success of the pregnancy is dependent on three factors; the baby, the placenta and the mother.

Every one of them has to be in absolutely good health to be able to have a healthy outcome for both the mother and the baby.

If we want to improve the health of the mothers and babies, we need to devote time, effort, resources and energy into screening for placental health, because that is far more likely to improve pregnancy outcomes than anything else "

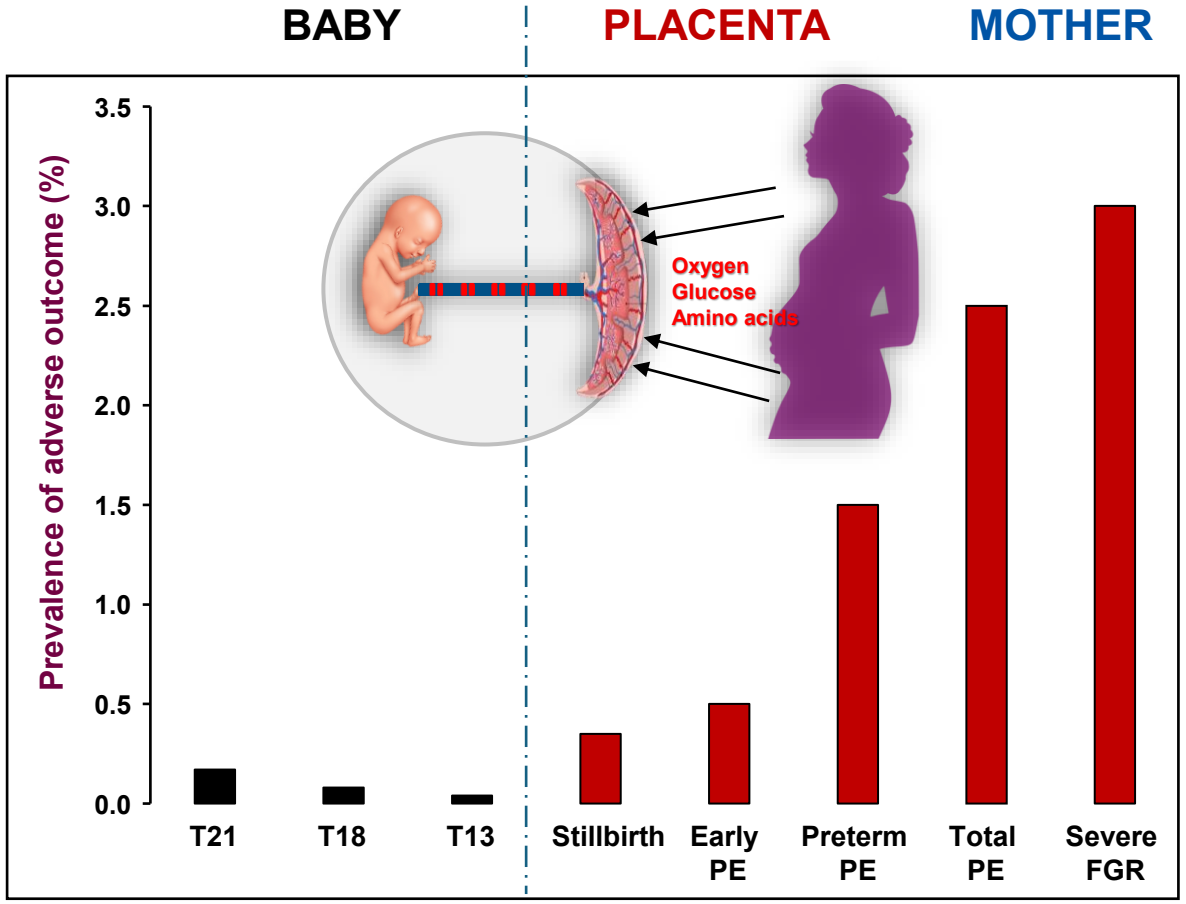
MAKING A BIG DIFFERENCE IN PREGNANCY CARE

PLACENTAL INSUFFICIENCIES,

especially preeclampsia leading to ADVERSE OUTCOMES of pregnancy

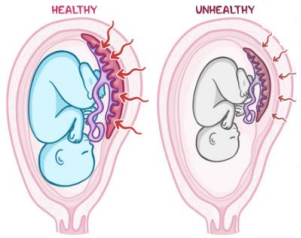
ARE MUCH MORE COMMON THAT ANEUPLOIDIES COMBINED.

BOTH MOTHER AND BABY ARE AFFECTED both short and long-term



Placental insufficiency is present in virtually every major obstetrical syndrome"

ROMERO, AM J OBSTET GYNECOL. 2011.

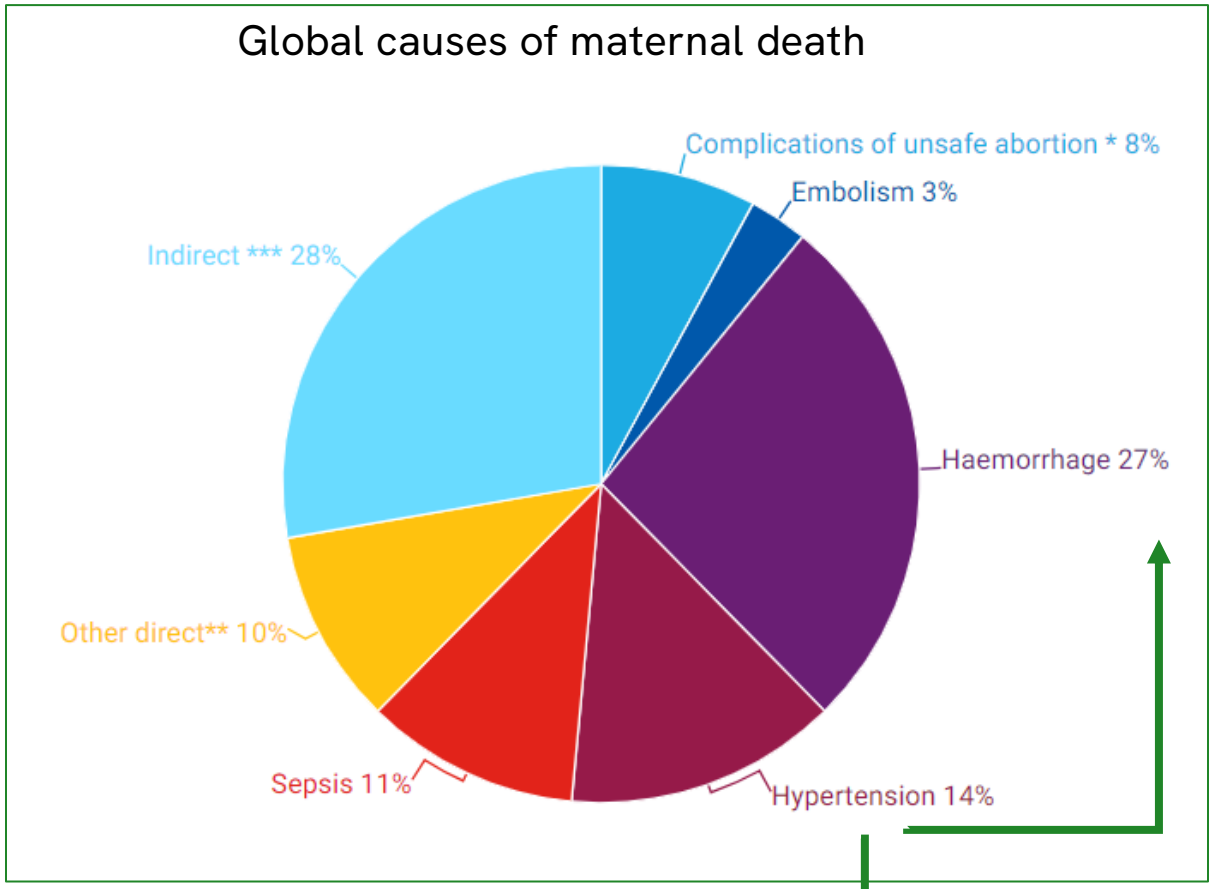


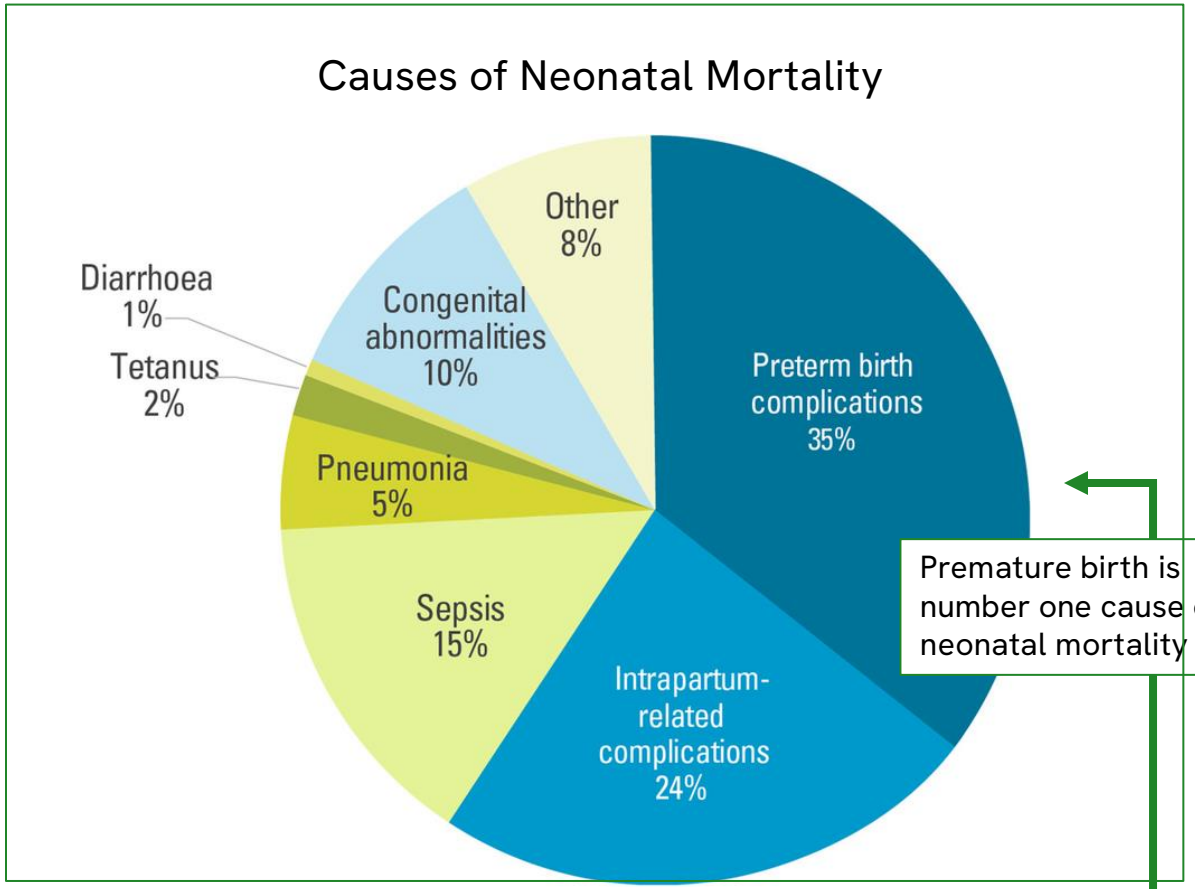
- **Trisomy 21 = 1 in 600 (0.17%)**
- **Trisomy 18 = 1:1200 (0.08%)**
- **Trisomy 13 = 1:4200 (0.02%)**

- **Stillbirth = 1:250 (0.40%)**
- **Early PE = 1:200 (0.5%)**
- **Preterm PE = 1:66 (1.5%)**
- **Total PE = 1:40 (2.5%)**
- **Severe FGR = 1:33 (3.0%)**

Parker S et.al Birth Defects Res A Clin Mol Teratol. 2010, Duley L. *Semin Perinatol* 2009, Romo A et al. Pediatr Endocrinol Rev. 2009, WHO media centre, fact sheet 2016. http://www.who.int/mediacentre/factsheets/fs363/en/

MATERNAL AND NEONATAL MORTALITY





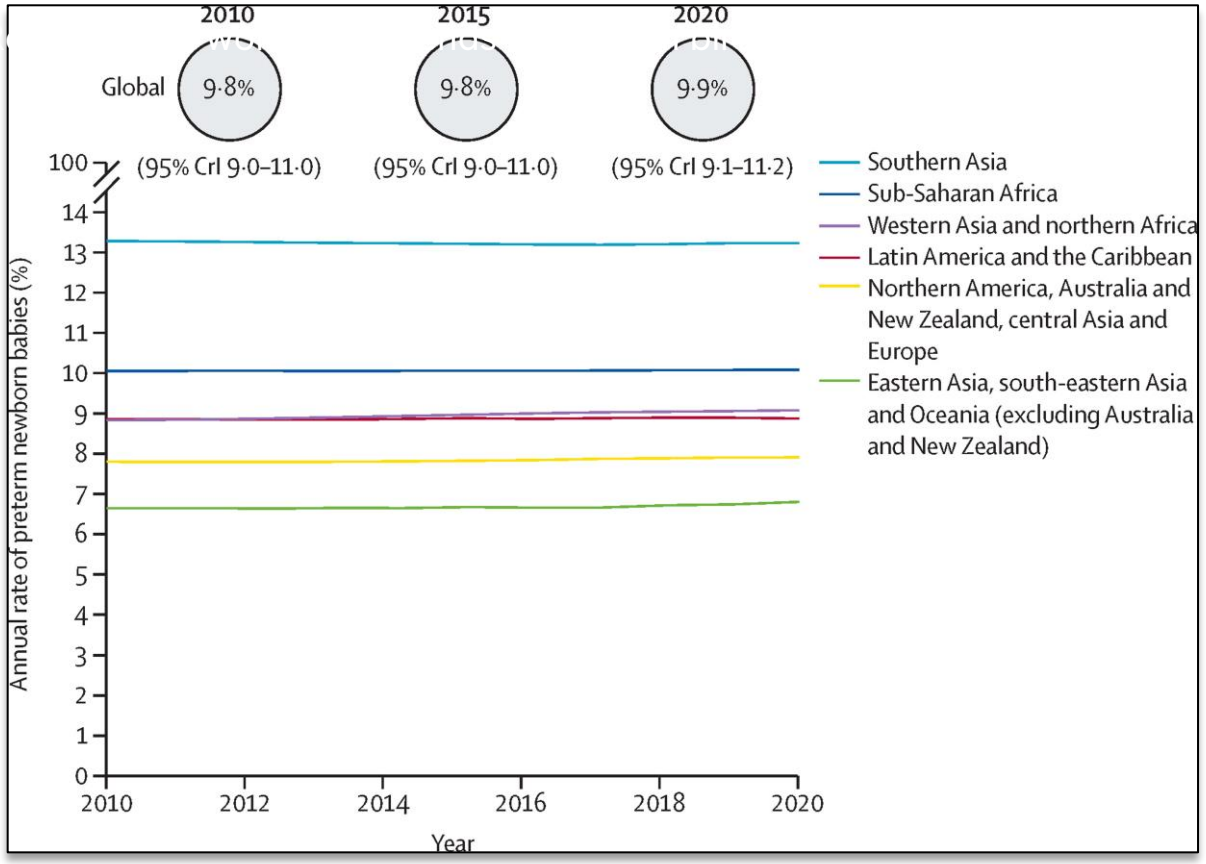
Premature birth is number one cause of neonatal mortality

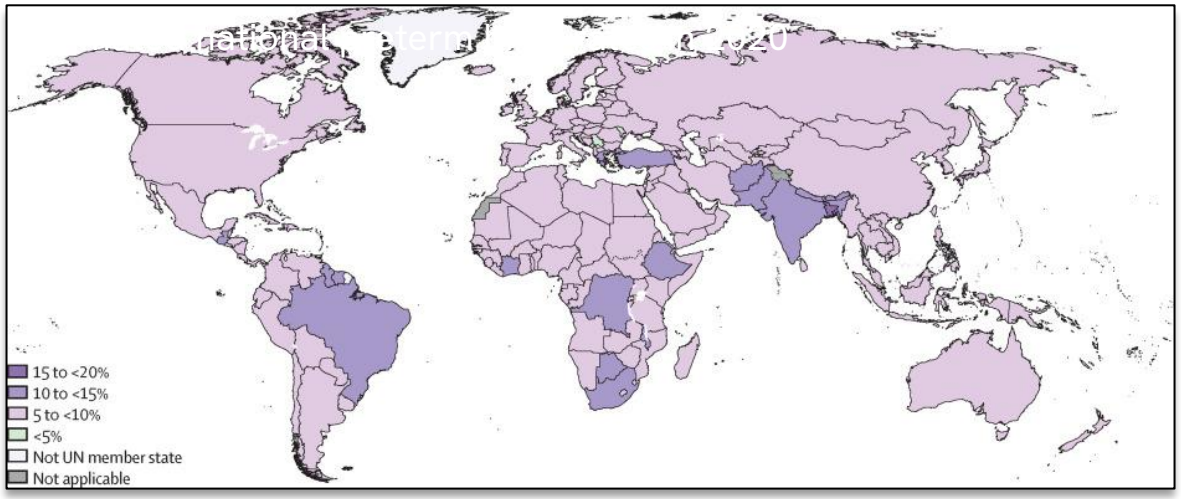
Pre-eclampsia, a hypertensive disorder, is one of the leading causes of maternal mortality

Pre-eclampsia often leads to premature delivery of the fetus

Source: WHO

National, regional, and global estimates of preterm birth in 2020, with trends from 2010 (Lancet, 2023)

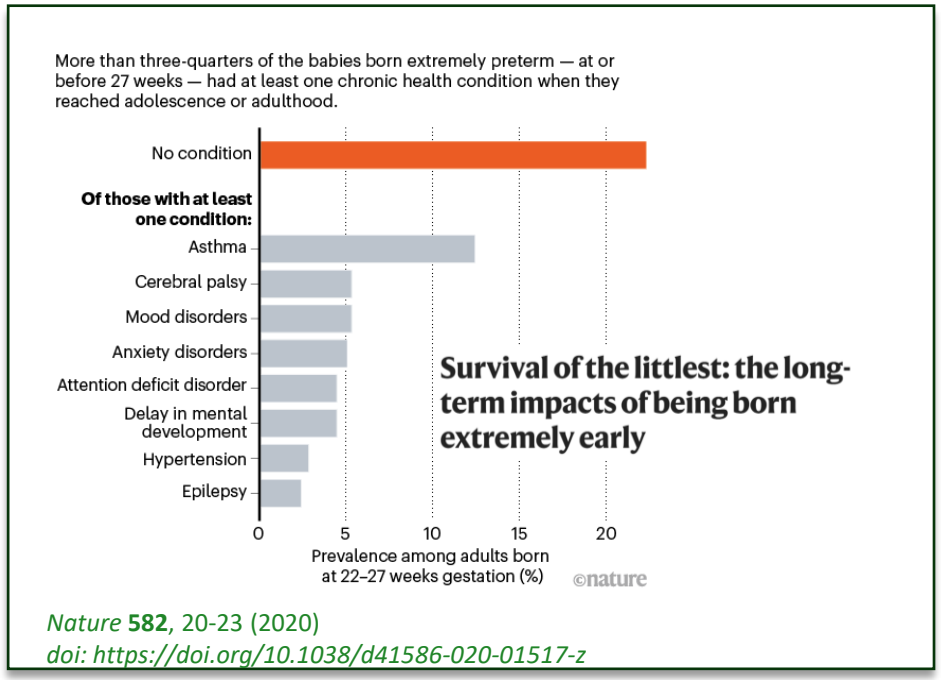




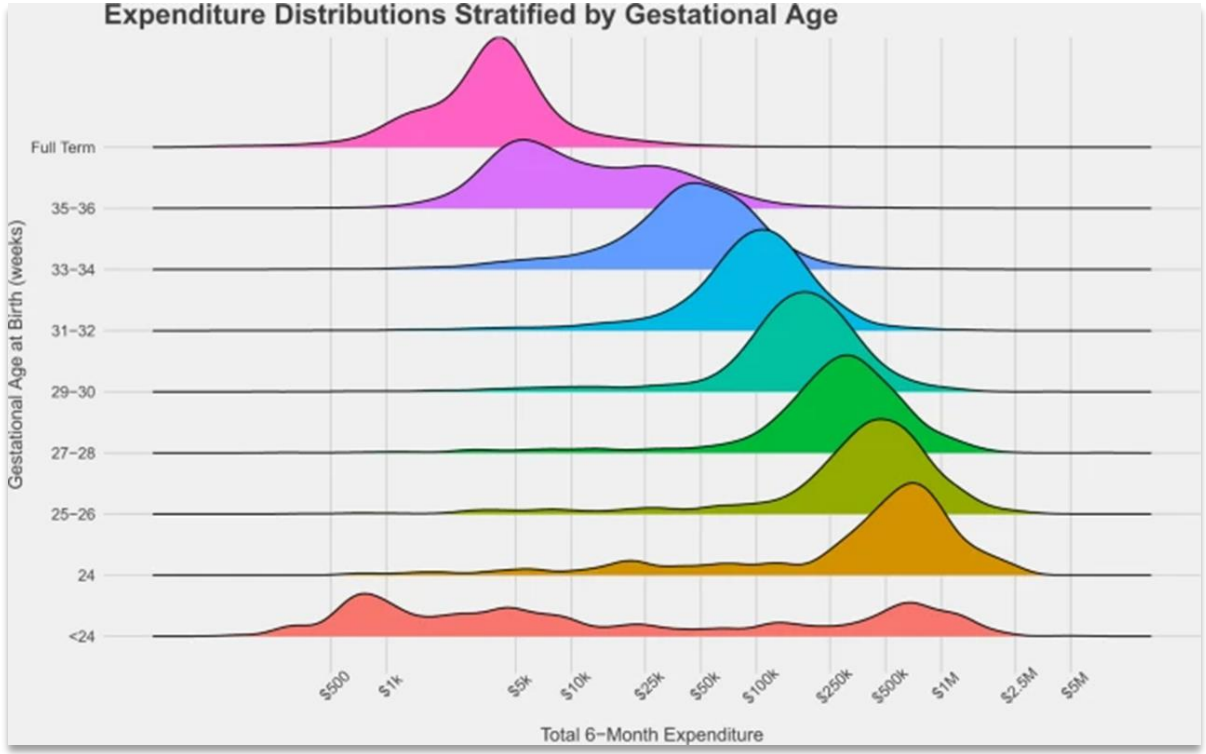
Prematurity numbers are not that different between countries.

...and have not been decreasing.

Effects of being survivor of premature: Morbidity and costs



Nature **582**, 20-23 (2020)
doi: https://doi.org/10.1038/d41586-020-01517-z

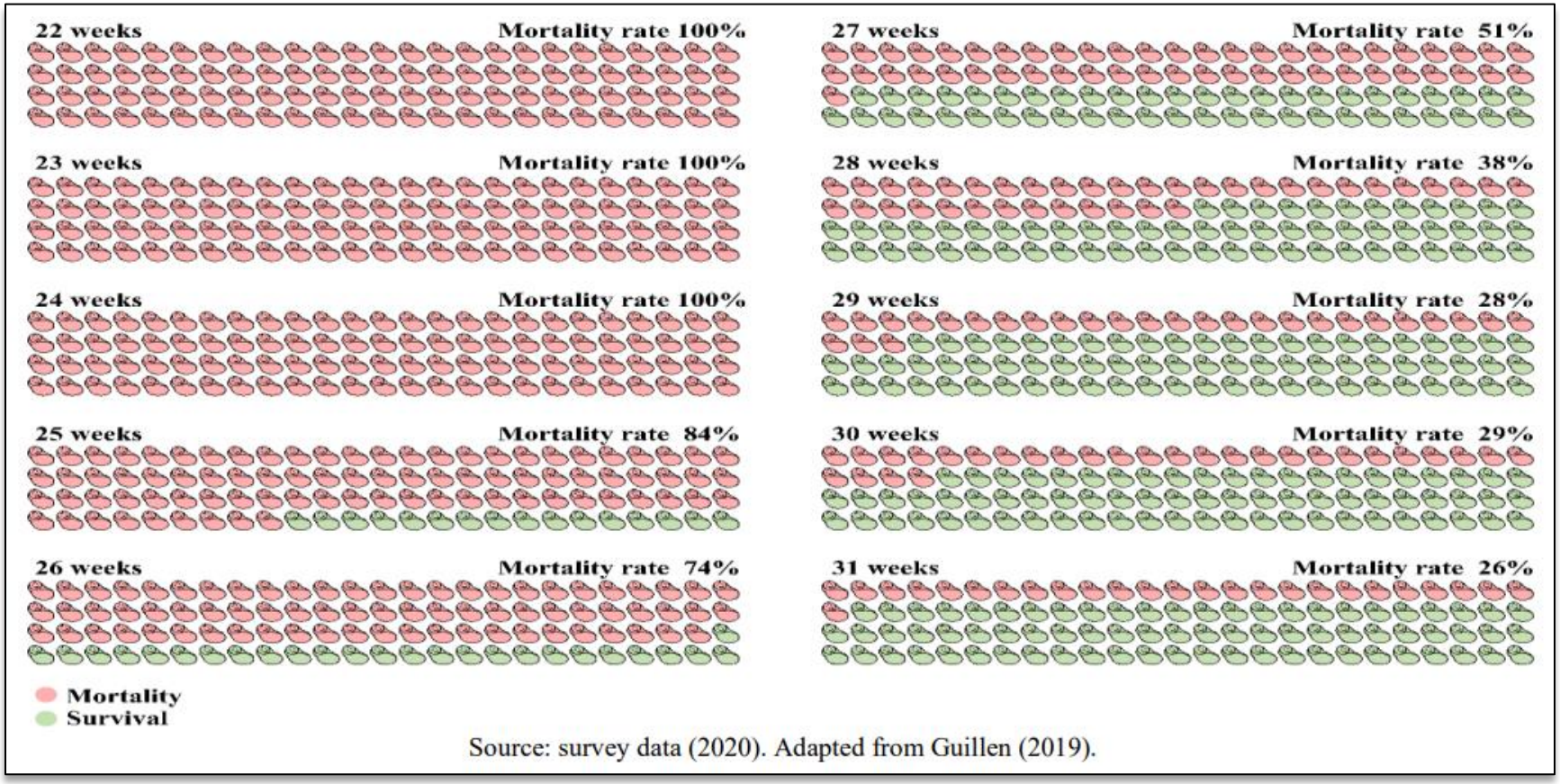


Frequency of death and major, intermediate and minor morbidity. Data are n (%).

Outcome	Delivery gestational age (weeks)															P for trend
	All (n=8334)	23 (n=43)	24 (n=114)	25 (n=124)	26 (n=169)	27 (n=159)	28 (n=196)	29 (n=213)	30 (n=262)	31 (n=312)	32 (n=451)	33 (n=639)	34 (n=1058)	35 (n=1477)	36 (n=3117)	
Death	119 (1.4)	19 (44.2)	36 (31.6)	15 (12.1)	19 (11.2)	13 (8.2)	4 (2.0)	4 (1.9)	4 (1.5)	3 (1.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	<.001
Major morbidity*	657 (7.9)	19 (44.2)	60 (52.6)	68 (54.8)	88 (52.1)	64 (40.3)	43 (21.9)	48 (22.5)	36 (13.7)	22 (7.1)	39 (8.7)	27 (4.2)	46 (4.4)	42 (2.8)	55 (1.8)	<.001
Minor morbidity†	3136 (37.6)	4 (9.3)	18 (15.8)	39 (31.5)	59 (34.9)	77 (48.4)	144 (73.5)	147 (69.0)	206 (78.6)	255 (81.7)	344 (76.3)	406 (63.5)	540 (51.0)	402 (27.2)	495 (15.9)	<.001
Survival without any of the above morbidities	4422 (53.1)	1 (2.3)	0 (0.0)	2 (1.6)	3 (1.8)	5 (3.1)	5 (2.6)	14 (6.6)	16 (6.1)	32 (10.3)	67 (14.9)	205 (32.1)	472 (44.6)	1033 (69.9)	2567 (82.4)	

Manuck TA, Rice MM, Bailit JL, Grobman WA, Reddy UM, Wapner RJ, Thorp JM, Caritis SN, Prasad M, Tita AT, Saade GR, Sorokin Y, Rouse DJ, Blackwell SC, Tolosa JE; Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Preterm neonatal morbidity and mortality by gestational age: a contemporary cohort. Am J Obstet Gynecol. 2016 Jul;215(1):103.e1-103.e14. doi: 10.1016/j.ajog.2016.01.004. Epub 2016 Jan 7. PMID: 26772790; PMCID: PMC4921282. Beam, A.L., Fried, I., Palmer, N. et al. Estimates of healthcare spending for preterm and low-birthweight infants in a commercially insured population: 2008-2016. J Perinatol 40, 1091–1099 (2020). https://doi.org/10.1038/s41372-020-0635-2

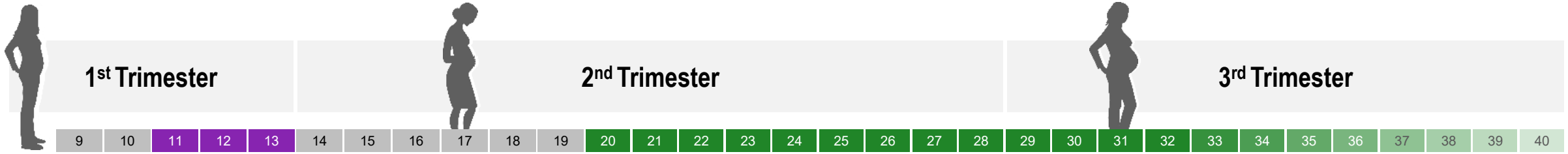
Infographic for parents on the mortality results among premature infants



Without efficient prediction & prevention, prematurity is still the primary management and outcome of preterm preeclampsia

Extreme prematurity in a public reference unit: morbidity, viability and mortality Research, Society and Development, v. 11, n. 6, e58311629468, 2022
 | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v11i6.2946

Traditional Pre-eclampsia screening for all – PE management for symptomatic



Pre-eclampsia screening
NO SYMPTOMS

SYMPTOMS of pre-eclampsia may appear
from wk 20 onwards

For all

Identify women with high risk for pre-eclampsia

Screening based on maternal/obstetric risk factors

Recent studies: **only ~40% are detected**

For symptomatic

Test (symptomatic) women with suspected pre-eclampsia

Diagnosing the preeclamptic with standard clinical tests

Are not specific to Pre-eclampsia,

Don’t provide a prognosis of PE

Don’t provide a prediction in the time,

Do not inform about fetal well being

60%

Of maternal deaths due to pre-eclampsia are preventable

Majority of long-term effects of PREECLAMPSIA SURVIVORS

3-4x times the risk of developing high blood pressure

2x times to develop heart disease

higher risk to develop diabetes

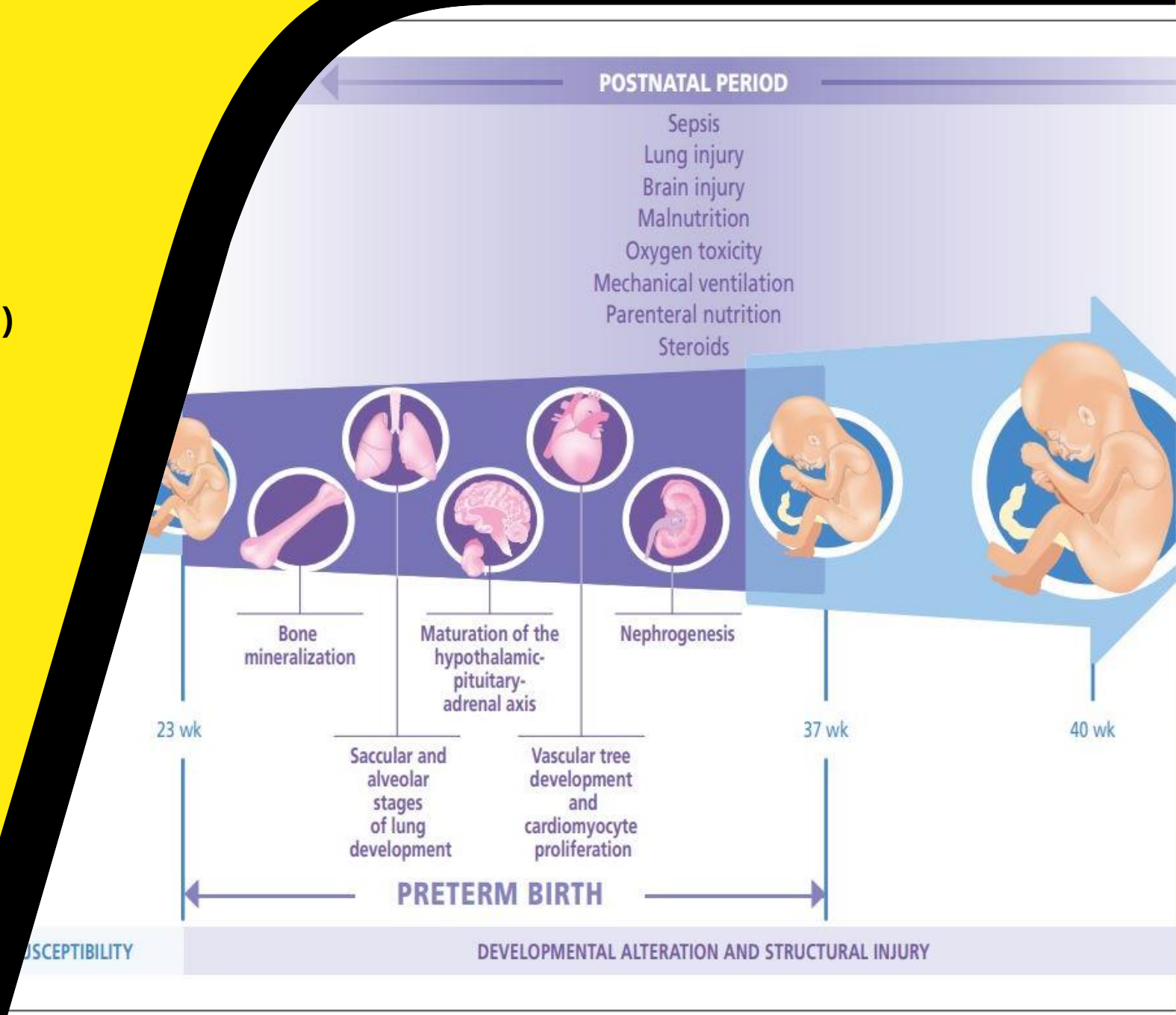
...could be prevented

Majority of long-term effects of PREECLAMPSIA SURVIVORS

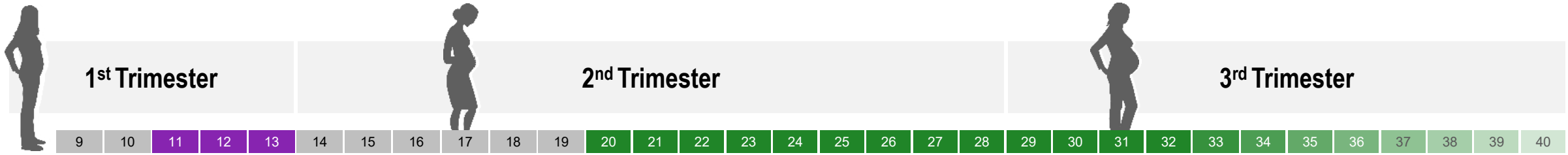
- Babies who survive can have
- **breathing issues, intestinal (digestive) problems, and bleeding in their brains**.

- Long-term problems may include **developmental delay** (not meeting the developmental milestones for his or her age), **CP, ADHD, Neurological disorders and lower performance in school**.

...could be prevented



Improved Pre-eclampsia screening for all – PE management for symptomatic



Pre-eclampsia screening
NO SYMPTOMS

SYMPTOMS of pre-eclampsia may appear from wk 20 onwards

For all

Identify women with high risk for pre-eclampsia

RECORD MEDICAL HISTORY + BLOOD TEST PIGF 1-2-3 + MEASURE BLOOD PRESSURE + MEASURE ULTRASOUND

The Fetal Medicine Foundation

For symptomatic

Test (symptomatic) women with suspected pre-eclampsia

PLGF ↓ sFlt-1 ↑

PREECLAMPSIA CARE IMPACT

NUMBER 1 GOAL

	UNTREATED	DIAGNOSED & MANAGED	SCREENED & PREVENTED
		+ PlGF + sFlt-1	+ PlGF
SHORT-TERM	Hypertension, coma, convulsions, kidney failure, liver failure, DEATH	Hypertension, kidney failure, liver failure, swollenness, headache	Normal pregnancy, Healthy mother
SHORT-TERM	Preterm birth, STILLBIRTH	Preterm birth, risk of DEATH	More mature in delivery

PREECLAMPSIA SURVIVORS

LONG-TERM	Cardiovascular disease, organ damage, risk for stroke
LONG-TERM	Delayed cognitive development, autism, death, chronic diseases

revvity

Complications of preeclampsia (hypertensive disorder of pregnancy)

SHORT-TERM

Hypertension, coma, convulsions, kidney failure, liver failure, DEATH

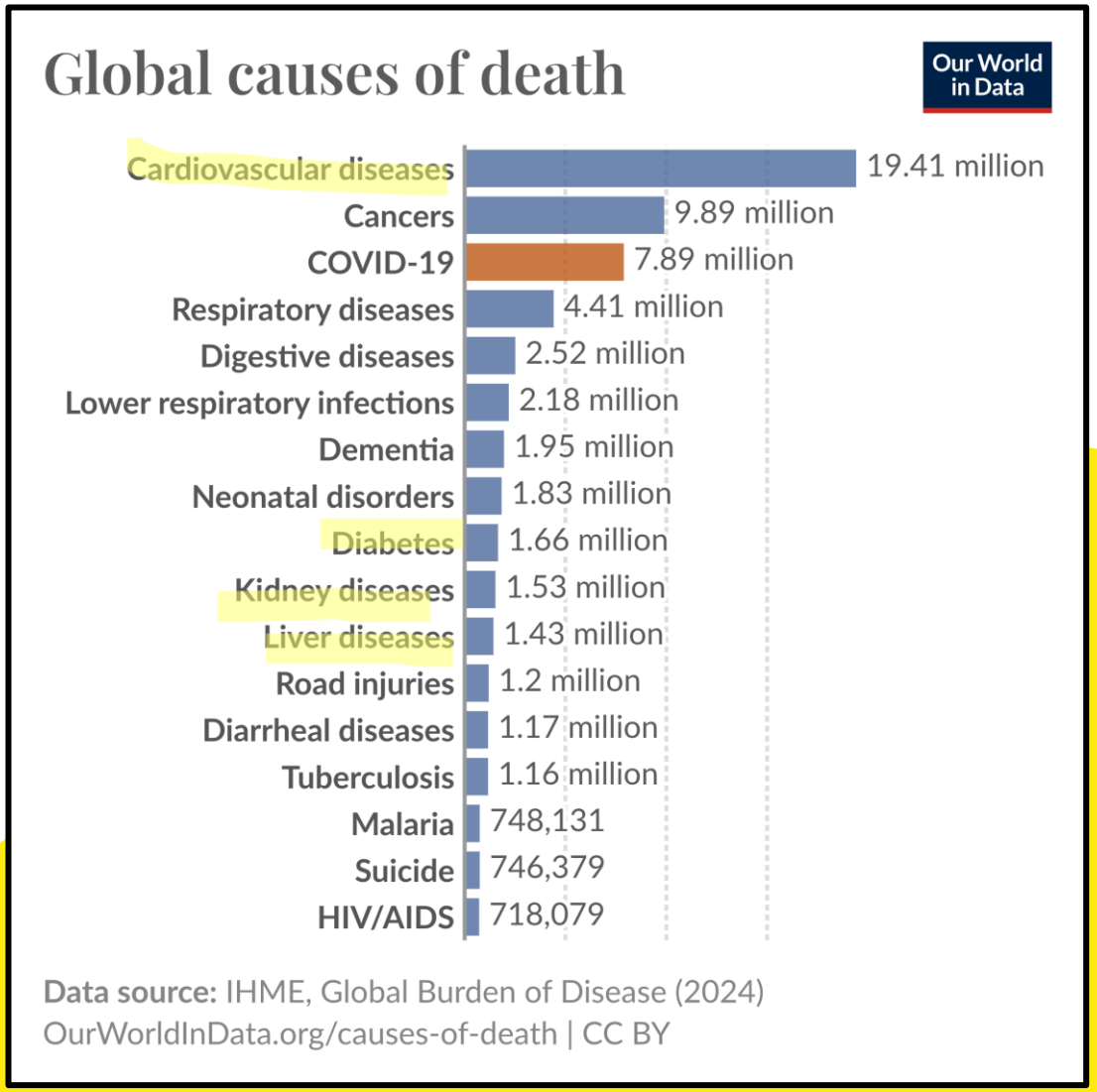
Preterm birth, STILLBIRTH

LONG-TERM

Cardiovascular disease, kidney damage, Liver disease, stroke, diabetes mellitus

Delayed cognitive development, autism, death, cardiovascular disease, Stroke, Diabetes mellitus

Preeclampsia survivors – health affected for lifetime



How to improve pregnancy care for preventing pre-eclampsia?

1T PRE-ECLAMPSIA SCREENING

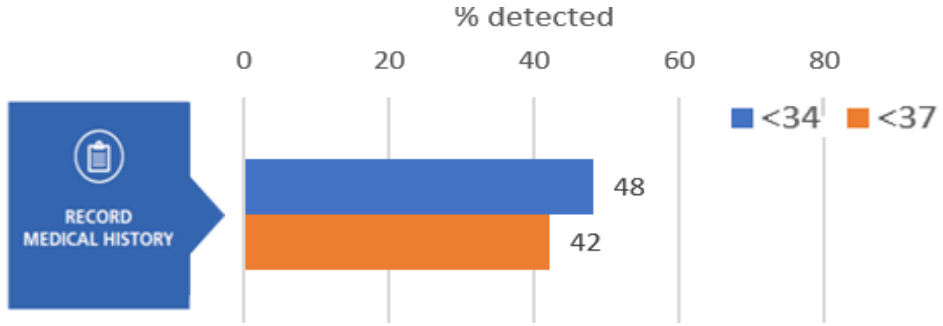
Traditional screening **method is simple but poor**

ACOG/NICE guidelines pre-eclampsia screening is based on maternal characteristcs and medical history

Moderate-risk factors
Nulliparity
Age >40 years
Inter-pregnancy interval >10 years
BMI at first visit >35 kg/m2
Family history of PE

High-risk factors
History of hypertensive disease in previous pregnancy
Chronic kidney disease
Autoimmune disease
Diabetes mellitus
Chronic hypertension
Multi fetal pregnancy

Simple and easy method to perform, but the DETECTION RATE IS POOR



Screening based on maternal/obstetric risk factors

Recent studies: **only ~40% are detected**

ACOG. First-trimester risk assessment for early-onset preeclampsia. Committee opinion No. 638. Obstet Gynecol 2015; 126: e25-7. Tan MY et al. Ultrasound Obstet Gynecol 2018; 51: 743-750.

The first step to better detection **combined screening with PLGF**

ACOG/NICE guidelines pre-eclampsia screening is based on maternal characteristcs and medical history

ACOG. First-trimester risk assessment for early-onset preeclampsia. Committee opinion No. 638. Obstet Gynecol 2015; 126: e25-7. Tan MY et al. Ultrasound Obstet Gynecol 2018; 51: 743-750.

funded by EU FP7
ASPRE project

EFFICACY OF SCREENING AND ASPIRIN
in reducing preterm pre-eclampsia

Combined pre-eclampsia screening

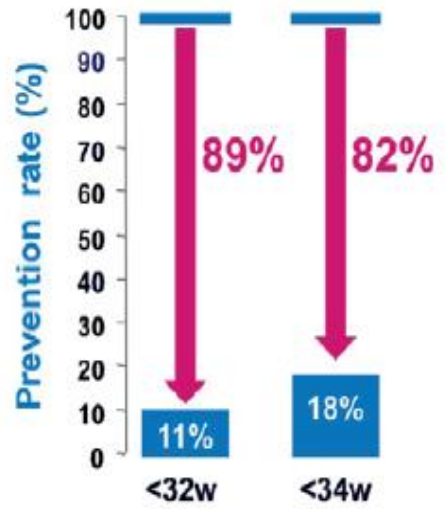
Weeks 11-13+6

RECORD MEDICAL HISTORY + BLOOD TEST PIGF 1-2-3 + MEASURE BLOOD PRESSURE + MEASURE ULTRASOUND

Identify women at high risk of pre-eclampsia

Aspirin in high risk women

150mg Aspirin



Screening enables timely intervention for reducing the incidence of pre-eclampsia

EFFECT OF PREVENTION
on length of stay in the NICU

Placebo Group	Aspirin Group
Mean NICU stay 2.06d	Mean NICU stay 660d

The findings have implications for both short and long-term

Prophylactic use of aspirin results in

68% reduction

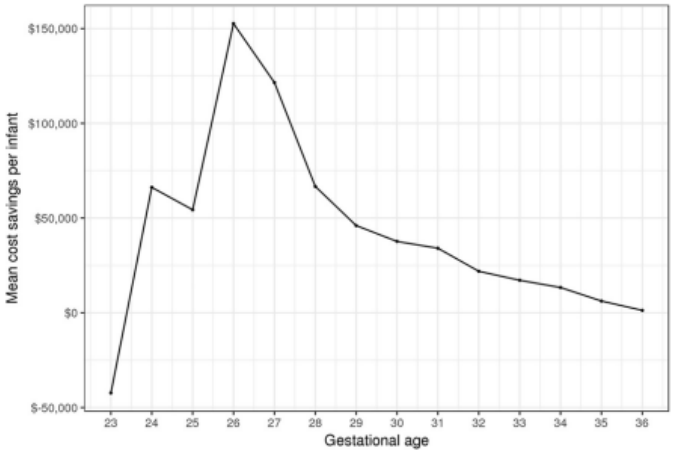
in the length of stay in NICU
(neonatal intensive care unit)

Healthcare costs | Infant survival

1. Rolnik DL et al. ASPRE trial; Aspirin versus Placebo in Pregnancies at High Risk for Preterm Preeclampsia. N Engl J Med. 2017;377(7):613-622. 2. Wright D et al. Aspirin for Evidence-Based Preeclampsia Prevention trial: influence of compliance on beneficial effect of aspirin in prevention of preterm preeclampsia. Am J Obstet Gynecol. 2017; 217:685.e1-5. 3. Poon LC et al. Aspirin for Evidence-Based Preeclampsia Prevention trial: effect of aspirin in prevention of preterm preeclampsia in subgroups of women according to their characteristics and medical and obstetrical history. *Am J Obstet Gynecol* 2017;217:585.e1-5. 4. Wright et al. Aspirin for Evidence-Based Preeclampsia Prevention trial: effect of aspirin on length of stay in the neonatal intensive care unit. Am J Obstet Gynecol. 2018; 218:612.e1-6

EFFECT OF PRE-ECLAMPSIA

on healthcare costs and infant survival



The costs are by gestational age.

Stevens. Short-term costs of preeclampsia in the US. Am J Obstet Gynecol 2017.

The earlier a baby is born, the higher the cost of care.

Table 1. Short-term costs of pre-eclampsia to the United States health care system. [11]

Estimated unit and total health care cost for pre-eclampsia patients in the United States, by gestational age at birth (2012) using California Office of Statewide Health Planning and Development and commercial claims data

Costs	<28 wks (3604)	28-33 wks (23,624)	34-36 wks (41,856)	37 wks or longer (87, 596)	All (156, 680)
Maternal cost per birth	$29,131	$24,063	$19,692	$17,021	$19,075
Infant cost per birth	$282,570	$59,803	$11,112	$6013	$21,847
Combined cost per birth	$311,701	$83,866	$30,804	$23,035	$40,922
Total health care cost	$1.2 billion	$2.0 billion	$1.3 billion	$2.0 billion	$6.4 billion
Total cost because of infant cost, %	91%	71%	36%	26%	

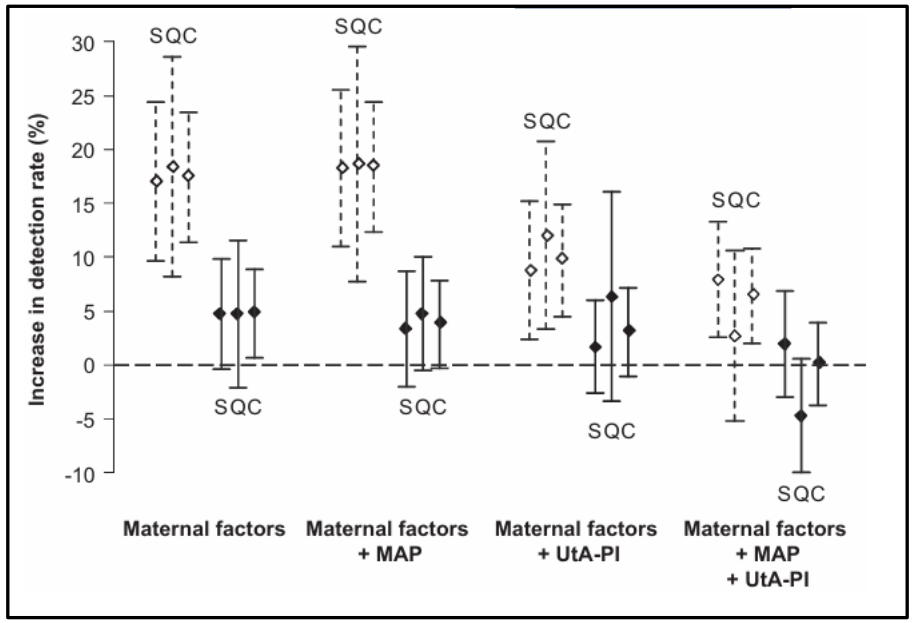
The earlier a baby is born, the higher the risk of death or serious disability.

- In 2019 preterm birth and low birth weight accounted for about **17% of infant deaths** in US.
- Babies who survive can have **breathing issues, intestinal (digestive) problems, and bleeding in their brains**.
- Long-term problems may include **developmental delay** (not meeting the developmental milestones for his or her age), **CP, ADHD, Neurological disorders and lower performance in school**.

Birth	Death <5 y	Cerebral palsy	Impaired work capacity
23-27w	80%	9.1%	10.6%
28-30w	40%	6.0%	8.2%
31-33w	11%	1.9%	4.2%
34-36w	2.3%	0.3%	2.4%
≥37w	0.6%	0.1%	1.7%

867,692 live births Norway 1967-1983
Moster et al. NEJM 2008;359:262

Why not PAPP-A? Performance review for prediction of pre-term PE (<37wks GA).



Increase in DR observed for a fixed 10% SPR

Screening Model	Base case	Base case plus PAPP-A	Base case plus PlGF
History	45.4%	4.7%	17.4%
History plus MAP	51.8%	3.8%	18.4%
History plus UTPI	63.8%	3.0%	9.7%
History plus UTPI & MAP	75.0%	0.0%	6.4%

Based on SPREE & Screening Quality Study. Both data sets reviewed individually and combined (25226 screens).

In total, 194 cases of pre-term PE.

Accepted: 22 December 2021 | Published Online 13 February 2022
DOI: 10.1111/1471-0528.17096
BJOG An International Journal of Obstetrics and Gynaecology
RESEARCH ARTICLE
Epidemiology

Serum PlGF compared with PAPP-A in first trimester screening for preterm pre-eclampsia: Adjusting for the effect of aspirin treatment

David Wright[1] | Min Yi Tan[2] | Neil O'Gorman[2] | Argyro Syngelaki[2] | Kypros H. Nicolaides[2]

Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health 42 (2025) 101270

Contents lists available at ScienceDirect

Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health

journal homepage: www.elsevier.com/locate/preghy

Review article

The diagnostic accuracy of the NICE risk–stratification algorithm in predicting pre-eclampsia: A systematic review with *meta*-analysis

James S Morris [a,*], Siraj Abualnaja [a], Miriam Baumgarten [b]

[a] University of Cambridge School of Clinical Medicine, Addenbrooke's Hospital NHS Foundation Trust, Hills Road, Cambridge CB2 0QQ, United Kingdom
[b] Department of Obstetrics and Gynaecology, Addenbrooke's Hospital NHS Foundation Trust, Hills Road, Cambridge CB2 0QQ, United Kingdom

- This systematic review of the NICE risk–stratification algorithm. Incorporating data from 17 eligible studies and 258,278 pregnancies.

- The NICE risk-stratification algorithm for preeclampsia performs remarkably poorly as a tool by which to allocate Aspirin prophylaxis.
  - 56.7% of preeclampsia cases missing
  - Costing £265000/year unnecessary prescriptions of Aspirin

- Should be replaced with an alternative tools like FMF tool.

Ultrasound Obstet Gynecol 2018
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.19039

Comparison of diagnostic accuracy of early screening for pre-eclampsia by NICE guidelines and a method combining maternal factors and biomarkers: results of SPREE

M. Y. TAN[1,2], D. WRIGHT[3], A. SYNGELAKI[1], R. AKOLEKAR[1,4], S. CICERO[5], D. JANGA[6], M. SINGH[7], E. GRECO[8], A. WRIGHT[3], K. MACLAGAN[9], L. C. POON[1,10#] and K. H. NICOLAIDES[1,2#]

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Efficacy and Mechanism Evaluation

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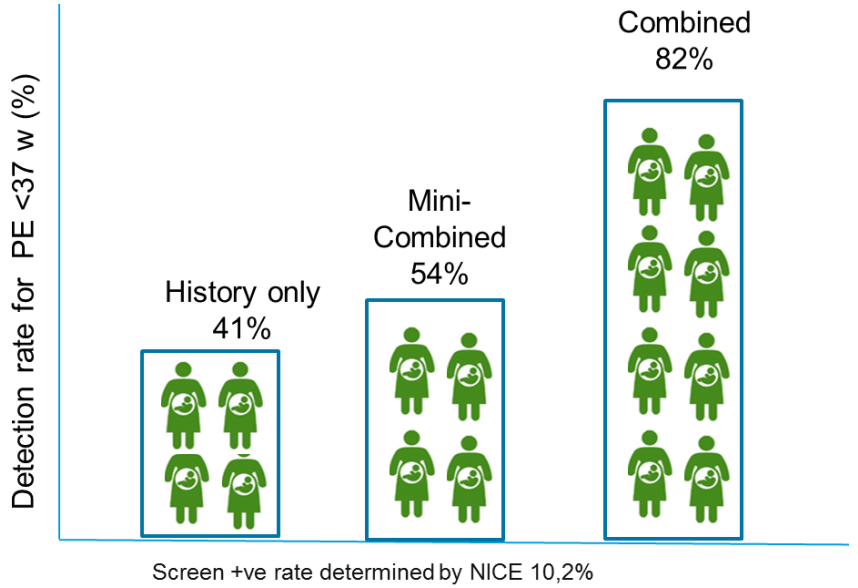
Mini-combined test compared with NICE guidelines for early risk-assessment for pre-eclampsia: the SPREE diagnostic accuracy study

Liona C Poon, David Wright, Steve Thornton, Ranjit Akolekar, Peter Brocklehurst and Kypros H Nicolaides

Showed low compliance to treatment if no proper screening and counselling is performed



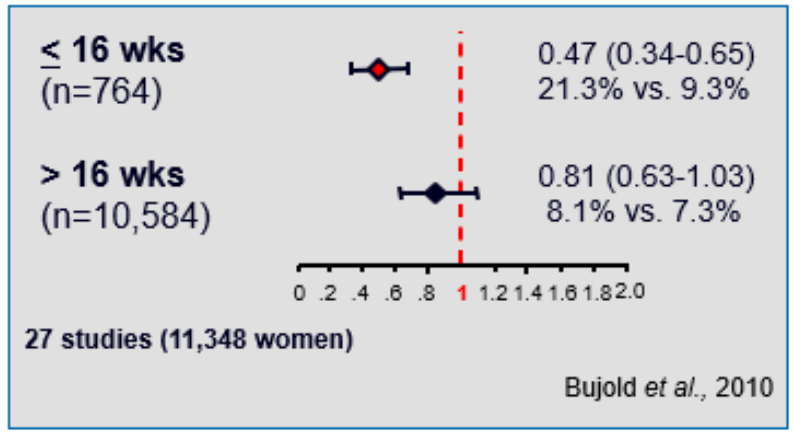
- Compliance to aspirin (Do high risk women take their tablets?)
  - 23% with NHS method (history only)
  - 85% with FMF method (Combined)

It is important that the women know their risk and it is based on specific assessment with measurement results.

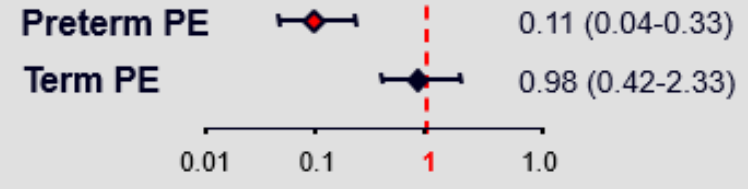
ASPIRIN – potential candidate for prevention - Timing?

Low-dose Aspirin from 12 wks

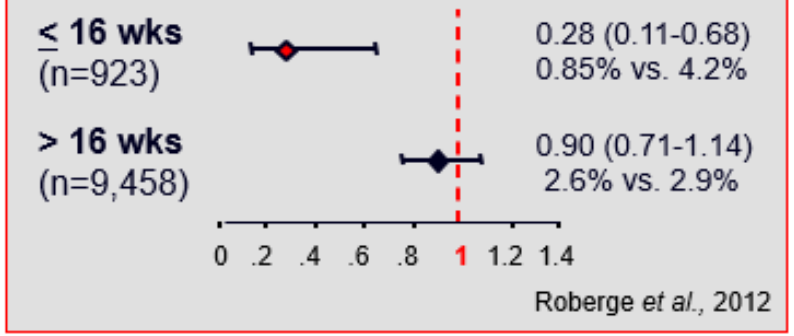
Meta analysis on prophylactic aspirin
31 randomized studies, 32217 patients
• Preeclampsia 0.90 (95% CI 0.84-0.97)
Askie *et al*, Lancet 2007



Aspirin ≤16 wks: early vs late PE



Perinatal death



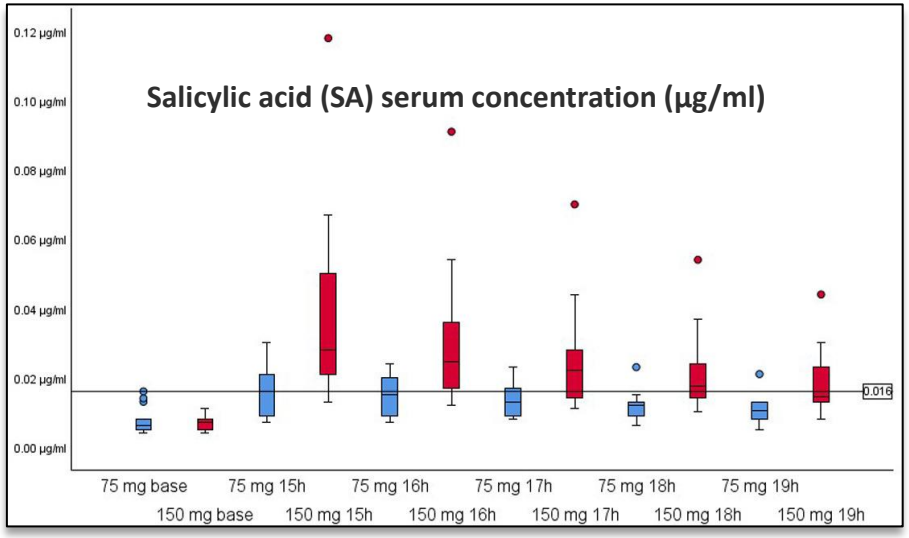
Significant difference in impact on pre-term PE and perinatal death, dependent on when Aspirin prophylaxis was started.

ASPIRIN – potential candidate for prevention - The dose?

A randomised crossover design study comparing the pharmacokinetics and pharmacodynamics of two single Doses of ORal Aspirin (75 mg v 150mg) in pregnant women at risk of pre-eclampsia (DORA): implications on assessing aspirin response and patient adherence to therapy.

Raya Vinogradov*†§c, Oisín N. Kavanagh*#◊, Jeremy Palmer#, Paul Murphy§, Emma Curtis§, Farhad Kamali §# & Stephen Robson†§.

The doses and the effect to thromboxane B2 levels from blood samples, in different timepoints post ingestion of aspirin



- 150 mg dose SA inhibits thromboxane more efficiently than the 75 mg dose.
- With a dose of 150 mg SA, plasma SA concentrations are consistently above baseline levels up to 12 hours after oral dosing
- Study was also able to demonstrate that thromboxane levels were fully recovered after a wash-out period of one week.

A Randomized Controlled Study Comparing the Efficacy of 75mg Versus 150mg Aspirin for the Prevention of Preeclampsia in High-Risk Pregnant Women

Nishi Sinha [1], Shruti Singh [1], Mukta Agarwal [2], Pramod K. Manjhi [1], Rajesh Kumar [1], Sunil Kumar Singh [1], Aakanksha Priya [1]

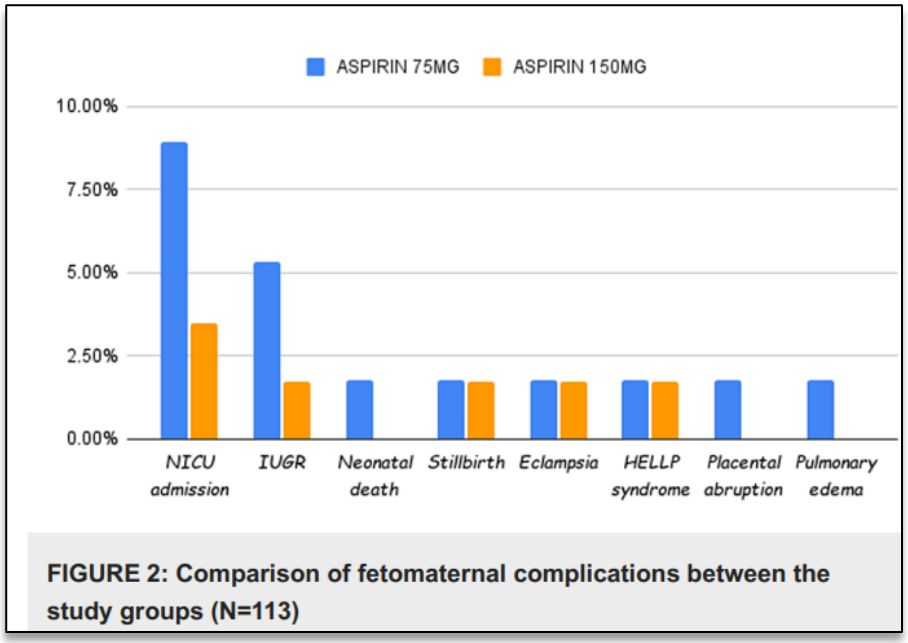


FIGURE 2: Comparison of fetomaternal complications between the study groups (N=113)

- With women who are at high risk of developing preeclampsia, Aspirin 150 mg once a day at bedtime is more effective than Aspirin 75 mg in preventing preeclampsia with similar adverse outcomes (NICU admission, IUGR, neonatal death, still birth, eclampsia, HELLP syndrome, placental abruption and pulmonary edema).

Am J Obstet Gynecol. 2025 Sep;233(3):e91-e93. doi: 10.1016/j.ajog.2025.04.046. Epub 2025 Apr 24.

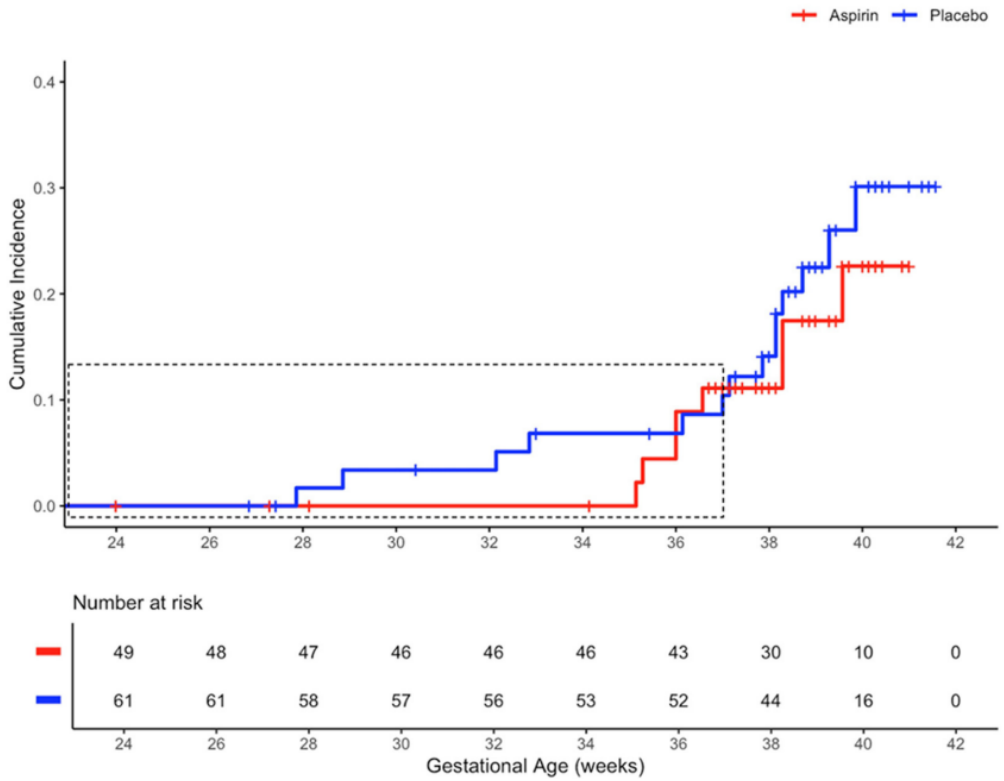
Aspirin delays preeclampsia in women with chronic hypertension

Emmanuel Bujold [1], Daniel L Rolnik [2], Liona Poon [3], Argyro Syngelaki [4], David Wright [5], Kypros H Nicolaides [4]

Affiliations + expand

PMID: 40287082 DOI: 10.1016/j.ajog.2025.04.046

FIGURE
Cumulative risk of PE among participants taking aspirin or placebo



Secondary analysis of the ASPRE data to better estimate the role of aspirin in women with chronic hypertension.

Aspirin use is associated with a shift in the cumulative risk of preterm PE to later gestational age (P=.051).

Findings suggest that, in women with chronic hypertension, aspirin shifts the distribution of delivery with PE to a later gestational age, in a similar fashion to that in high-risk women without chronic hypertension.

Women with chronic hypertension often have PE with delivery very early in gestation. Aspirin delays PE by several weeks and certainly reduces perinatal morbidity and neonatal hospitalizations.

Aspirin does not specifically reduce the number of preterm PE.

Consequently, women with chronic hypertension benefit from aspirin during pregnancy by reducing the earliest cases of PE.

Aspirin in prevention of preeclampsia: Universal aspirin – Side effects

Aspirin use during pregnancy and the risk of bleeding complications: a Swedish population-based cohort study.
Hastie, R. et al. (2021). *American journal of obstetrics and gynecology*, *224*(1), 95.e1–95.e12.

Complication	Aspirin (n=4,088)	No aspirin (n=309,536)	Odds ratio (95%CI)
Intrapartum hemorrhage	117 (2.9%)	4.695 (1.5%)	1.63 (1.30,2.05)
Postpartum hemorrhage	411 (10.2%)	24,036 (7.8%)	1.23 (1.08,1.39)
Neonatal intracranial hemorrhage	3 (0.07%)	17 (0.01%)	9.66 (1.88, 49.48)

Problems: Aspirin use defined as any tablet taken for any reason

Systematic review and meta-analysis of adverse events of low-dose aspirin and clopidogrel in randomized controlled trials.
McQuaid, K. R., & Laine, L. (2006). *The American journal of medicine*, *119*(8), 624–638

Complication (n=75,000 non-pregnant)	Aspirin	No aspirin	RR (95%CI)
Major bleeding	26,673	26,712	1.71 (1.41, 2.08)
Major gastrointestinal bleeding	28,686	28,719	2.07 (1.61, 2.66)
Intracranial bleeding	27,671	27,712	1.65 (1.12, 2.44)

Absolute annual increase: Major bleeding 0.13%, Gastrointestinal bleeding 0.12%, Intracranial bleeding 0.03%, non-pregnant)

Utero Exposure to Aspirin and Risk of Asthma in Childhood.
Chu, S. et al (2016). *Epidemiology (Cambridge, Mass.)*, *27*(5), 726–731.

Complication	Aspirin (n=11,215)	No aspirin (n=8,677)	aOR (95%CI)
Childhood asthma	552 (5%)	352 (4%)	1.3 (1.1, 1.6)

The risk of childhood asthma was increased by 30%

In utero drug exposure and hearing impairment in 2-year-old children A case-control study using the EFEMERIS database.
Foch, C., et al (2018). *International journal of pediatric otorhinolaryngology*, *113*, 192–197.

Complication	Abnormal hearing (n=1,245)	Normal hearing (n=28,046)	aOR (95%CI)
In-utero ASA exposure	28 (2.2%)	396 (1.4%)	1.61 (1.09, 2.37)

The risk of hearing disorders was increased by 60%

Implementation of First-Trimester Screening and Prevention of Preeclampsia: A Stepped Wedge Cluster-Randomized Trial in Asia. Nguyen-Hoang et al; FORECAST Collaborators Circulation. 2024 Oct 15;150(16):1223-1235.

Complication	High risk with aspirin	High risk without aspirin
Postpartum hemorrhage	2.05%	1.44%
Fetal structural defects	0.72%	0.64%
Fetal chromosomal defects	0.1%	0
At least one serious adverse event	3.15%	2.08%

The risk of PE was screened

Aspirin versus Placebo in Pregnancies at High Risk for Preterm Preeclampsia.
Rolnik, D. L., et al (2017)*The New England journal of medicine*, *377*(7), 613–622.
ASPRE study

Complication	Aspirin (n=798)	Placebo (n=822)	P-value
Vaginal bleeding	29 (3.6%)	21 (2.6%)	0.27
Nasal bleeding	16 (2.0%)	27 (3.3%)	0.15
Abruption without PE	5 (0.62%)	9 (1.09%)	0.31
Neonatal IVH ≥ G2	2 (0.25%)	1 (0.12%)	0.55

The risk of PE was screened

revvity

Aspirin should be given only to women screened as high-risk to prevent increasing adverse effects of aspirin.

Received: 8 April 2025 | Revised: 10 June 2025 | Accepted: 14 July 2025
DOI: 10.1111/aogs.70026

ORIGINAL RESEARCH

Placental growth factor before 11 weeks for screening of preterm preeclampsia: The PreMoM study

Rocío López Mármol[1,2] | José Alejandro Ávila Cabreja[3] | Teresa de Haro Romero[4] | Catalina de Paco Matallana[5] | Olga Ocón Hernández[2,6] | Otilia González-Vanegas[2,6] | Pilar Carretero Lucena[2,6] | María Paz Carrillo[1] | Juan Luis Delgado[5] | Valeria Rolle[7] | Uzay Gormus[8] | Liza Oraha[8] | María M. Gil[9,10] | Francisca S. Molina[2,6]

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[3]Fundación Pública Andaluza para la Investigación Biosanitaria Andalucía Oriental, Granada, Spain
[4]Clinical Laboratory Management Unit, Hospital Universitario Clínico San Cecilio, Granada, Spain
[5]Department of Obstetrics and Gynecology, Hospital Universitario Virgen de la Arrixaca, Murcia, Spain
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[7]Biostatistics and Clinical Research Unit, Hospital Universitario de Torrejón, Madrid, Spain
[8]Department of Clinical Laboratory, Revvity Omics Sweden, Sollentuna, Sweden
[9]Department of Obstetrics and Gynecology, Hospital Universitario de Torrejón, Madrid, Spain
[10]School of Medicine, Universidad Francisco de Vitoria, Pozuelo de Alarcón, Madrid, Spain

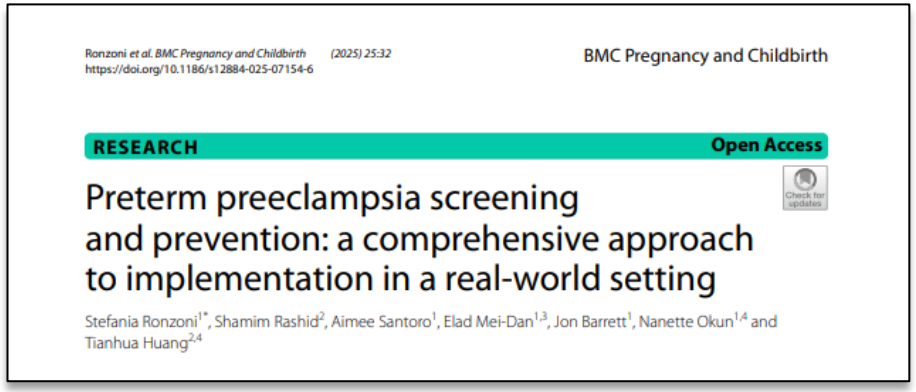
8-10+6 weeks vs 11-13+6 weeks screening performance

- The best discrimination (AUROC: 0.863; 95% CI, 0.754–0.971) and calibration were achieved by the model using PlGF between 11 and 13+6 weeks.

- PlGF measured before 11 weeks did not improve preterm PE screening performance

Preterm preeclampsia screening and prevention: a comprehensive approach to implementation in a real-world setting

2025 Jan 15;25(1):32. doi: 10.1186/s12884-025-07154-6.



Ronzoni et al. BMC Pregnancy and Childbirth (2025) 25:32
https://doi.org/10.1186/s12884-025-07154-6

BMC Pregnancy and Childbirth

RESEARCH Open Access

Preterm preeclampsia screening and prevention: a comprehensive approach to implementation in a real-world setting

Stefania Ronzoni[1*], Shamim Rashid[2], Aimee Santoro[1], Elad Mei-Dan[1,3], Jon Barrett[1], Nanette Okun[1,4] and Tianhua Huang[2,4]

The study confirms the feasibility of integrating comprehensive preeclampsia screening into real-world clinical practices

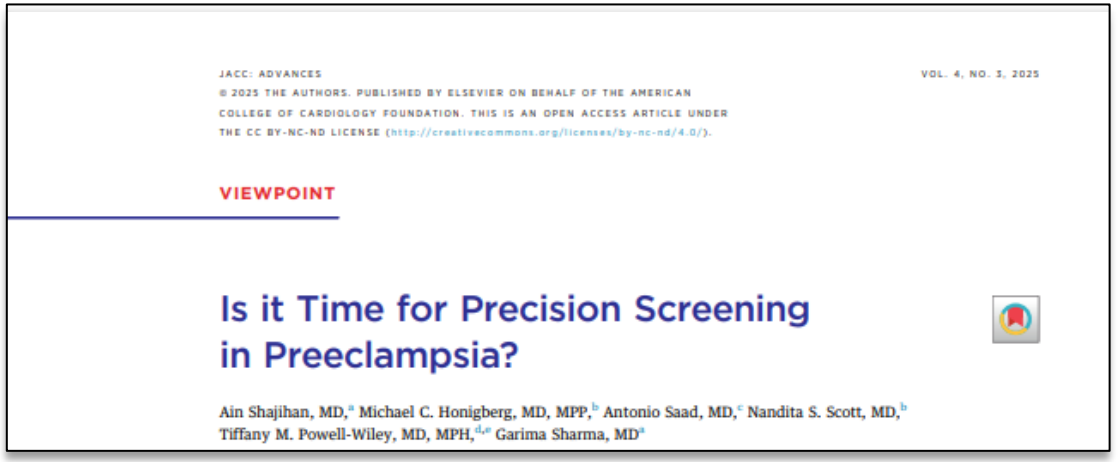
- The integration of preeclampsia screening had a minimal effect on the time required for aneuploidy screening, with results obtained within a rapid turnaround time.
- While the FMF algorithm provides better performance when all parameters (UtAPI, PlGF, and PAPP-A) are included,
- FMF algorithm can deliver a personalized risk score even if one or both placental markers are missing. Therefore, the protocol is applicable to lower-resource settings where not all parameters may be available.

Table 2 Time used for each component of the screening test and turnaround time of the screening test

Time Interval	Median (p5, p95)
History Collection (min)	2.0 (1.0, 4.25)
Blood Pressure Collection (min)	3.0 (2.0, 4.0)
Nuchal Translucency Scan (min)	25 (20,40)
Uterine artery Doppler measurement (min)	2.0 (1.0,2.5)
Time between blood sample collection and blood sample receipt (days)	1(1,2)
Time between sample receipt and results report (days)	2(1,3)

Is it Time for Precision Screening in Preeclampsia?

JACC Adv. 2025 Mar;4(3):101585. doi: 10.1016/j.jacadv.2025.101585.



JACC: ADVANCES VOL. 4, NO. 3, 2025

VIEWPOINT

Is it Time for Precision Screening in Preeclampsia?

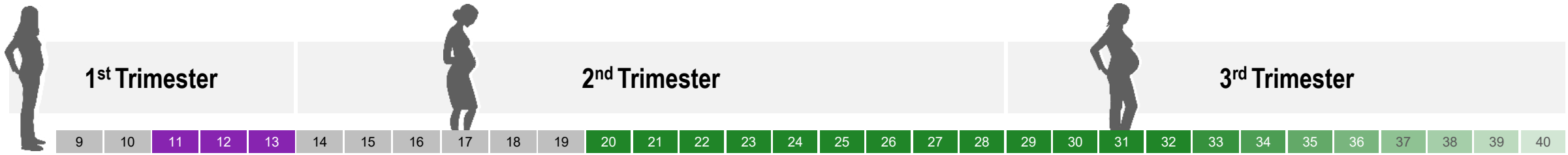
Ain Shajihan, MD,[a] Michael C. Honigberg, MD, MPP,[b] Antonio Saad, MD,[c] Nandita S. Scott, MD,[b] Tiffany M. Powell-Wiley, MD, MPH,[d,e] Garima Sharma, MD[a]

Improved first-trimester preeclampsia screening would

1. reduce costs for patients and hospitals by
   - decreasing unnecessary hospitalizations and
   - identifying early-onset preeclampsia patients that need close monitoring during pregnancy.
2. It would also alleviate patient anxiety and provide additional information to help clinicians to risk-stratify patients.

Utilizing the proposed models, providers can capture a larger portion of high-risk patients in order to allocate aspirin appropriately, leading to improved morbidity, maternal outcomes, and future cardiovascular health.

Effective screening reduces health care costs and improves quality of life

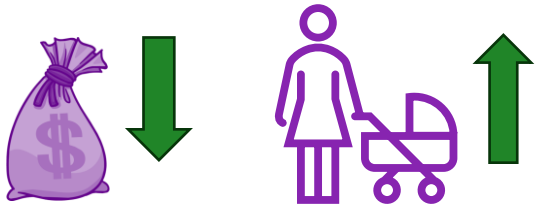


Pre-eclampsia screening

For **all pregnant** in 1T
Identify pregnant women who has high risk for pre-eclampsia

Prevention
with better compliance

Reduction
of pre-eclampsia incidence

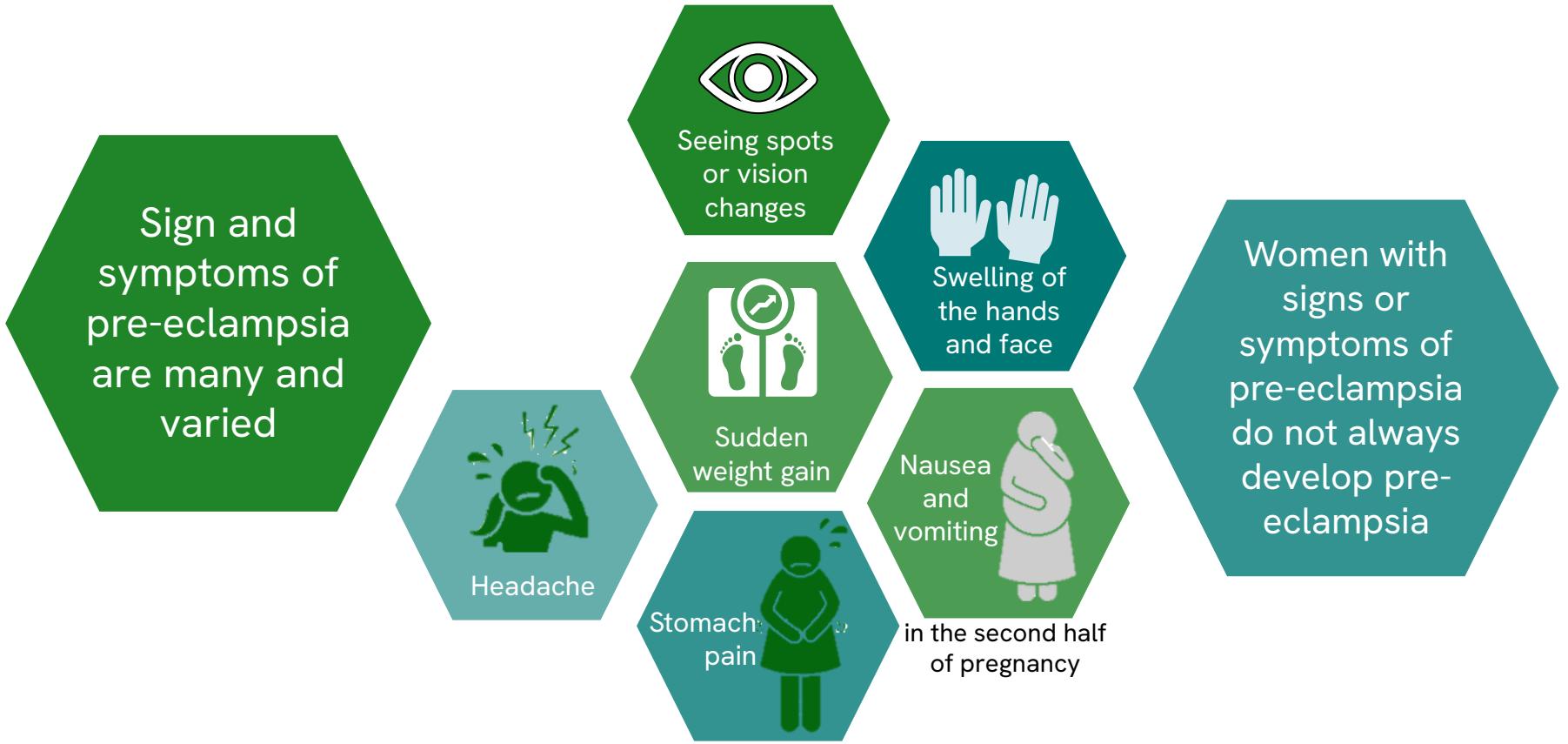


How to enhance pre-eclampsia management?

2T/3T PRE-ECLAMPSIA SHORT-TERM PREDICTION & AID IN DIAGNOSIS

revvity

Pre-eclampsia related sign or **symptoms are not specific for pre-eclampsia**



25%

of women with gestational hypertension will progress to pre-eclampsia

Magee L et al. Pregnancy Hypertension. 2022; 27: 148–169. Revvity does not endorse or make recommendations with respect to research, medication, or treatments. All information presented is for informational purposes only and is not intended as medical advice. For country specific recommendations, please consult your local health care professionals.

Standard clinical care **tests are not specific to pre-eclampsia**

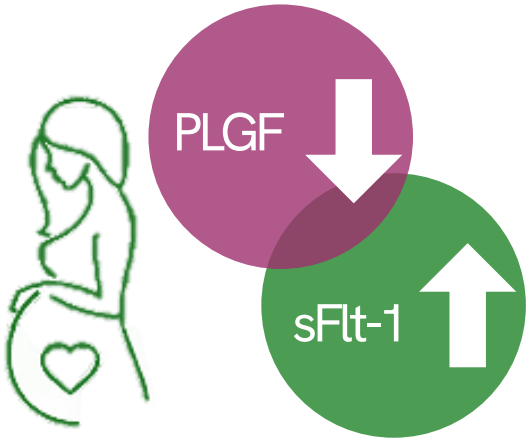
The standard clinical diagnostic assessments in case of suspected pre-eclampsia contain comprehensive set of tests

BUT, tests:

- Are not specific to Pre-eclampsia
- Don’t provide a prognosis of PE
- Don’t provide a prediction in the time
- Lead to overdiagnosis and unnecessary hospital admission
- May lead to incorrect patient management
- Do not inform about fetal well being
- May lead to delay in diagnosis

For symptomatic women PLGF based testing improves pre-eclampsia management

During 2T and 3T
PlGF and sFlt-1 are both predictive and diagnostic for pre-eclampsia

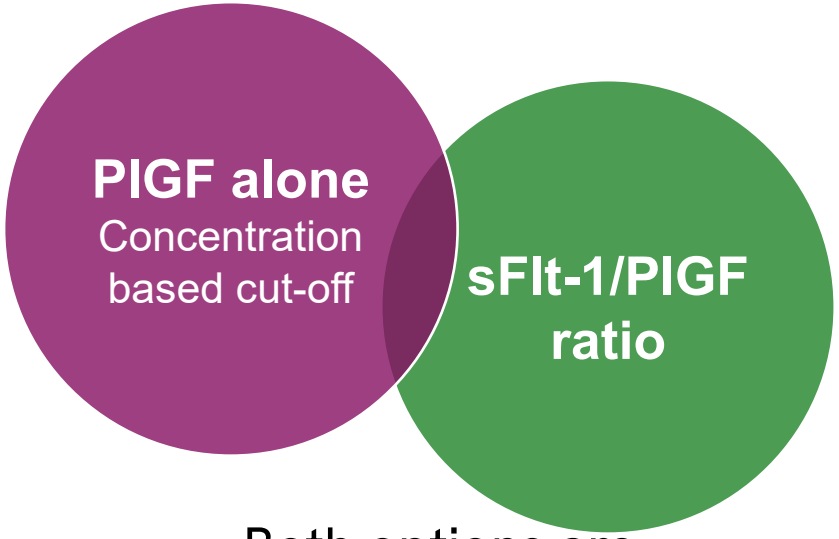


Biomarker levels also correlate with severity of disease

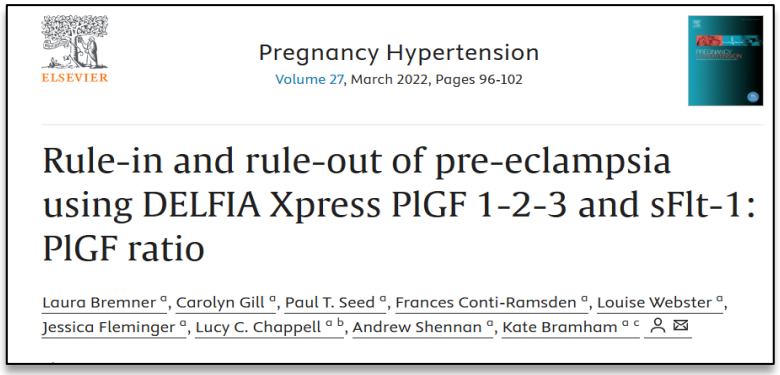
PLGF BASED TESTING in addition to standard clinical assessment ENHANCE CLINICAL CARE

NICE Diagnostic guidance: DG23. PlGF-based testing to help diagnose suspected pre-eclampsia, 2016.

For symptomatic women **PLGF based testing – two alternatives**



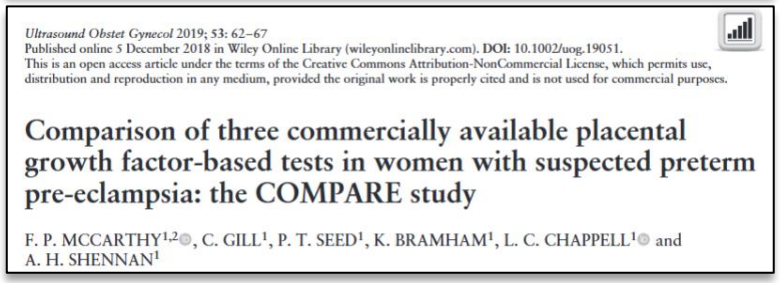
Both options are
equally recommended
for clinical use


ELSEVIER

Pregnancy Hypertension
Volume 27, March 2022, Pages 96-102

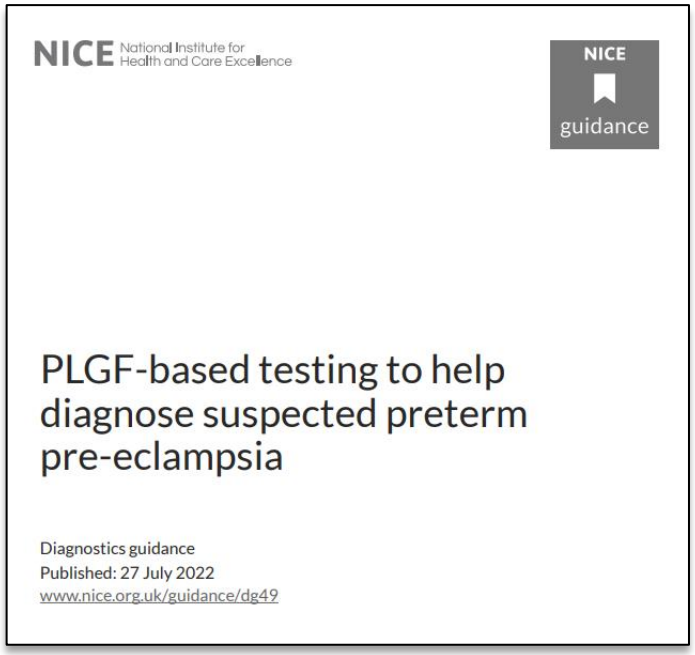
Rule-in and rule-out of pre-eclampsia using DELFIA Xpress PlGF 1-2-3 and sFlt-1: PlGF ratio

Laura Bremner [a], Carolyn Gill [a], Paul T. Seed [a], Frances Conti-Ramsden [a], Louise Webster [a], Jessica Fleminger [a], Lucy C. Chappell [a b], Andrew Shennan [a], Kate Bramham [a c]


Ultrasound Obstet Gynecol 2019; 53: 62–67
Published online 5 December 2018 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.19051.
This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

Comparison of three commercially available placental growth factor-based tests in women with suspected preterm pre-eclampsia: the COMPARE study

F. P. MCCARTHY[1,2], C. GILL[1], P. T. SEED[1], K. BRAMHAM[1], L. C. CHAPPELL[1] and A. H. SHENNAN[1]


NICE National Institute for Health and Care Excellence

NICE guidance

PLGF-based testing to help diagnose suspected preterm pre-eclampsia

Diagnostics guidance
Published: 27 July 2022
www.nice.org.uk/guidance/dg49

PlGF,
as single marker,
has a comparable
performance
to sFlt-1/PlGF ratio

Based on the studies
there is no need
for two analytes,
PlGF alone
is sufficient

PLGF alone,
with concentration
based cut-offs,
could provide a
simpler solution

PLGF alone,
use of one kit,
could offer more
affordable
alternative

Bremner L et al. Cardiovascular Health 2022; 27: 96–102. NICE Diagnostic guidance: DG23. PlGF-based testing to help diagnose suspected pre-eclampsia, 2016. McCarthy F et al. Ultrasound Obstet Gynecol 2019; 53: 62–67.

Increasing implementation and interest

Preeclampsia SCREENING/DIAGNOSING growth 2025 – supporting signals

Supporting data

Increasing amount of data showing the efficacy of screening and added value of PlGF and sFlt-1:

- FORECAST
- PREVAL
- PRECISE
- PRAECIS
- (RANSPRE, IMPACT

Supporting guidelines

International guidelines FIGO, ISSHP, ISUOG,

Local guidelines (screening): Germany, Austria, Switzerland, Denmark, Estonia, Canada, Brazil...Updating: Spain, Sweden

Local guidelines (management): Lithuania, UK, Finland, Germany, Austria, Switzerland, Spain, Canada, Brazil

Increasing implementation

National implementation studies in:

- Denmark
- France
- UK

New countries:

- USA

GRANTs:

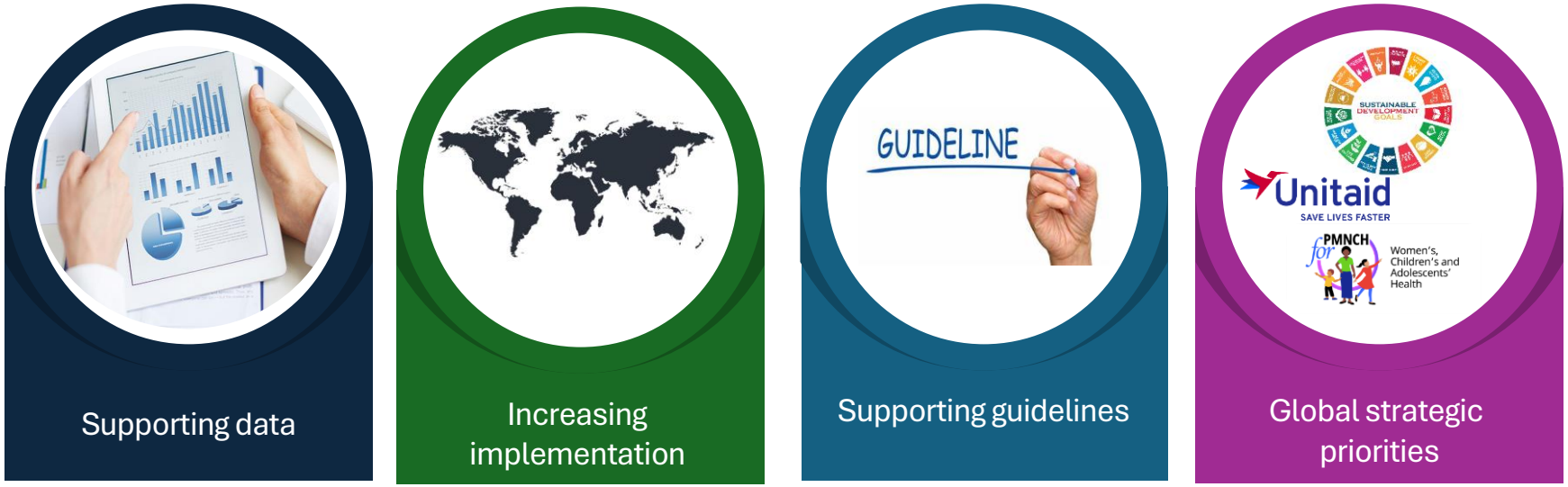
- UNITAID
- Gates

Global strategic priorities

Organization with supporting strategies to accelerate reduction of maternal, newborn and child health

Hypertensive disorders of pregnancy being acknowledge as one of the leading causes of maternal mortality andmorbidity

Increasing interest for preeclampsia screening



	2017	2018	2019	2020	2021	2022	2023	2024	2025
Screening	ASPRE project		FIGO Poland		ISSHP		ISUOG Brazil	Australia New Zealand	
Both		Czech	Romania Bulgaria	Italy Spain Thailand	Estonia	Japan Canada		Germany Austria Swizerland	
Management	UK (NICE) Brazil	Malaysia ISUOG ESC	South Africa		Finland FIGO ISSHP	Sri Lanka	Australia New Zealand Lithuania Scotland	USA	Denmark

Still majority of countries lacking the support from National Health Board

Increasing interest for preeclampsia screening

GRANTs and open calls:

Call for proposals: Improving access to lifesaving tools for prevention, diagnosis, and management of pre-eclampsia and maternal anemia

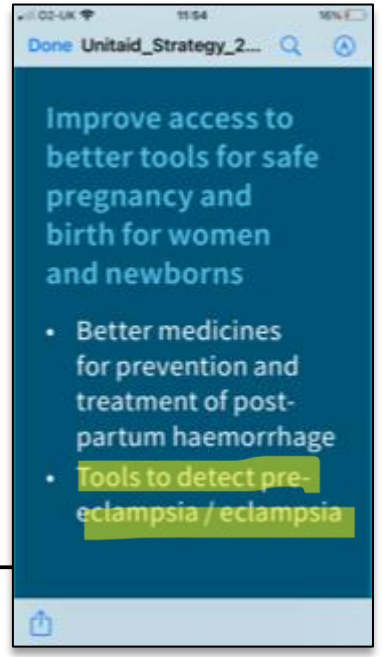
Unitaid
SAVE LIVES FASTER

Date posted
21 November 2024

Call status
CLOSED

Organizational strategies to accelerate reduction of maternal, newborn and child health

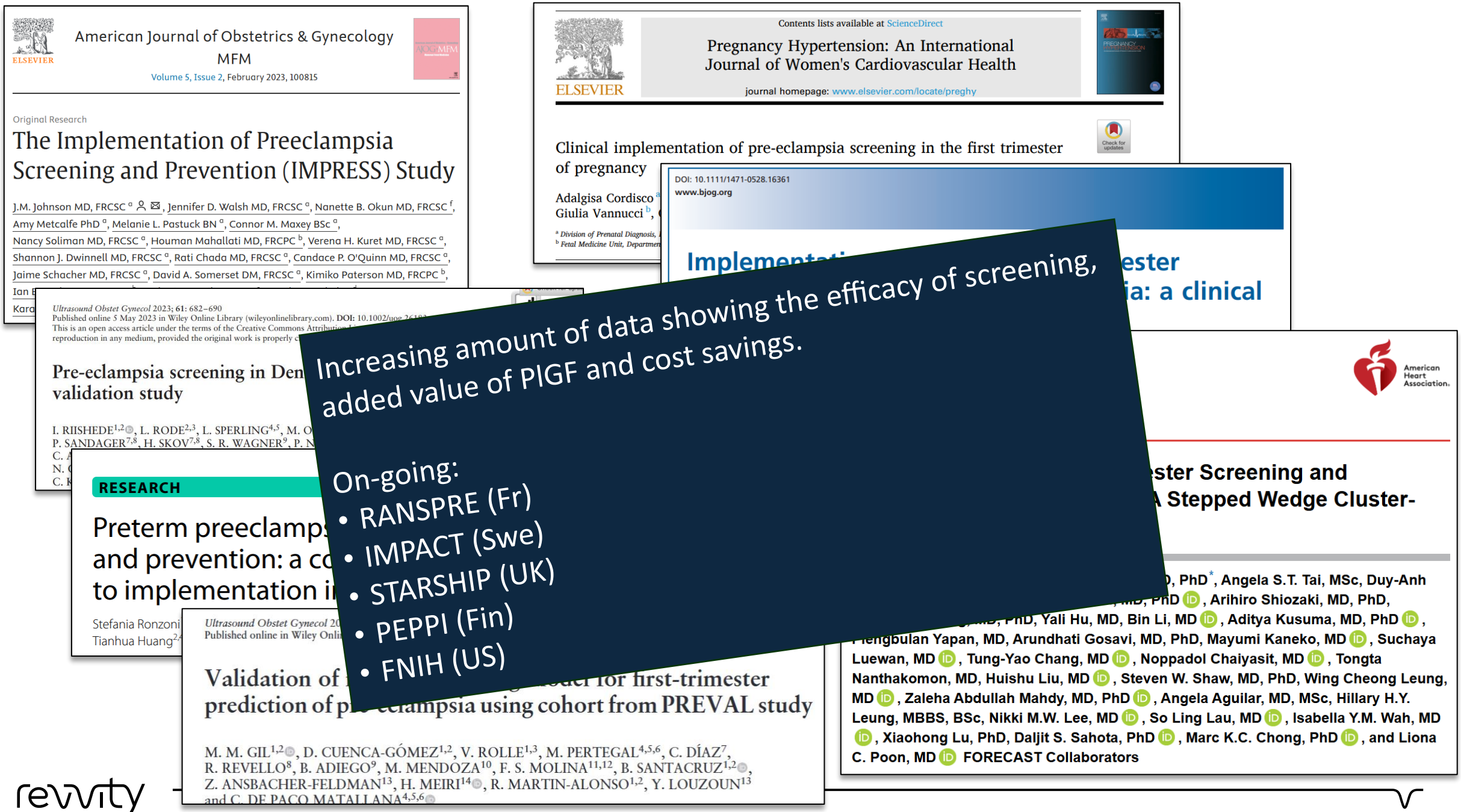
- Hypertensive disorders of pregnancy being acknowledge as one of the leading causes of maternal mortality and morbidity (16%)



Mar 8, 2025

Many pregnancy-related complications going undetected and untreated – WHO

Haemorrhage – severe heavy bleeding – and hypertensive disorders like preeclampsia are the leading causes of maternal deaths globally, according to



J.M. Johnson MD, FRCSC [a], Jennifer D. Walsh MD, FRCSC [a], Nanette B. Okun MD, FRCSC [f], Amy Metcalfe PhD [a], Melanie L. Pastuck BN [a], Connor M. Maxey BSc [a], Nancy Soliman MD, FRCSC [a], Houman Mahallati MD, FRCPC [b], Verena H. Kuret MD, FRCSC [a], Shannon J. Dwinnell MD, FRCSC [a], Rati Chada MD, FRCSC [a], Candace P. O'Quinn MD, FRCSC [a], Jaime Schacher MD, FRCSC [a], David A. Somerset DM, FRCSC [a], Kimiko Paterson MD, FRCPC [b],

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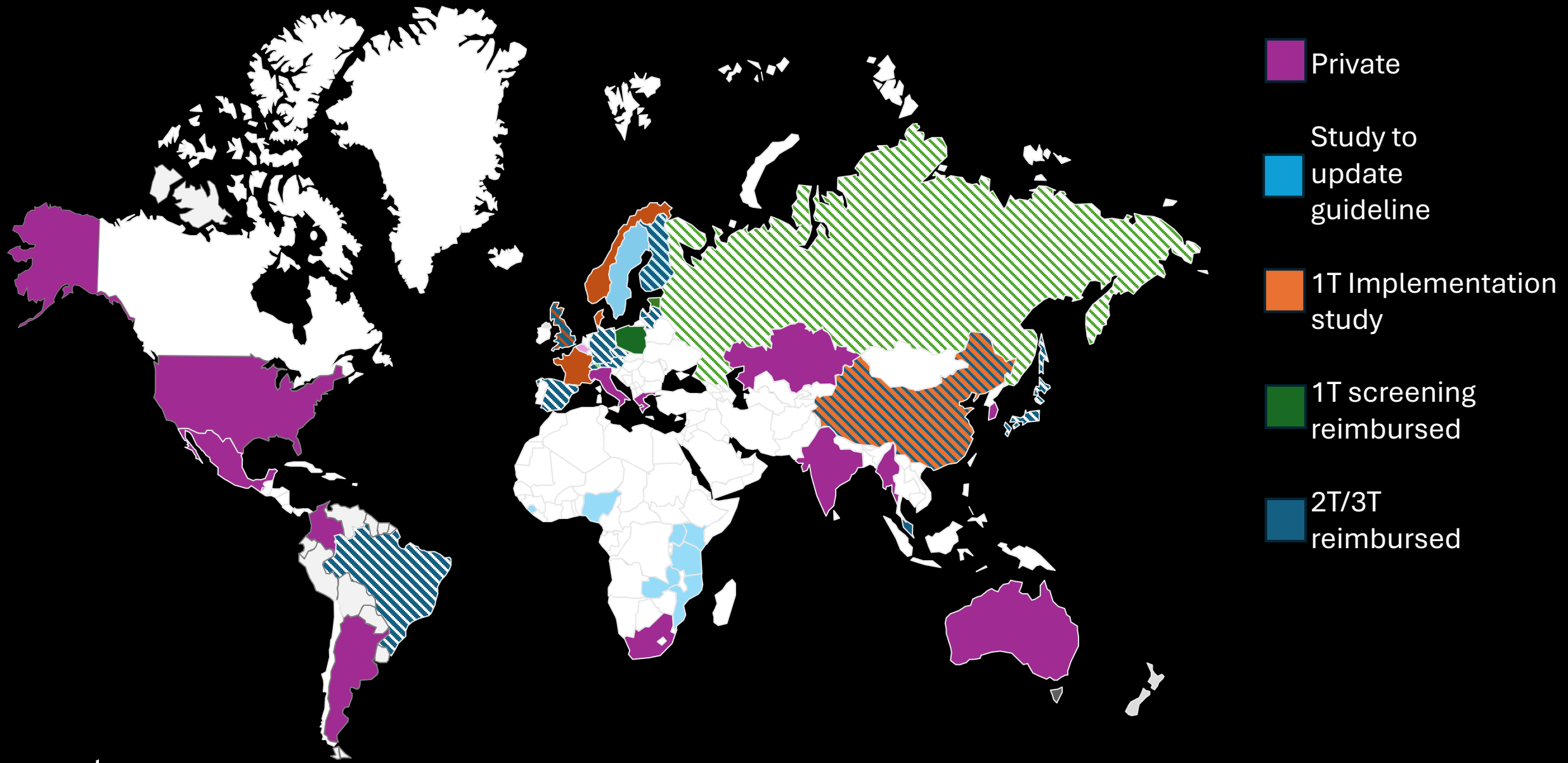
N. C
C. K

Stefania Ronzoni
Tianhua Huang[2]

M. M. GIL[1,2], D. CUENCA-GÓMEZ[1,2], V. ROLLE[1,3], M. PERTEGAL[4,5,6], C. DÍAZ[7], R. REVELLO[8], B. ADIEGO[9], M. MENDOZA[10], F. S. MOLINA[11,12], B. SANTACRUZ[1,2], Z. ANSBACHER-FELDMAN[13], H. MEIRI[14], R. MARTIN-ALONSO[1,2], Y. LOUZOUN[13] and C. DE PACO MATALLANA[4,5,6]

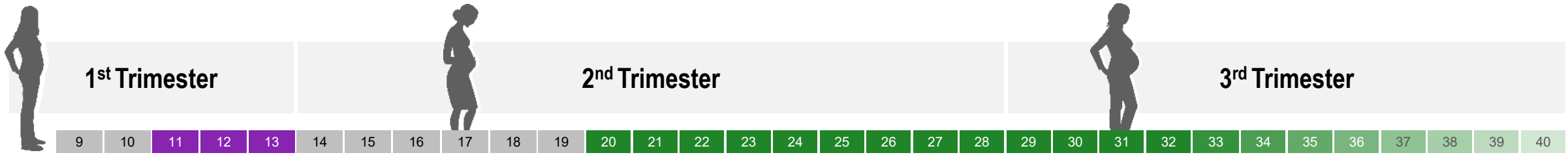
, PhD*, Angela S.T. Tai, MSc, Duy-Anh , PhD, Arihiro Shiozaki, MD, PhD, , PhD, Yali Hu, MD, Bin Li, MD, Aditya Kusuma, MD, PhD, Piengbulan Yapan, MD, Arundhati Gosavi, MD, PhD, Mayumi Kaneko, MD, Suchaya Luewan, MD, Tung-Yao Chang, MD, Noppadol Chaiyasit, MD, Tongta Nanthakomon, MD, Huishu Liu, MD, Steven W. Shaw, MD, PhD, Wing Cheong Leung, MD, Zaleha Abdullah Mahdy, MD, PhD, Angela Aguilar, MD, MSc, Hillary H.Y. Leung, MBBS, BSc, Nikki M.W. Lee, MD, So Ling Lau, MD, Isabella Y.M. Wah, MD, Xiaohong Lu, PhD, Daljit S. Sahota, PhD, Marc K.C. Chong, PhD, and Liona C. Poon, MD FORECAST Collaborators

PE testing maturity level - Readiness to adopt



revvity

Pre-eclampsia screening for all – PE management for symptomatic



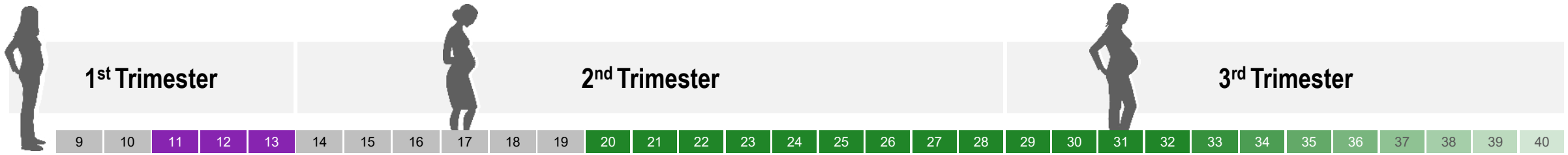
Pre-eclampsia screening

For all pregnant in 1T
Identify pregnant women who has high risk for pre-eclampsia

Symptoms of pre-eclampsia may appear from wk 20 onwards

Test (symptomatic) women with suspected pre-eclampsia later in pregnancy (3-10% of pregnant)
Short-term prediction & aid in diagnosis

Pre-eclampsia screening for all – PE management for symptomatic



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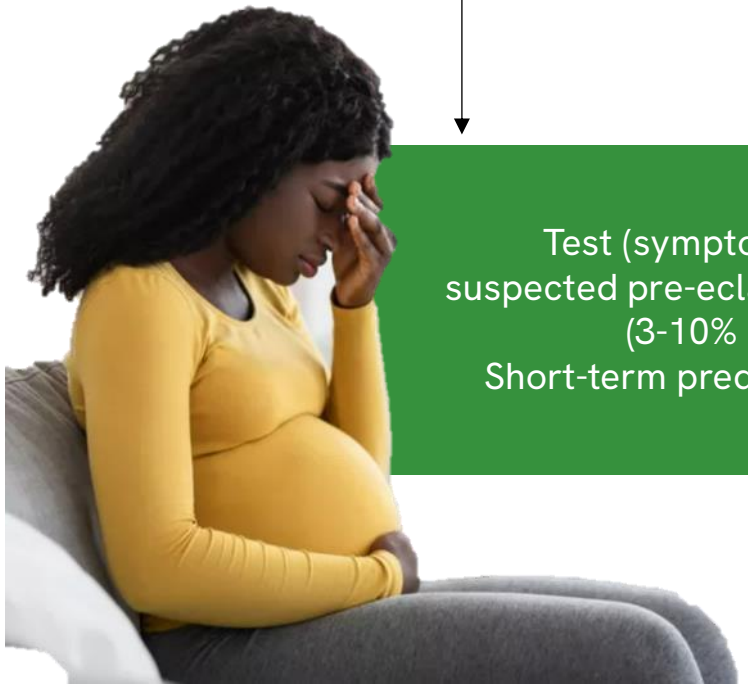
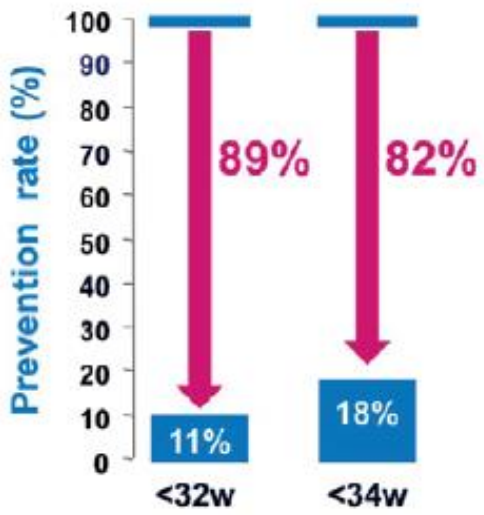


Test (symptomatic) women with suspected pre-eclampsia later in pregnancy (3-10% of pregnancies)
Short-term prediction & aid in diagnosis

Preeclampsia affects both mother and the child also later in life

PREVENT

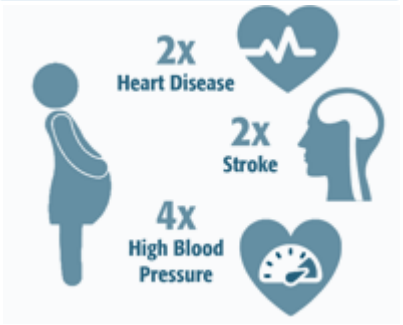


Rolnik et al. N Engl J Med 2017;377:613

BETTER OUTCOMES

Birth	Death <5 y	Cerebral palsy	Impaired work capacity
23-27w	80%	9.1%	10.6%
28-30w	40%	6.0%	8.2%
31-33w	11%	1.9%	4.2%
34-36w	2.3%	0.3%	2.4%
≥37w	0.6%	0.1%	1.7%

867,692 live births Norway 1967-1983
Moster et al. NEJM 2008;359:262



REDUCED COSTS

Cost of NICU Care

Gestational Age (completed weeks)	N	Mean (US $)
24	486	222,563
25	678	233,538
26	756	207,637
27	900	178,080
28	1,091	146,121
29	1,226	115,801
30	1,556	92,882
31	1,995	68,446
32	2,799	46,117
33	4,719	30,145
34	14,541	10,535
35	25,077	6,007
36	44,922	3,444
37	92,421	2,027

Prophylactic use of aspirin results in

68% reduction

in the length of stay in NICU

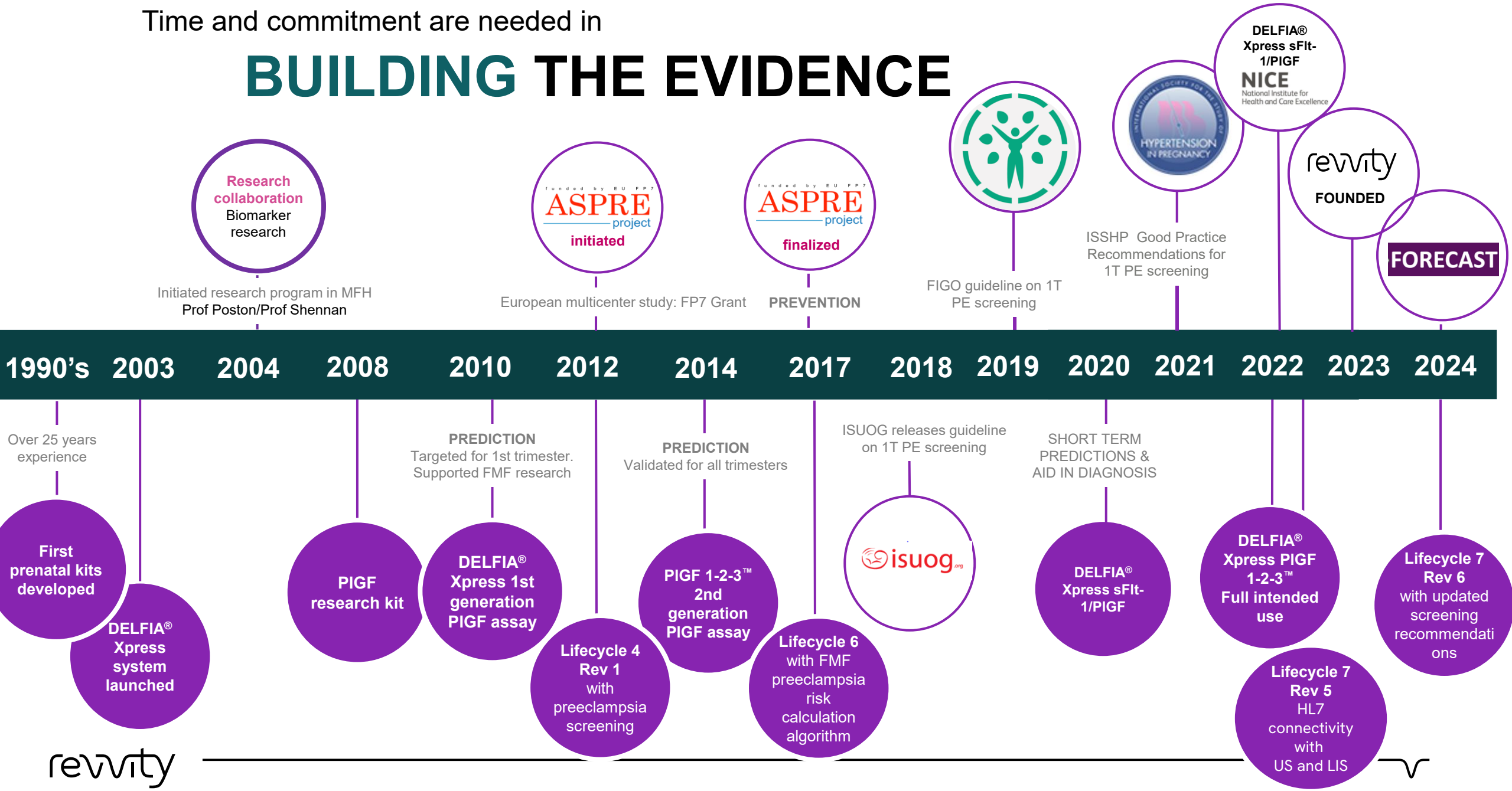
MANAGE BETTER

RAPID & ACCURATE TRIAGE

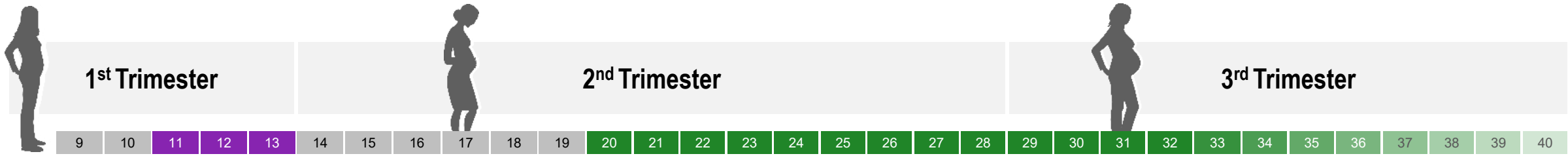
THIS CONDITION WOULD BRING SUBSTANTIAL IMPROVEMENTS TO MATERNAL AND FETAL HEALTH AND COSTS

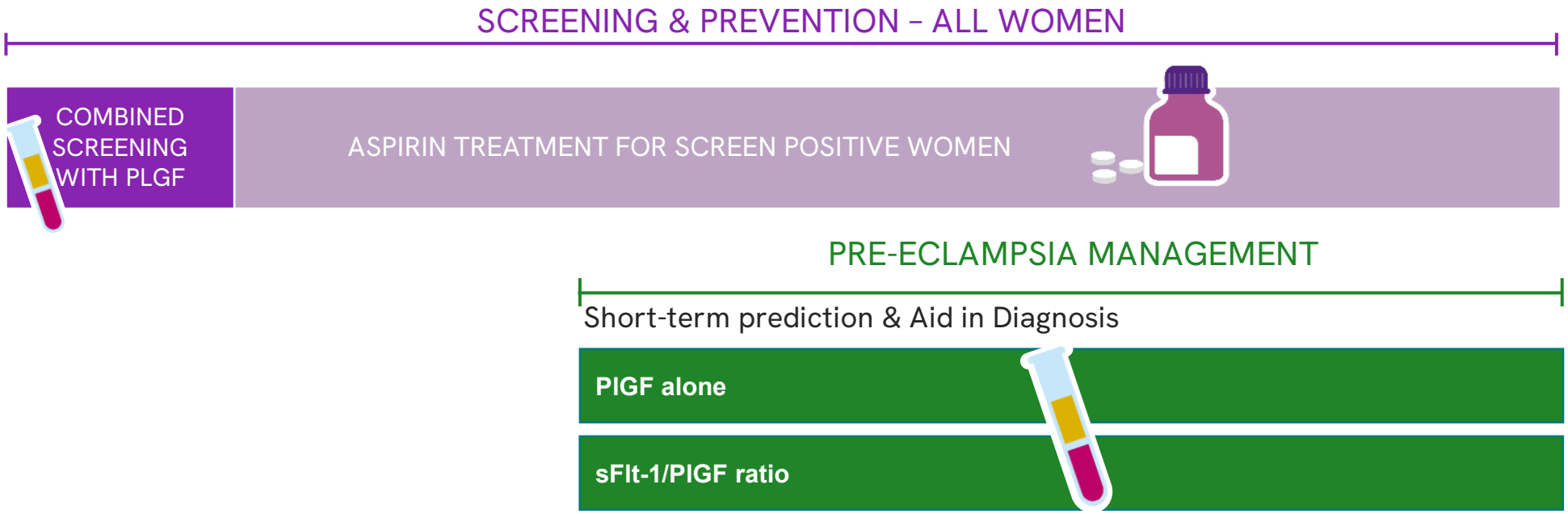
Time and commitment are needed in

BUILDING THE EVIDENCE



Pre-eclampsia

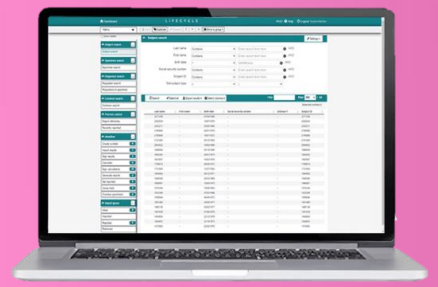




Bremner L et al. Cardiovascular Health 2022; 27: 96–102. Rolnik DL et al., .N Engl J Med. 2017 Aug 17;377(7):613-622. Giblin et al. Pregnancy Hypertension 21 (2020) 35–37.

Customer-Driven Innovation and Continuous Improvement

- Demographic entry to LifeCycle



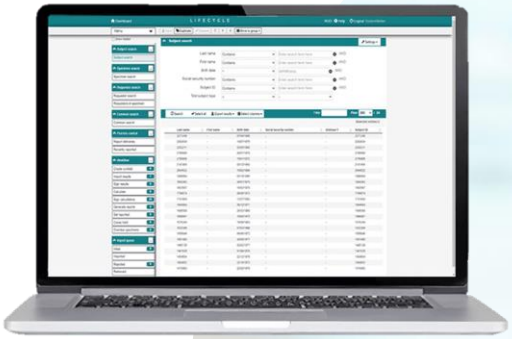
- Worklist transferred automatically from LifeCycle to DELFIA Xpress

- When test is ready, results are transferred from DELFIA Xpress to LifeCycle

- **Comprehensive**
  Multiple screening strategies are supported
- **Effective data management with LifeCycle**
  Simplifies the data collection and workflow processes
- **Easy to set up, learn and use**
  Simple and flexible user interface with performance monitoring dashboard

LifeCycle
Leading risk calculation software for prenatal screening

- Trusted system since 2000
- Over 800 users
- Supports all prenatal screening models
- Enables aneuploidy screening and pre-eclampsia screening



Simple, flexible and reliable LifeCycle™ Prenatal Screening risk calculation software

- ✓ Complete data management solution for prenatal screening laboratories
- ✓ Simple and flexible user interface with a performance monitoring dashboard
- ✓ Comprehensive – Multiple screening strategies are supported
- ✓ Tailored to population – Optimized risk calculation to your population
- ✓ Accessible – Remote access for external users and connectivity to 3rd party applications
- ✓ Trusted solution over 20 years

revvity

Innovations for future

DIFFERENT NEEDS – DIFFERENT SOLUTIONS

TARGET CUSTOMERS

FROM CENTRALIZED TO DECENTRALIZED

Central laboratories & large hospitals

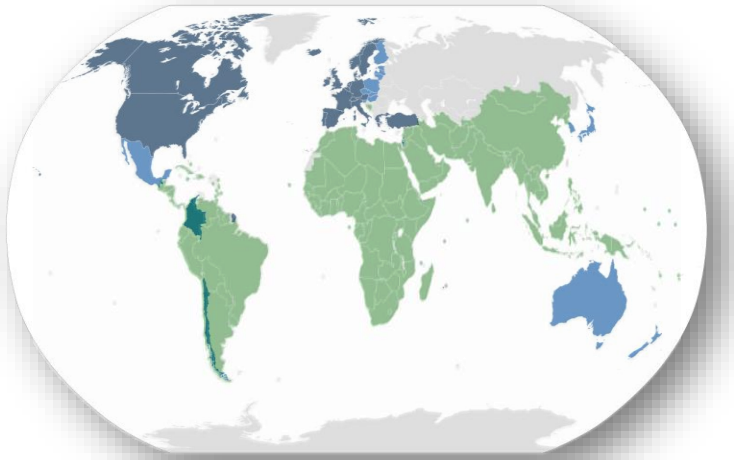
District hospitals

Private Obstetrics

Remote Healthcare workers

TARGET COUNTRIES

FROM LOW TO HIGH INCOME COUNTRIES REMOTE TO NEAR HOSPITAL

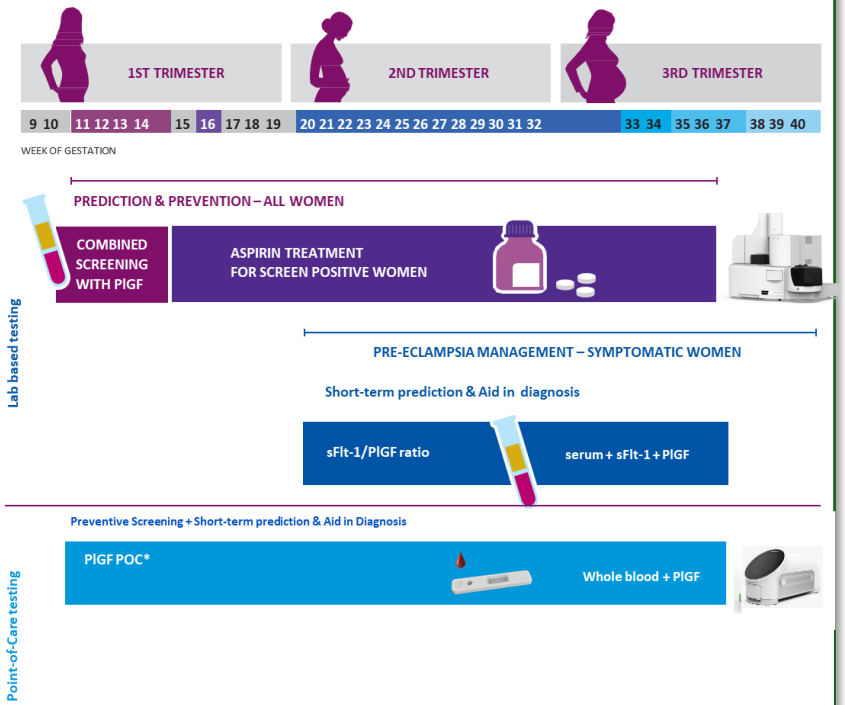


Training
Infrastucture

Throughput
Complexity
Costs
Time-to-Result

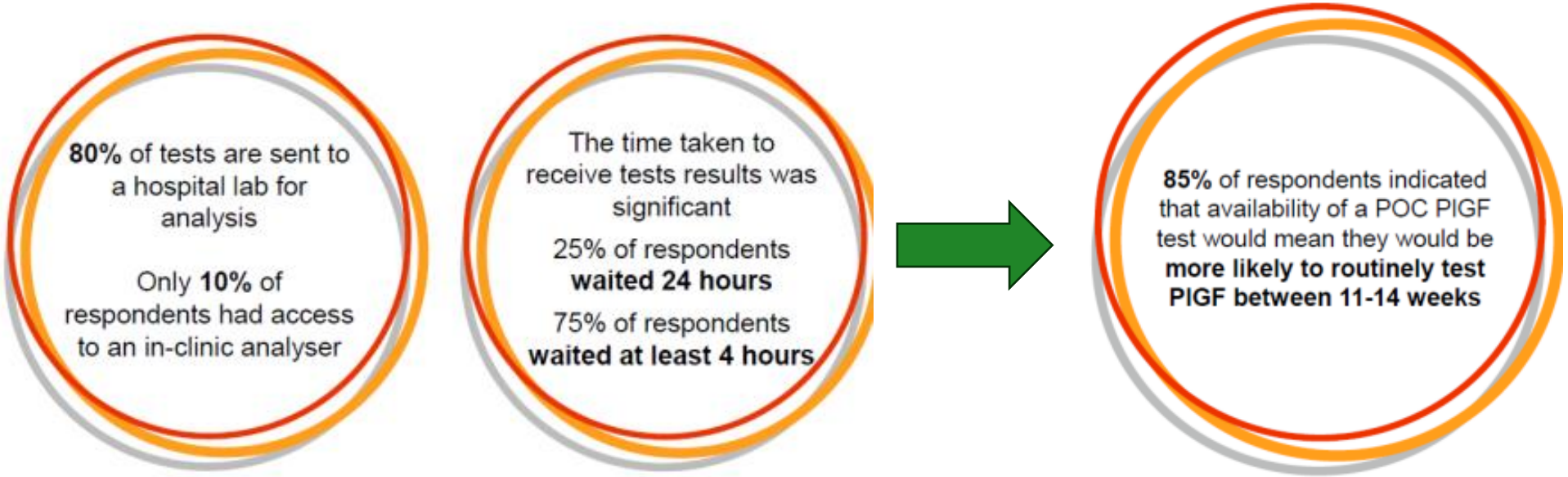
TARGET PATIENTS

FROM SCREENING TO MANAGEMENT



These tests are typically sent to a hospital laboratory & it can take up to 24 hours to receive a result

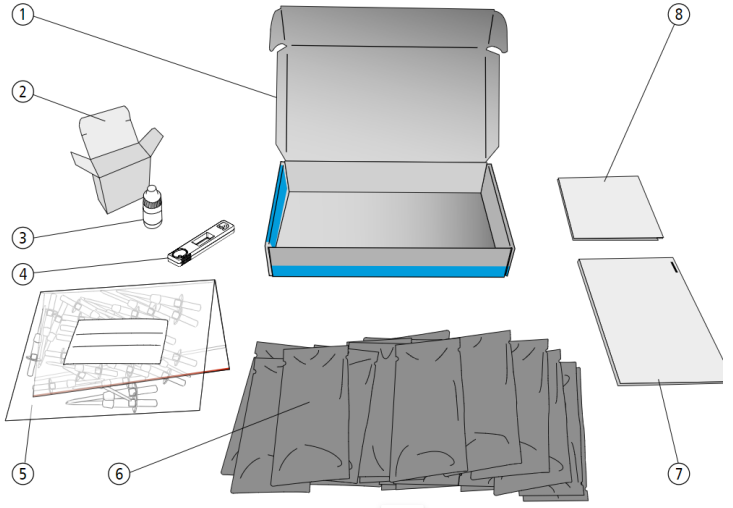
Data from Europe




RONIA™ Platform

RONIA™ Platform

- **Quantitative Placental Growth Factor (PlGF) results**
- **Portable reader** (can run on batter)
- **No maintenance/service**
- **No need for laboratory facilities**
- **Whole blood** = no pre-treatment (centrifugation /laboratory skills) necessary. Serum also an option.
- **10µl sample volume**
- **No sample shipping:** immediate results = fast treatment, effective care
- **Short assay time (30 min), <2 min in the reader.**
- **Lot specific calibration** enabled **with RFID**



RONIA™ Platform

Result simply from whole blood finger prick

1. Add buffer to reaction tube

2. Collect finger prick sample

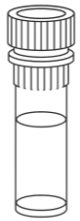
3. Add sample to the reaction tube - mix

4. Incubate 15 min

5. Add reaction to the cassette
6. Incubate another 15 min and measure

PlGF assay Total time ~ 30 min

RONIA PlGF Advanced kit workflow

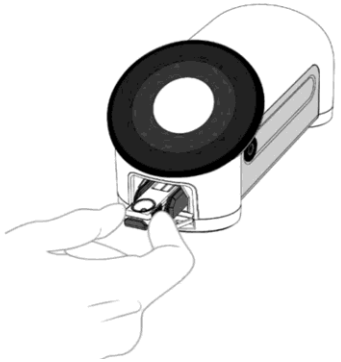


1 Transfer 100 µL of Buffer to the Reaction tube (mix)

3 Incubate Reaction for 15 min

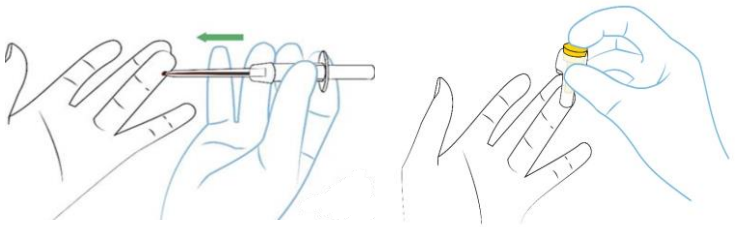
4 Transfer all of reaction mix to the RONIA Cassette

5 Incubate the RONIA Cassette for 15 min



6 Insert the RONIA Cassette into the RONIA Reader and measure (2 min)

2 Add 10 µL of sample to the Reaction Tube (mix)



Thank you!