The BMJ Awards 2020 Entry Form

Entry criteria
The awards are open to clinically led teams based in the UK with projects active in 2019.

Judges will be interested in the scale of the problem that your project was addressing, the impact of the project, and whether the project took an innovative and original approach. Additionally they will also be looking at the size of the benefit your project produced, what you learnt from this experience, how much it cost, and the potential for wider application. As *The BMJ* is seeking to advance partnership with patients, we are also asking entrants to describe how they included patients in the design and evaluation of their projects.

Where applicable, your written answers should include supporting evidence and data. Limited supplementary material can be uploaded but should be limited to non-text items (tables, graphs and figures). Judges will only refer to this material if there is a clear and specific reference to it within the written entry form. Any numbers or key points must be included in your written answers.

Please note the following:

- Answers to each question should be between 100-200 words. Any text that goes beyond 200 words will not be seen by judges.
- Please ensure you save your document with a title that is only letters and numbers.
- Please do not include any symbols as you may have problems uploading this.

Please see entry form on page 2

New testing for pre-eclampsia

Questions

1. What problem were you addressing and why was it important?

What is the problem?
Pregnant women can develop pre-eclampsia, a common and potentially serious complication. For the last 100 years, we have relied on measuring blood pressure and dipping their urine for protein. But the clinical presentation is varied, with complications occurring before diagnosis is confirmed. Conversely hypertension or proteinuria can occur without progression to pre-eclampsia.

How did you know?
The national guidelines have recognised that we need better ways of monitoring women with suspected pre-eclampsia. Our work with the patient support group, Action on Pre-eclampsia, and our Patient and Public Involvement and Engagement Groups, show that women often have difficulties and delays in diagnosis, or require frequent, inconvenient monitoring with little certainty on risk of developing pre-eclampsia or needing early delivery.

Who was it affecting?
Around 10% of women have pregnancy hypertension, equating to around 70,000 in the UK each year, and are at risk of pre-eclampsia. Many more will have suspected pre-eclampsia with other symptoms and signs such as a small baby or headaches.

Why had it not been entered before?
In 2019, we reached several key landmarks: we published the first trial of a new diagnostic test, and NHS England started support for implementation of diagnostic testing.

2. What did you do to understand the scale of the problem?

What is the scale of the problem?
The scale of the problem is established in the literature, with more than 70,000 women per year in the UK having suspected disease. In previous work, we measured 58 different biomarkers in 625 women with suspected pre-eclampsia in a national multicentre prospective cohort study (Duckworth Obstet Gynecol 2016). Of these, 55% (346 women) went on to develop pre-eclampsia.

What were our baseline results?
We demonstrated that Placental Growth Factor (PlGF) was far superior to any other marker (selected as promising for pre-eclampsia detection in the literature) in predicting need for delivery within two weeks of testing. We established clinical rule-in (<12pg/ml) and rule-out (100pg/ml) thresholds. The test had very high sensitivity (96%; 95%CI 89%-99%) and negative predictive value (98%; 93-99.5%) for this endpoint (Chappell Circulation 2013). The test was superior to all other commonly used tests in clinical practice.

What did we measure?
We determined that PlGF can reliably rule out the need for delivery for pre-eclampsia in two weeks in women with suspected disease. We also measured stillbirth/ neonatal death rates and demonstrated that all seven stillbirths or neonatal deaths in the cohort were predicted with low PLGF (100% sensitivity).

3. What did you do?

What was our intervention?
We developed a new test, measuring a protein called Placental Growth Factor (PlGF), to be used as a diagnostic adjunct in pregnant women with suspected pre-eclampsia.

How did we engage stakeholders?
We engaged the relevant stakeholders, particularly pregnant women, through the patient support groups including Action on Pre-eclampsia, Tommy's Charity and with our local Pregnancy Hypertension Public and Patient Involvement groups, who told us what the challenges were from their perspective and why a new diagnostic test was important. We have also worked with healthcare professionals, the test manufacturers, and more recently with NHS England and the Academic Health Sciences Networks involved in roll-out of the test.

How was the intervention developed and evaluated?
We developed the intervention through robustly evaluating the new test in

- a case-control study (Chappell AJOG 2002),
- a multicentre prospective cohort study (Chappell Circulation 2013)
- a multicentre randomised controlled trial (Duhig Lancet 2019)
- a cost-effective analysis (Duhig BJOG 2019)

We undertook every appropriate stage of evaluation before launch into NHS clinical practice in order to show that it was a high-performing diagnostic test, with impact on time to diagnosis and on adverse maternal outcomes.

4. What impact did your project have?

Our project has achieved impact with:

a. **Benefit to women:** The multicentre randomised controlled trial of revealed PlGF testing in 1035 women with suspected pre-eclampsia demonstrated shorter time to diagnosis, from 4 days to 1.9 days (time ratio 0.36, 95%CI 0.15–0.87; p=0.027) and reduced maternal severe adverse outcomes (5.4% to 3.8%; adjusted odds ratio 0.32, 95%CI 0.11–0.96; p=0.043), translating into meaningful benefit for women, with speedier diagnosis and fewer complications.

b. **Benefit to the health service:** The health economic evaluation showed that PlGF testing is cost-saving at around £147 per patient, mainly through reduced maternal outpatient attendances.

c. **Academic publications:** The studies have been published in high-impact journals with far reach, including the cohort study (Chappell Circulation 2013), main trial (Duhig Lancet 2019) and cost-effectiveness evaluation (Duhig BJOG 2019).

d. **National guidance:** PlGF testing has been adopted into national guidance for diagnostic testing (https://www.nice.org.uk/guidance/dg23) and into the new guidance for pregnancy hypertension (https://www.nice.org.uk/guidance/ng133).

e. **NHS implementation:** PlGF-based testing has been adopted by NHS England through its Accelerated Access Programme (https://www.england.nhs.uk/ourwork/innovation/accel-access/), Pathway Transformation Fund (https://www.england.nhs.uk/aac/what-we-do/how-can-the-aac-help-me/pathway-transformation-fund/), and Innovation and Technology Payment Programme (https://www.england.nhs.uk/ourwork/innovation/innovation-and-technology-payment-itp-2019-20/)

f. **Media**: including widespread coverage in print journals, BBC breakfast, BBC today programme and social media.

5. What lessons have you learnt?

The long journey has been challenging, but PlGF-based testing is now implemented into clinical care. Seeing a change in care and outcomes for women has been the motivating driver.

Women have provided overwhelmingly positive support. They describe how difficult the uncertainty around diagnosis and risk stratification is, when they are unsure whether they are higher-risk (welcoming increased surveillance) or lower-risk (continuing without additional unnecessary anxiety).

Healthcare professionals have also been strongly supportive, welcoming a new test that improves on methods used for the last century (measuring blood pressure and dipping urine) that are imperfect, poorly reproducible, and do not always predict which women need delivery.

The challenges have included

- Validating and evaluating the novel test before introduction into clinical practice
- Building a community of practice, for the research then implementation work, requiring activation energy both.
- Maintaining ongoing momentum

We have kept the clinical need (for women and the health service) at the forefront, using the strong support from women and patient support groups and building a multidisciplinary research group to address the problem. Use of multicentre research studies increased the generalisability and ownership by the UK pregnancy community. The intervention is now being embedded into routine practice.

6. Did your project offer value for money?

The development of the test was through conventional academic funding, including joint funding (£400,000) from Tommy's charity and investigator-led commercial collaboration (providing minority support) and funding from the National Institute for Health Research (NIHR) Research for Patient Benefit programme (£350,000). The research was delivered across UK maternity units with the backing of the NIHR national Clinical Research Network, with their associated financial support. Salary and consumable costs were covered by these grants.

The cost savings were initially estimated based on a budget impact analysis using data from concealed testing in our cohort study (Duckworth PLOS One 2016) and then updated using data from the NHS healthcare setting from the trial of revealed testing (Duhig BJOG 2019). The real-world trial data confirmed a cost saving, of £147 per patient, with PlGF testing, driven by maternal antenatal care being better targeted to those who need it most (higher-risk women), with a reduction in outpatient attendances for those with normal PlGF results who are at lower risk of needing preterm delivery or having complications.

These cost saving data have been used by NHS England to support the adoption and implementation of PlGF-based testing into maternity units to ensure that it is sustainable.

7. Was your project innovative and original?

The use of PLGF testing in clinical practice in the assessment of women with suspected pre-eclampsia is entirely novel. It has provided a fundamentally new way of assessing pregnancy risk and influencing care. Previous assessment was reactive to downstream indicators of 'damage' caused by the disease (such as hypertension and proteinuria). Low concentrations of PlGF in the woman's blood are related to the cause of the disease, unlike all previously used tests, (as it comes from the placenta) and allows accurate and timely diagnosis. It now may provide a target for new interventions in preventing the disease.

PlGF is cost-saving to the health service. In a cost-effectiveness analysis, performed on real data from our implementation trial, we have demonstrated that £150 per patient is saved, representing a potential saving of nearly £3million per year to the NHS. Additional savings in reduction to life-long morbidity related to neonatal care could be substantially more.

8. **Did you co-produce your project with patients?**

All our research is performed in close collaboration with patient support groups. Lay members of Action on Pre-eclampsia (APEC), a national charity dedicated to pre-eclampsia, have been closely involved in all studies, directly influencing design, delivery, trial committee and management group representation, interpretation and dissemination (including media coverage) of the work.

Much of our research (including for PlGF testing) starts with co-design with women through our Patient and Public Involvement and Engagement Groups in Pregnancy Hypertension established at Guy's and St Thomas' NHS Foundation Trust. Women are asked to identify what research is important to them, and how we might address the gaps in clinical care. We recently formalised this through a James Lind Alliance Priority Setting Partnership in Pregnancy Hypertension, building on our patient partnership work.

Marcus Green, APEC Chief Executive Officer, whose partner had pre-eclampsia, has been instrumental in raising awareness of the disease, campaigning for appropriate research and clinical care, and promoting UK implementation of PlGF-based testing. He has been a co-author on many of our pre-eclampsia publications, from original research to opinion pieces (Lancet 2017; BMJ 2018 & 2019).

We also work closely with Tommy's charity, who have provided invaluable funding support at all stages.

9. **Conflicts of interest**

Are there any relevant conflicts of interest (COI) that the judges would expect to be made aware? (NB: shortlisted candidates will be asked for a more detailed COI declaration)

Alere provided some support for the original PELICAN study (paid to institution). Alere no longer markets PLGF.