



## Section 1 Need identification.

Preeclampsia (defined as new hypertension presenting after 20 weeks with significant proteinuria) is a serious complication affecting 1 in every 10 pregnancies. Annually, preeclampsia claims the lives of 50,000 mothers and 500,000 babies, making it one of the world's deadliest pregnancy complications.

At present, birth of the baby is the only treatment and the safest option for the mother. However, such pre-term delivery is associated with a significant risk of long-term neurodevelopmental infant morbidity and mortality; and accounts for a huge proportion of annual admissions to neonatal ICU. Even a minor improvement in gestation at delivery would confer a significant infant survival benefit, such that every day *in utero* counts. Accurate risk stratification would reduce these enormous preeclampsia risks for mothers and babies, facilitating early intervention before severe complications have occurred. Therefore, there is an urgent, unmet challenge to develop accurate risk stratification tools for preeclampsia.

While tests to 'rule out' preeclampsia are in clinical use, no test is currently available to meet the crucial clinical challenge of 'rule in' or diagnosis of preeclampsia. Clinical diagnosis can be extremely challenging, even in the most experienced of hands, and complementary diagnostic tests are an urgent unmet need. Furthermore, clinical criteria for severity of preeclampsia correlate poorly with maternal and foetal outcome, meaning that there is no test that can predict how the mother's health will progress, once diagnosed with preeclampsia. Accurately identifying mothers with preeclampsia who will not progress to a severe phenotype could prevent unnecessary preterm/emergency delivery with all associated complications. Moreover, due to the increasing prevalence of preeclampsia and the fact that survivors of the disease and their babies have a lifelong increased risk of developing other chronic health problems; any improvements in clinical decision-making would have enormous impact.

## Section 2 Use of data analytics (and/or) AI.

We are a multidisciplinary team led by biomedical, medical and data scientists from UCD, together with a team of clinicians and laboratory scientists from three of Ireland's largest and busiest maternity hospitals – the National Maternity, the Rotunda, and the Coombe Hospitals, in collaboration with data scientists and machine learning experts from the SAS Institute. Collectively our team has over 150 years of basic research, clinical and data science acumen, which has enabled us to put all the pieces in place to deliver a cutting-edge and unique AI-powered solution- AI\_PREMie- in the management of preeclampsia.

Our AI\_PREMie method incorporates holistic data from patients including demographics, medical history, clinical assessments and other investigation data as well as the novel blood-based preeclampsia biomarkers developed by the team. On top of this we have accurate and reliable ground truth for preeclamptic cases that has been collected by the clinicians on our team. Our initial analysis of this data focused on the novel biomarkers and using mixed effect modelling to examine the relationships between these and risk of preeclampsia. As we found non-linear relationships between the biomarkers and preeclamptic risk, we were motivated to pursue a machine learning approach to preeclampsia risk stratification that uses information from all variables/data collected.



To this end, data was imported into SAS Viya and preprocessed before model building. All data was merged, cleansed, and observations with insufficient or missing data either rejected or imputed using mean imputation where statistically appropriate. In SAS Visual Data Mining and Machine Learning (VDMML), a pipeline was created containing a variety of different machine learning models (ranging from a simple logistic regression to more sophisticated support vector machine models). Performance was assessed to select a champion model for AI\_PREMie. To estimate the capacity for preeclampsia to be modelled from the features available, a 10-fold cross validation with performance measured using Area under ROC (AUROC) was used. The best performing model to accurately separate high-risk from low risk patients was a Support Vector Machine (SVM) with an average AUROC of 0.839.

Although our current model is based on a dataset from 150 pregnant women with suspected preeclampsia, it is a robust indicator of the viability of the approach that we are taking and gives us confidence in moving forwards. Moreover our method returns an easily interpretable risk score to the clinician, and will be delivered as a cloud based function as a service, or potentially an embedded AI model on the edge device to augment clinical evaluation in real-time.

### **Section 3: Social benefit achieved.**

The challenge of maternal health is of strategic national importance and is globally relevant. Our team have applied extensive interdisciplinary knowledge to deliver a new and simplified bespoke solution for risk stratification in preeclampsia that will enable timely delivery decisions, transforming the lives of pregnant mothers, their babies, their families & their extended communities. Improving quality of life in this way not only aligns to the UN priority goal of Sustainable Development Goal 3 (Good Health & Well-Being) but also to Sustainable Development Goal 5: Gender Equality & Sustainable Development Goal 10: Reducing Inequality, which is not only a moral imperative but critical for sustaining international growth.

A 2015 WHO report acknowledges that many maternal and infant deaths are preventable and could be avoided with effective and timely clinical interventions. The key, they state, would be to ensure that high-risk pregnancies and complications are recognized early and managed appropriately. Thus, new diagnostics are urgently required, and AI\_PREMie will fill this gap. This report also outlines specific targets in global maternal & newborn mortality rates to be achieved by 2030 under SDG3. However, these targets will only be achieved if there is a significant investment in maternal health research, as between 2009-2019 there was no statistically significant change in the rate of direct maternal deaths from any cause, including preeclampsia in the UK & Ireland. Moreover, the rate of severe maternal morbidity is increasing, including morbidity from preeclampsia (*National Perinatal Epidemiology Centre 2019 report*). AI\_PREMie will enable Ireland to lead on contributing to achievement of these nationally important and globally relevant targeted reductions by 2030.

Through our stakeholder engagement to date, we have learnt that our AI\_PREMie tool has the capacity to completely alter the clinical approach to the management of preeclampsia and will allow careproviders to personalise patient care to achieve the best possible outcomes for both mother and baby. For obstetric careproviders, including doctors and midwives, this test will transform diagnosis and risk prediction: *“It is difficult to sometimes know what to do: whether to deliver a baby because we fear for the mother’s safety or to keep baby in utero for as long as possible.”* For critical care end



users, this test will direct treatment for severely unwell women: *“We are presuming the diagnosis is correct. Our decision is influenced by what the diagnosis is. If we are wrong, then a devastating intracranial haemorrhage or a blood clot could happen, which could be fatal”*. Our solution also creates value for all members of the multidisciplinary team including laboratory staff: *“We have more job satisfaction if we really are helping a woman who is sick- I love to be involved in patient care”*. Finally, for careproviders in secondary centres, who may not have frequent exposure to severe, potentially life-threatening cases of preeclampsia, uncertainty arising from lack of experience can pose a risk.

Preeclampsia diagnosis often resulted in the transfer of women from their own local area to tertiary level units for care, and women talked about the experience of being separated from their normal environment due to clinical uncertainty about prognosis. Women spoke of the challenges of running a family life from a distance and trying to maintain normality in a time of constant worry. Families also spoke of their devastating memories of preeclampsia, which reverberated for years. Several people we spoke to also confided to us that this was the first time they had spoken openly since their devastating experiences and that they were immensely worried about any future pregnancy as well as the health of their baby.

The independent consensus of all stakeholders interviewed to date is that a high-quality, reliable test for risk stratification of preeclampsia, which could be performed in the clinic and provide results within hours, **is urgently needed**. Women, their families, and clinicians all spoke of the value of information in making decisions. Many women told us how challenging it was to *“stay relaxed”* when they constantly worried about what was going to happen to them or their baby. Clinicians told us that they will use AI\_PREMie to guide their management on the appropriate time to administer antenatal steroids, to transfer women, to advise delivery and ultimately to reduce morbidity and mortality. These informed delivery decisions can transform the lives of pregnant mothers, their babies, their families & extended communities.

### **Section 4 Evidence of impact.**

Trialling AI\_PREMie in three of Ireland’s largest and busiest maternity hospitals (The National Maternity Hospital, The Rotunda Hospital and The Coombe Hospital), representing 50% of all births in Ireland, has demonstrated compelling evidence that our technology works to accurately separate high-risk from low risk patients and will be used by care providers in a busy hospital setting. Firstly, by accurately diagnosing preeclampsia, which can be challenging even for experienced staff. Second, by predicting progression to severe disease, potentially permitting more accurate timing of delivery, allowing a baby to remain *in utero* for several more precious hours/days impacting their survival and long-term neurodevelopmental health. In short, AI\_PREMie arms care providers with an affordable risk stratification tool to closely observe pregnancies complicated by preeclampsia, helping to prevent unnecessary adverse outcomes for mother and baby.

We have raised public awareness of of preeclampsia and our AI\_PREMie test through multiple engagements during 2020 & 2021 including winning the 2021 NovaUCD Invention of the Year award, several newspaper articles, participation in the *‘Technology for Good’* panel event at the Science Foundation Ireland Summit 2020 and in SFI’s *“I’m a Scientist...”*, where AI\_PREMie was used to illustrate the real-life impact of maths. Our reach has also included events with >600 primary and



secondary school students. We continually engage with patient organizations, including the Irish Neonatal Health Alliance and a US-based preeclampsia support group, to ensure the impact of AI\_PREMie will be disseminated as early and broadly as possible. We use the hashtags: #myPETexperience to understand women’s preeclampsia experiences on social media platforms and raise awareness of the condition and #AI\_PREMie to raise general awareness, reaching >0.5M impressions based on 3-4 key posts.

## Section 5 Future plans.

Funded by Science Foundation Ireland, we are currently extending our AI\_PREMie prospective clinical management study to several maternity hospitals across Ireland and our AI-powered solution will continually learn and evolve as we implement it into more widespread clinical practice. Dashboards and automated alerting of model performance with governance oversight will ensure that intelligent decisions continually learn and improve. As more data is gleaned, the relative importance of all of our collected variables will improve the sensitivity of the models in production and we will be able to stratify preeclampsia prediction into risk bands. Continuous model development will take place concurrently with production, so that challenger models would be ready to deploy if necessary. Once we have such a hybrid biomarker/AI test operational in multiple sites, it excitingly opens the potential to further develop similar augmented intelligent solutions for chronic illnesses that have proven difficult to address .

## Section 5 The AI\_PREMie team & logos.



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