Anti-PLA2R Antibody Testing for the Diagnosis of Primary Membranous Nephropathy: An Early Cost-Effectiveness Analysis

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BACKGROUND

- **Membranous nephropathy (MN)** is a type of nephrotic syndrome (NS) associated with risk of **renal failure** and **high treatment costs.**
- **Renal biopsy** is the gold standard for diagnosing NS, but this procedure is **costly** and **invasive**.
- ~80% of **primary MN (pMN)** cases are attributed to an autoimmune process involving the PLA2R1 antigen. **Anti-PLA2R testing** could help diagnose those patients and **avoid unnecessary biopsies**, but there is a lack of consensus on this approach.

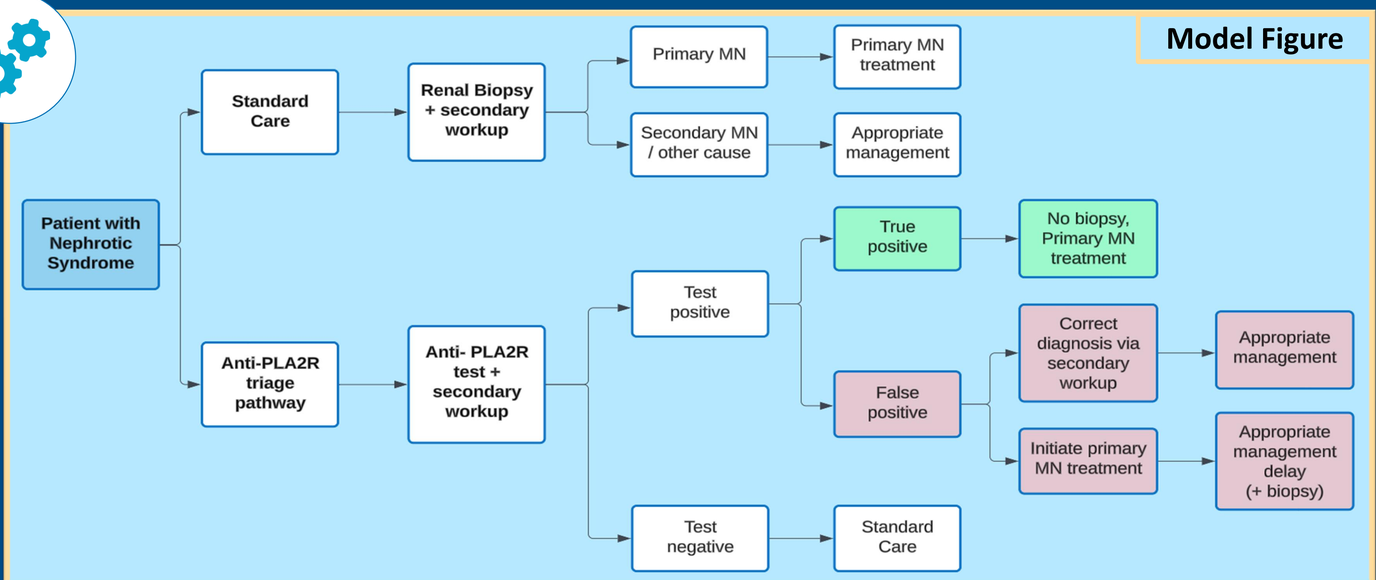
METHODS

- A systematic review identified **no existing economic evaluations** of test-directed management for patients with pMN or NS.
- A **short-term probabilistic decision tree** was used to assess the potential utility of anti-PLA2R testing (biopsy if negative) vs. standard care (biopsy all) from a **UK NHS perspective.**
- Primary outcomes included **costs**, **biopsies saved**, and **life years gained.**

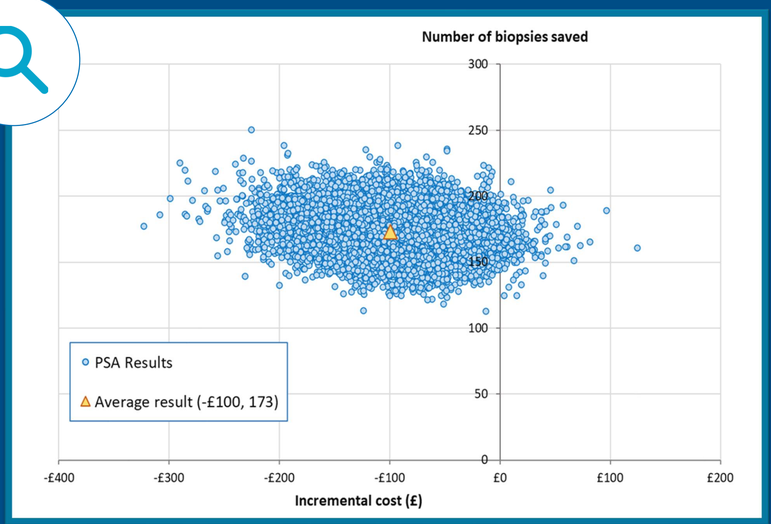
KEY FINDINGS

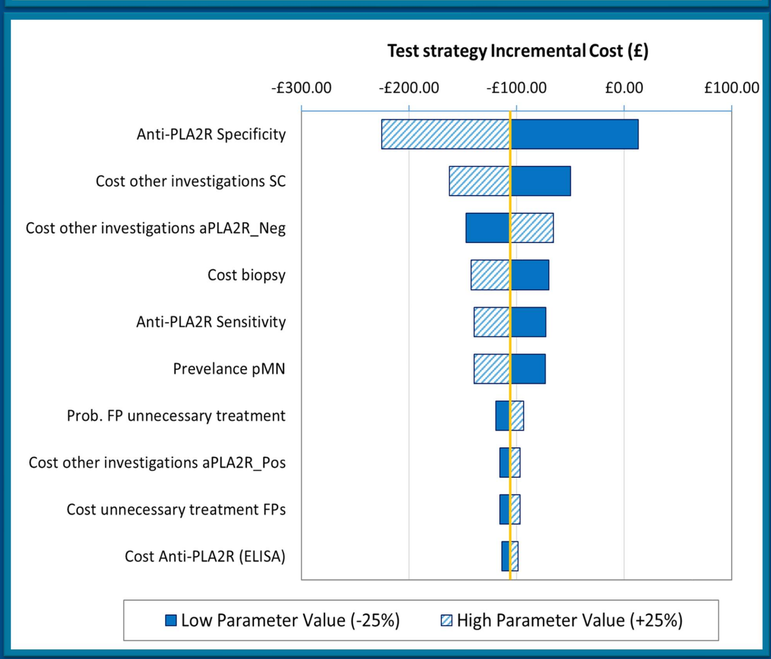
- Anti-PLA2R testing could **save costs**, **avoid unnecessary biopsies**, and **reduce morbidity and mortality** associated with biopsies.
- There is a **lack of data** to inform management and outcomes for patients with a **FP test result**.
- Research could help to address this uncertainty e.g. **clinical consensus on safety netting approaches**, and a **real-world implementation study**.

Model Figure



- Anti-PLA2R test accuracy was based on a recent **meta-analysis (n=33 studies): 63.1% sensitivity, 95.5% specificity** (in press).
- The prevalence of pMN was set to **24.7%** based on **Scottish registry data (2021)**.
- All patients receive **standard secondary workup tests** including virology, immunology and ultrasound tests.
- Some patients receive **additional tests** (blood tests, imaging, endoscopy) according to proportions from published UK data (Hamilton et al. 2019).
- No data was available to inform outcomes in the False Positive (FP) group. The base case assumes:
  - **50% FPs correctly diagnosed via secondary workup/ additional investigations;**
  - **50% receive pMN treatment (Rituximab). They are correctly identified via biopsy after ≤6 months with no negative health impacts.**
- **Threshold analysis** was conducted to identify the total quality adjusted life years **(QALY) loss** that would be required in the FP group to render the test strategy not cost-effective.





BASE CASE RESULTS:

- In a cohort of 1,000 patients, anti-PLA2R testing **saves £99,405, avoids 173 unnecessary biopsies**, and **gains 2.87 life years** (via reduced biopsy mortality, assuming average UK pop. life expectancy).
- Over 10,000 PSA runs, the testing strategy has **98% probably of being cost saving**, and **100% probability of reducing biopsies**.

SENSITIVITY ANALYSIS:

- The test was **no longer cost saving** if **>90% FPs receive Rituximab.**
- Other influential parameters included test **specificity**, the **cost** of other **diagnostic investigations and biopsy**, and pMN **prevalence.**

THRESHOLD ANALYSIS:

- Greater than **4.99 QALY loss** in the FP group would render the test no longer cost-effective, assuming a £20,000/QALY Willingness to pay (WTP) threshold.

TAKE AWAY MESSAGE

- **There is clear potential for the anti-PLA2R test to save NHS costs. Future research should address uncertainty around outcomes for FP cases.**

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