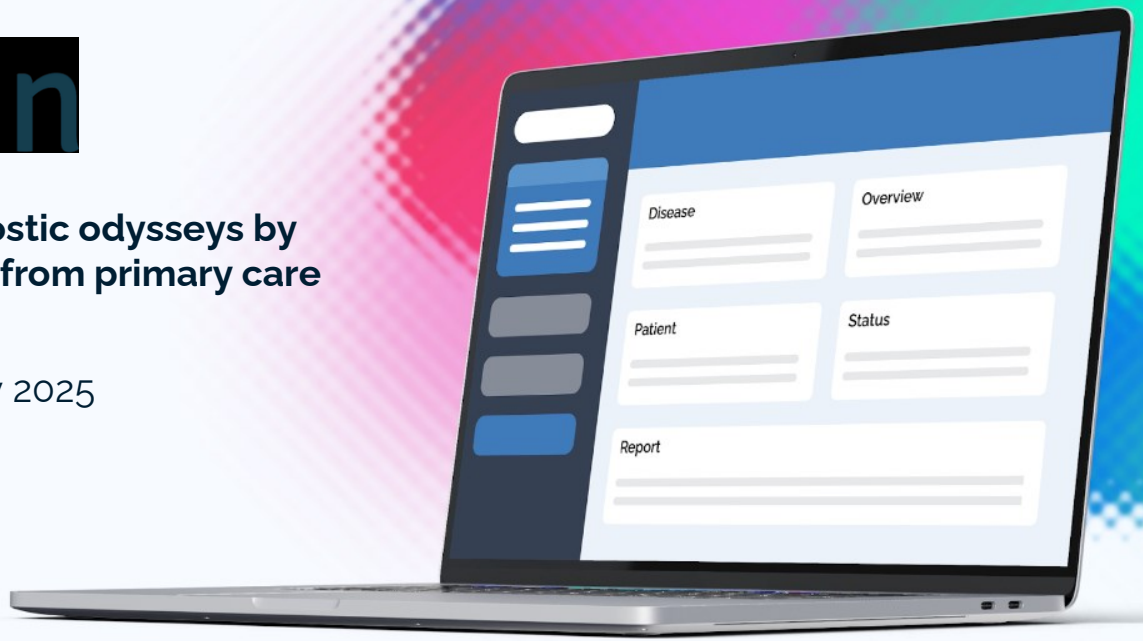
mendelian

MendelScan - shortening diagnostic odysseys by identifying rare disease at scale from primary care record

Clinical AI Interest Group - 22 July 2025

Dr Peter Fish



UK-Based MedTech Company Tackling the RD Diagnostic Odyssey

Hadley Mahon
Commercial & Product Director

Liz Varones
Head of Industry Partnerships

Dr Calum Grant
Clinical Lead and Sr. Data Scientist

Elena Marchini
Product Lead

Dr Freya Boardman-Pretty
Sr. Data Scientist

Rand Dubis
Data Scientist

Dr Alan Warren
Lead Software Engineer

Jack Sams
DevOps Engineer

Daniel Ollenershaw
Software Engineer

Chanaka Ranawickrema
NHS Partnerships

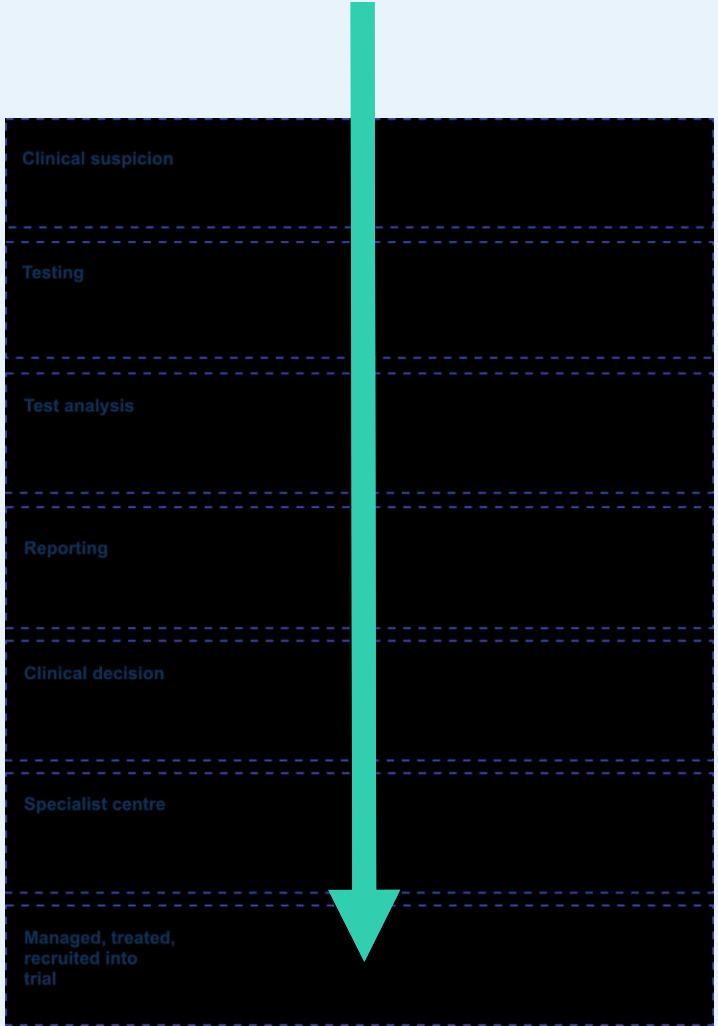
Dr Will Evans
Clinical Advisor (GP)

Dr Lara Menzies
Clinical Advisor (Geneticist)

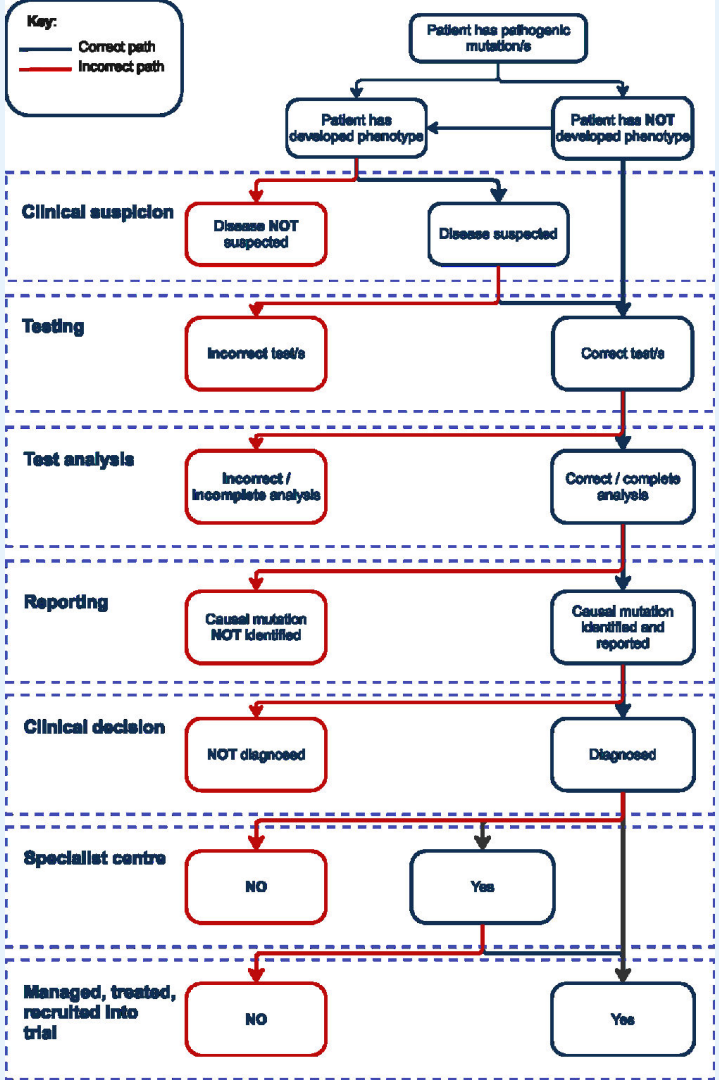
Dr Peter Fish
CEO

Fran Garcia
Co-founder & Non-executive Chairman

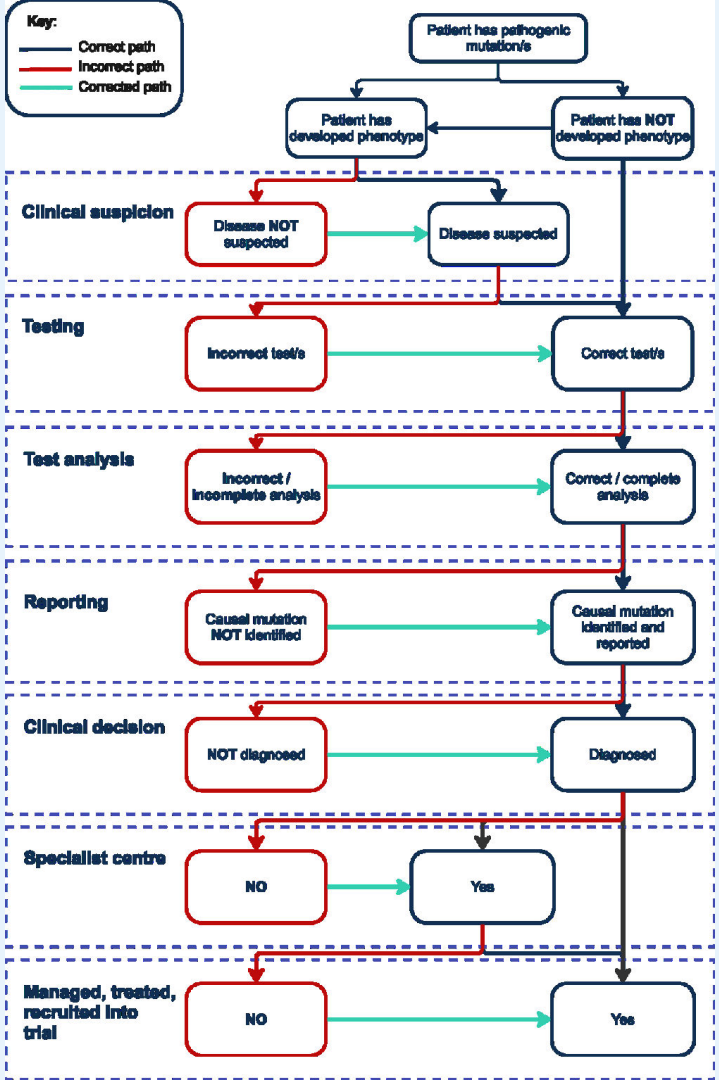
Mendelian's Approach



Mendelian's Approach



Mendelian's Approach



Clinical Suspicion is a Key Barrier to Treatment in PNH

Jenny, 38: Undiagnosed PNH (paroxysmal nocturnal haemoglobinuria)

1 **Early signs**

2 **Cause missed**

m

3 **High burden**

4 **Poor outcomes**

3 **Case identified**

4 **Diagnosed**

5 **Optimal management & outcomes**

*Mock patient story. Based on real patient journeys.

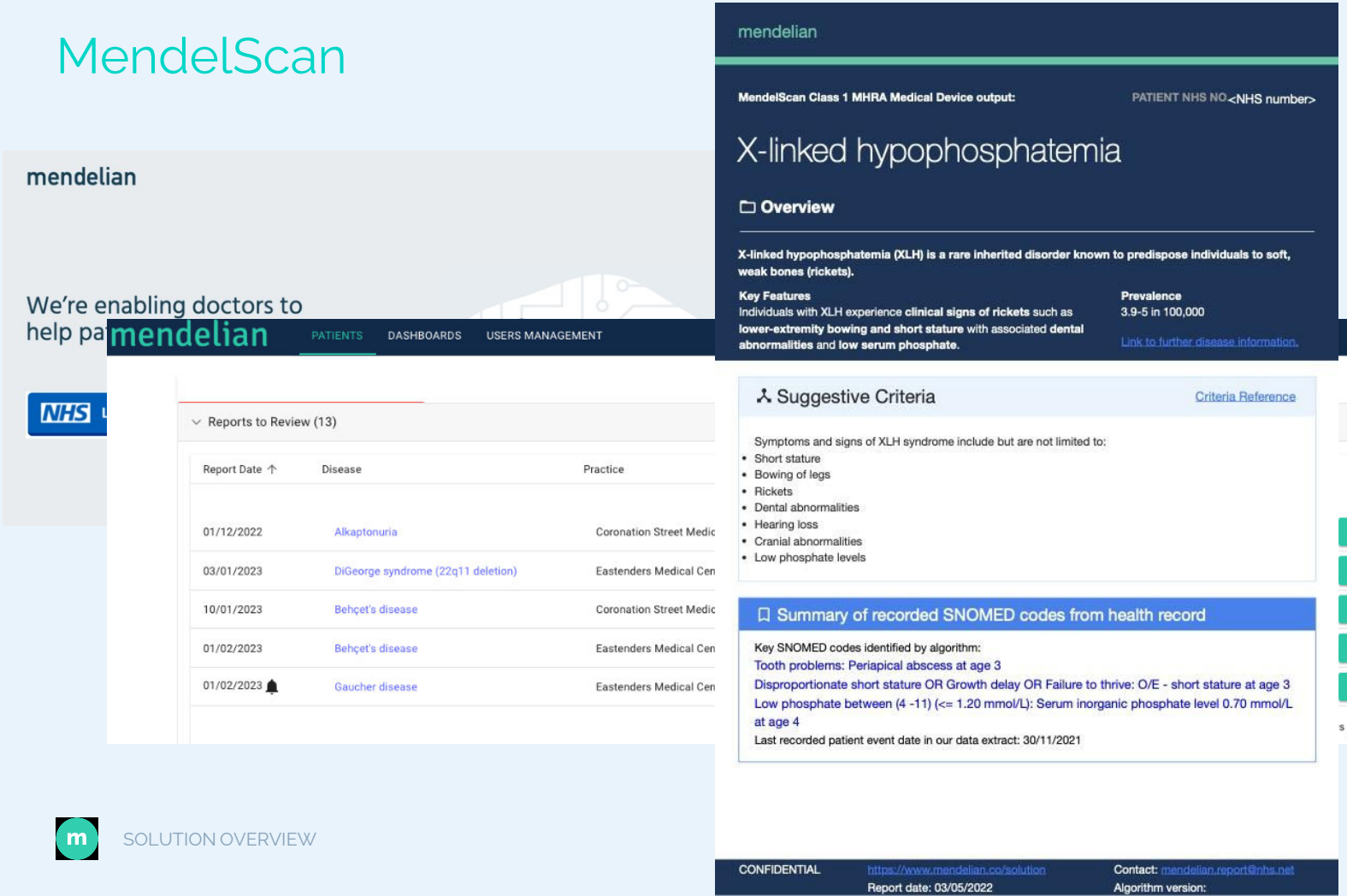
MendelScan

Asynchronous, multi-disease, case-finding platform - class I medical device (MDD)

EHRs Scanned, Case Reports Generated → **Digital Clinical Review** → **Patient Outreach** → **Referral & Testing**

Outcomes generated to support health system change

MendelScan


mendelian
We're enabling doctors to help pa
mendelian
PATIENTS
DASHBOARDS
USERS MANAGEMENT
LOGOUT
NHS
Reports to Review (13)
Report Date
Disease
Practice
01/12/2022
Alkaptonuria
Coronation Street Medic
03/01/2023
DiGeorge syndrome (22q11 deletion)
Eastenders Medical Cen
10/01/2023
Behçet's disease
Coronation Street Medic
01/02/2023
Behçet's disease
Eastenders Medical Cen
01/02/2023
Gaucher disease
Eastenders Medical Cen
FILTER
REVIEW COMPLETE
HISTORY
s per page: 5
1–5 of 13
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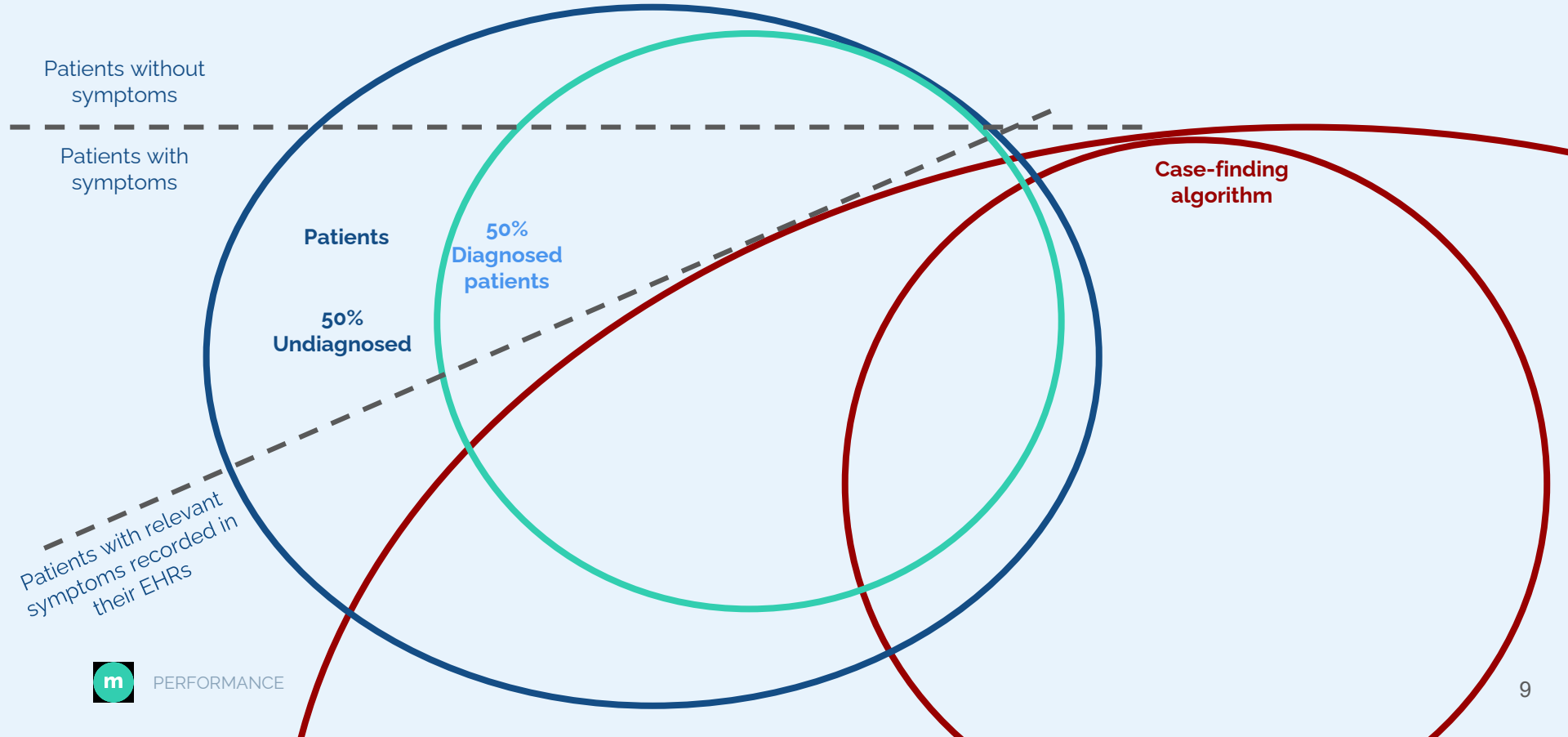
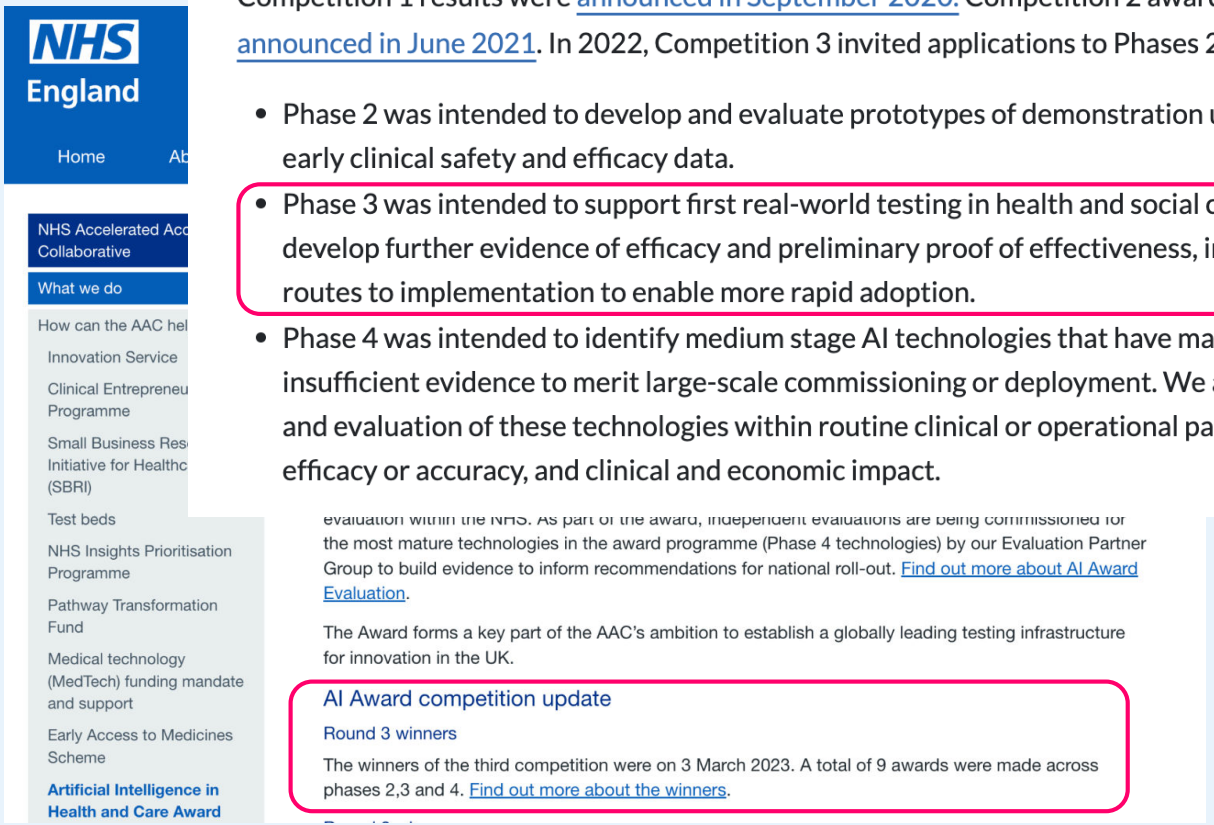
MendelScan Class 1 MHRA Medical Device output:
PATIENT NHS NO <NHS number>
X-linked hypophosphatemia
Overview
X-linked hypophosphatemia (XLH) is a rare inherited disorder known to predispose individuals to soft, weak bones (rickets).
Key Features
Individuals with XLH experience clinical signs of rickets such as lower-extremity bowing and short stature with associated dental abnormalities and low serum phosphate.
Prevalence
3.9-5 in 100,000
Link to further disease information.
Suggestive Criteria
Criteria Reference
Symptoms and signs of XLH syndrome include but are not limited to:
Short stature
Bowing of legs
Rickets
Dental abnormalities
Hearing loss
Cranial abnormalities
Low phosphate levels
Summary of recorded SNOMED codes from health record
Key SNOMED codes identified by algorithm:
Tooth problems: Periapical abscess at age 3
Disproportionate short stature OR Growth delay OR Failure to thrive: O/E - short stature at age 3
Low phosphate between (4 -11) (<= 1.20 mmol/L): Serum inorganic phosphate level 0.70 mmol/L at age 4
Last recorded patient event date in our data extract: 30/11/2021
CONFIDENTIAL
https://www.mendelian.co/solution
Report date: 03/05/2022
Contact: mendelian.report@nhs.net
Algorithm version:

Patient Cohorts and Algorithm Performance



NHS AI Award



Phases and specifications

Competition 1 results were announced in September 2020. Competition 2 awarded projects were announced in June 2021. In 2022, Competition 3 invited applications to Phases 2-4 of the AI Award.

- Phase 2 was intended to develop and evaluate prototypes of demonstration units and generate early clinical safety and efficacy data.
- Phase 3 was intended to support first real-world testing in health and social care settings to develop further evidence of efficacy and preliminary proof of effectiveness, including evidence for routes to implementation to enable more rapid adoption.
- Phase 4 was intended to identify medium stage AI technologies that have market authorisation but insufficient evidence to merit large-scale commissioning or deployment. We are supporting testing and evaluation of these technologies within routine clinical or operational pathways to determine efficacy or accuracy, and clinical and economic impact.

NHS AI in Health and Care Award

18-Month evidence generation project, fully funded by the Department of Health and Social Care

MendelScan - An innovative AI case-finding platform to accelerate the diagnosis of rare diseases using primary care electronic health records

Apr 2023 to Nov 2024

Aim: To evaluate for indications that MendelScan can:

- Reduce time-to-diagnosis
- Increase overall diagnosis rates
- Reduce avoidable healthcare activity associated with the pre-diagnosis phase
- Be implemented practically, ethically and affordably

NHS AI in Health and Care Award

We're building three evidence layers required for nationwide NHS commissioning and adoption

1. **Retrospective validation:** Large scale validation on 23m NHS anonymised primary care patient records

$341B
by 2027

2. **Implementation research:** Various smaller studies:
    a. Public sentiment survey
    b. Patient acceptability
    c. Clinician acceptability and usability
    d. Health resource impact modeling
3. **Real-world deployment:** MendelScan deployed on 725,000 primary care records in NHS GP practices

WP2: Analytical Validation

1. Retrospective case-control study
2. All cases, 2-million controls
3. 42 algorithms (34 diseases)
4. Lots of considerations…

WP2: Analytical Validation

Validation stats: DiGeorge syndrome (22q11 deletion) (v4.7)

> *Date scanned: 05/03/2024*
> *Report generated: 01/10/2024*

DiGeorge syndrome (22q11 deletion) (v4.7) is a non-scoring algorithm.

Overall coded disease prevalence is **4.65 in 100,000** . Prevalence from literature is **21 in 100,000** (taken from Calum's update of the Prevalence project winter 2022: see Disease prevalence).

Total patients scanned: **2,000,945 (1,051 cases, 1,999,894 controls)** .

106 patient(s) with diagnostic codes for DiGeorge syndrome (22q11 deletion) were found in the "control" group of 2,000,000 and removed, leaving 1,999,894 controls.

Total cases (dx code present): **1051**

Total cases (dx code present) with 3 years of case history before dx: **445**

Total cases with any clinical feature(s) of the disease present: **872**

All cases

	Cases	Controls
Flagged	238	620
Not flagged	813	1,999,274

Cases with clinical history

	Cases	Controls
Flagged	80	620
Not flagged	365	1,999,274

Cases with clinical features

	Cases	Controls
Flagged	238	620
Not flagged	634	1,999,274

WP2: Analytical Validation

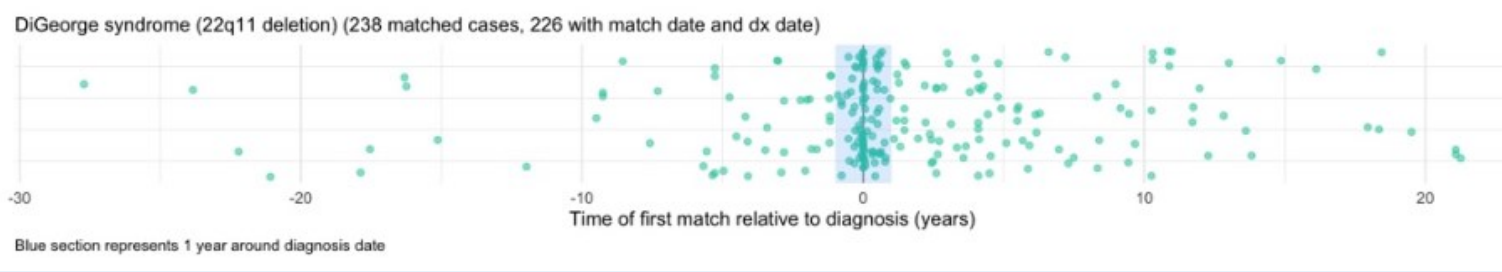
Results

Statistic	All cases	Clinical history	Clinical features
Patients scanned	2,000,945	2,000,339	2,000,766
Cases	1,051	445	872
Controls	1,999,894	1,999,894	1,999,894
Coded prevalence	4.65 in 100,000	1.97 in 100,000	3.86 in 100,000
Literature prevalence	21 in 100,000	21 in 100,000	21 in 100,000
Flagged cases (true positives)	238	80	238
Flagged controls (false positives)	620	620	620
Non-flagged cases (false negatives)	813	365	634
Non-flagged controls (true negatives)	1,999,274	1,999,274	1,999,274
Sensitivity	22.65% (20.15 - 25.30%)	17.98% (14.52 - 21.87%)	27.29% (24.36 - 30.38%)
Specificity	99.9690% (99.9665 - 99.9714%)	99.9690% (99.9665 - 99.9714%)	99.9690% (99.9665 - 99.9714%)
PPV (unadjusted)	27.74% (25.08 - 30.56%)	11.43% (9.44 - 13.77%)	27.74% (25.14 - 30.50%)
PPV (adjusted for coded prevalence)	3.29% (2.88 - 3.75%)	1.13% (0.91 - 1.39%)	3.29% (2.89 - 3.74%)
PPV (adjusted for literature prevalence)	13.30% (11.80 - 14.96%)	10.86% (8.96 - 13.10%)	15.61% (13.92 - 17.45%)
Flag rate (based on coded prevalence)	32.05 in 100,000	-	-
Flag rate (based on literature prevalence)	35.75 in 100,000	-	-

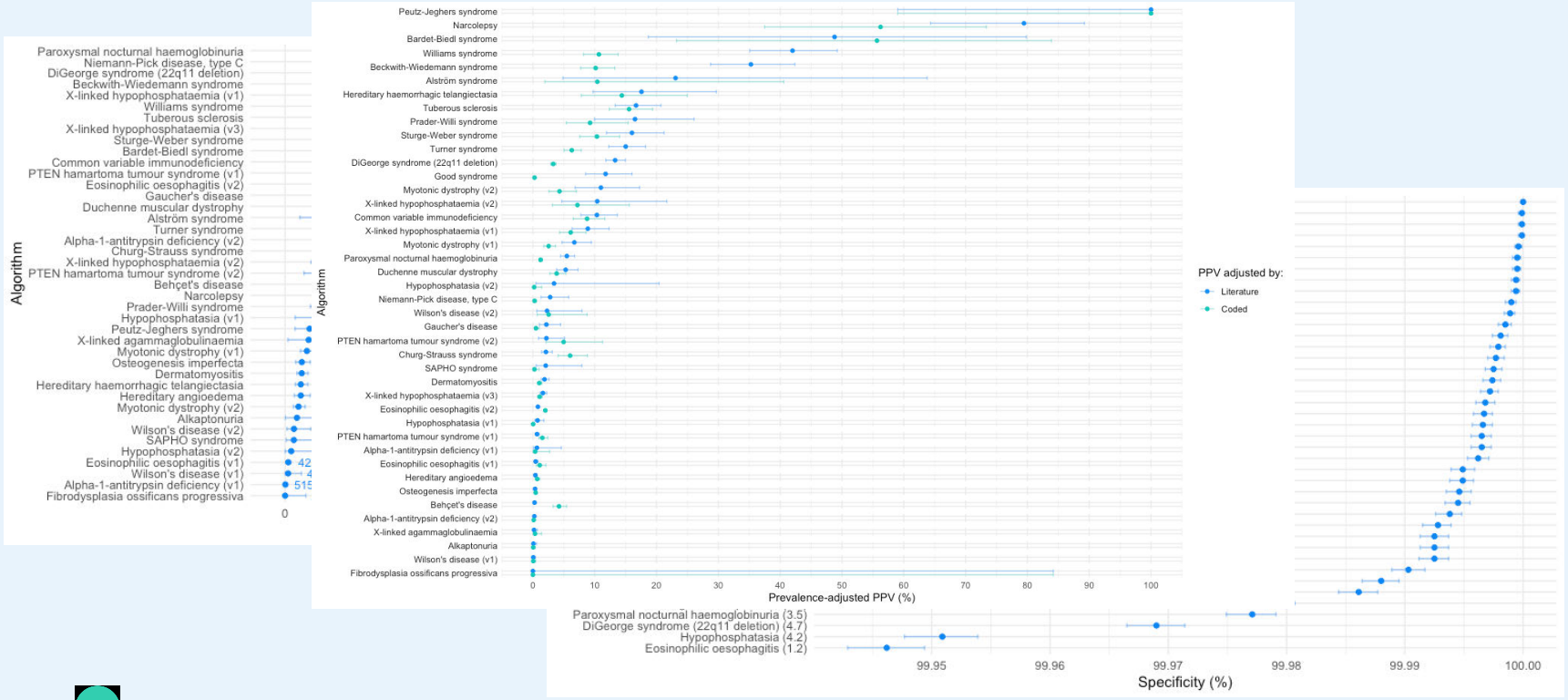
WP2: Analytical Validation

Number flagged before diagnosis	73	41	73
% flagged before diagnosis*	32.3%	60.3%	32.3%
Number flagged 1 year+ before diagnosis	47	27	47
% flagged 1 year+ before diagnosis (early match rate)*	19.7%	33.8%	19.7%
Mean months flagged before dx (of those flagged before)	57	64	57
Median months flagged before dx (of those flagged before)	24	41	24
Mean months flagged before dx (of all with a dx date)	-16	5	-16
Median months flagged before dx (of all with a dx date)	-5	2	-5

* *% calculated using only flagged cases with dx and match dates*



WP2: Analytical Validation

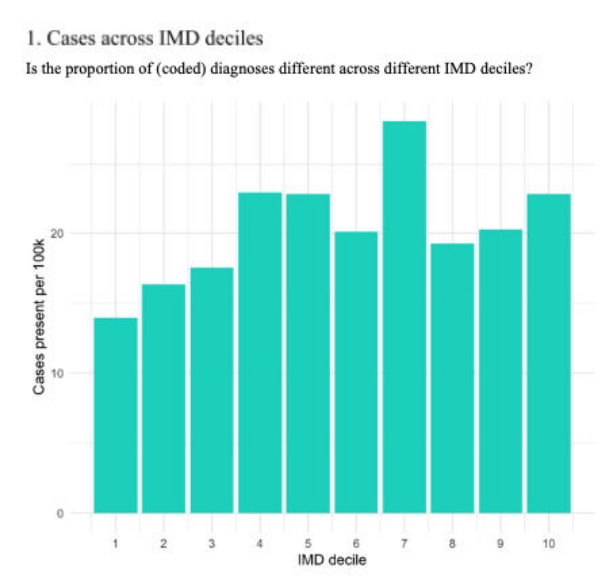


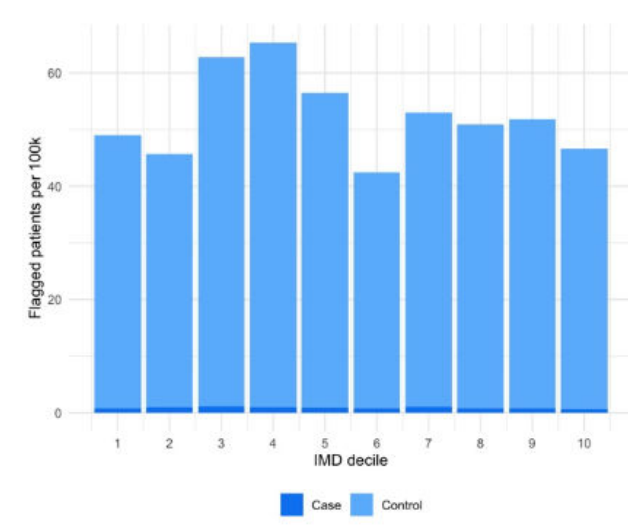
WP2: Analytical Validation - Publication

Evaluating Algorithmic Approaches to Rare Disease Case-Finding: A Retrospective Validation Study Using Electronic Health Records

Freya Boardman-Pretty*, Jyothika Kumar*, Calum Grant, Elena Marchini, Will Evans, Lara Menzies, Ashley Kieran Clift, Rand Dubis, Amanda Worker, Elizabeth Varones, Alan Warren, Jack Sams, Daniel Ollerenshaw, Jez Stockdale, Hadley Mahon, Peter Fish

WP2: Analytical Validation - Equality (AAT)

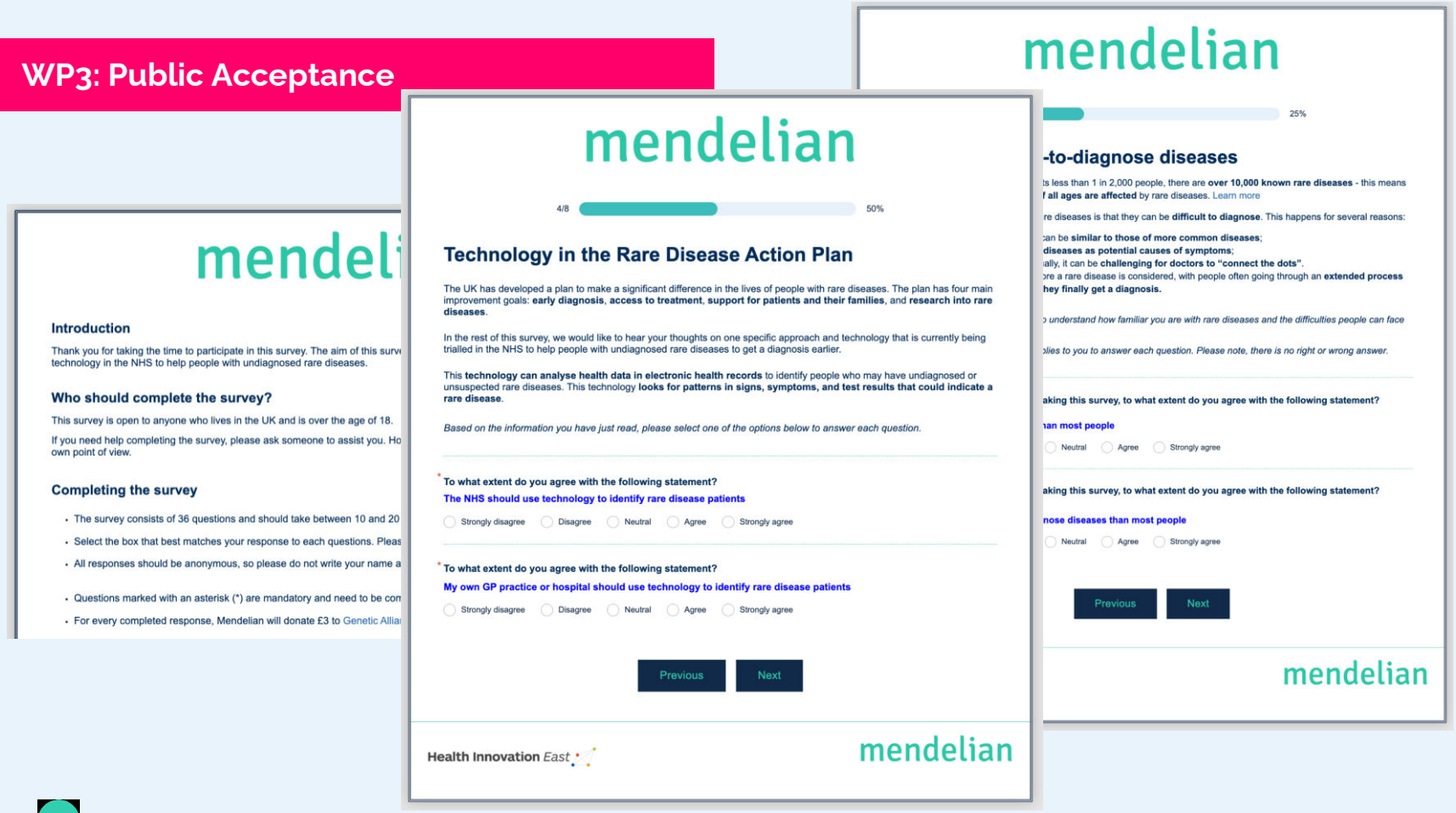




WP3: Public and NHS Acceptance

- Public sentiment survey
- NHS stakeholder engagement (focus group)

WP3: Public Acceptance

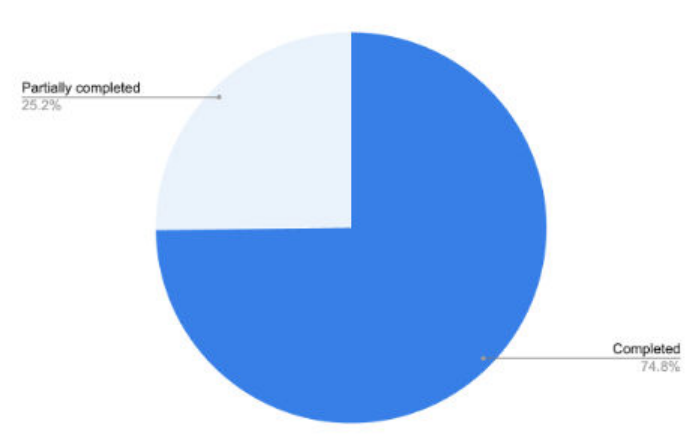


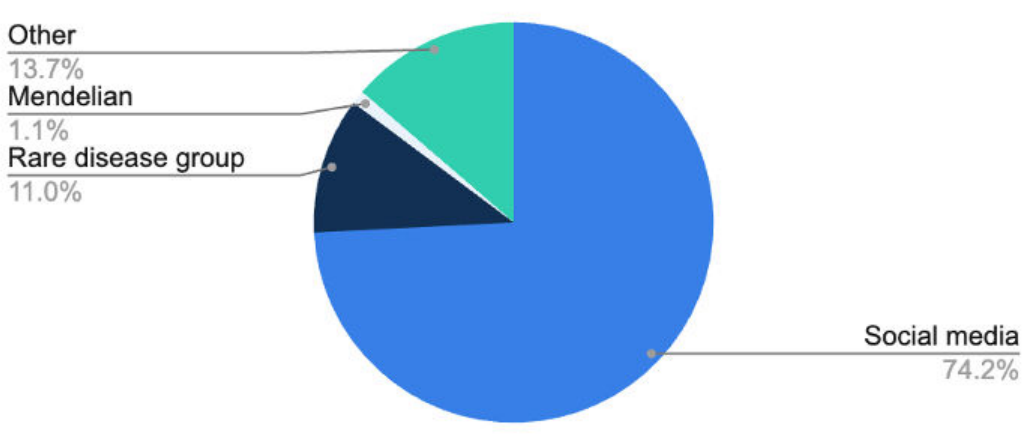
WP3: Public Acceptance

254
Respondents

93%
Endorsed the use of EHR data to identify undiagnosed rare disease patients

90%
Anticipated feeling grateful that their health data had been included



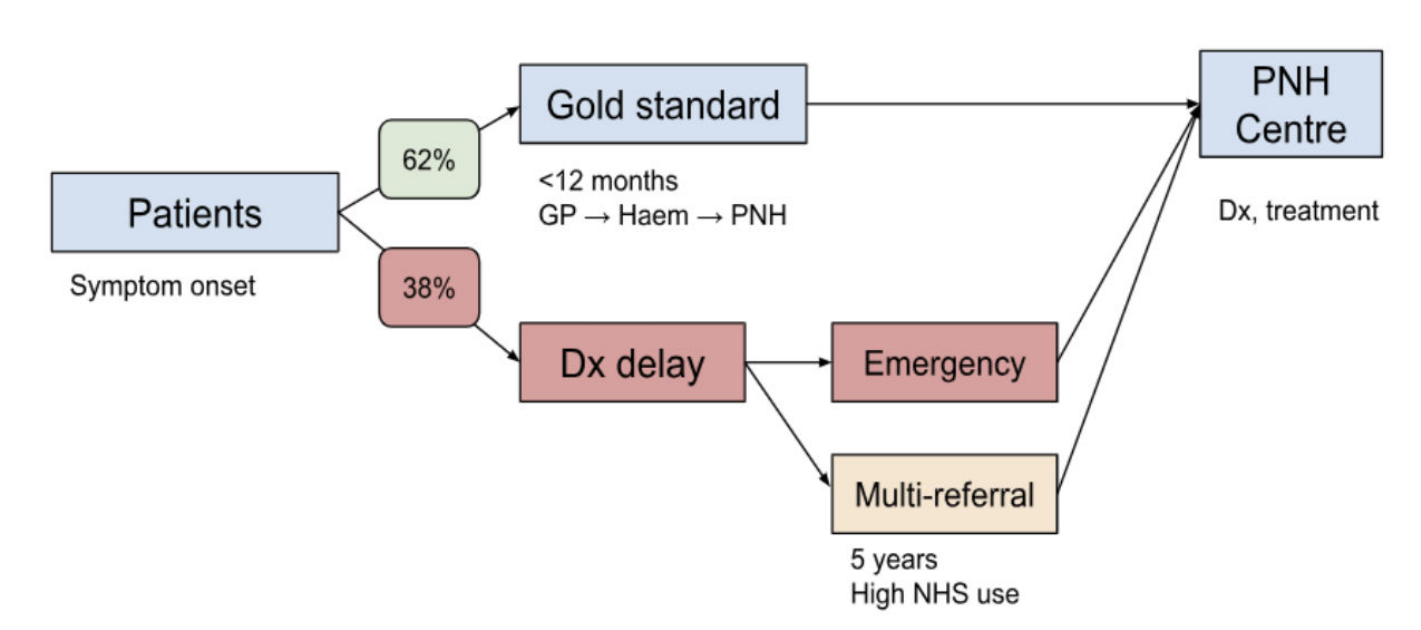


WP3: Public Acceptance

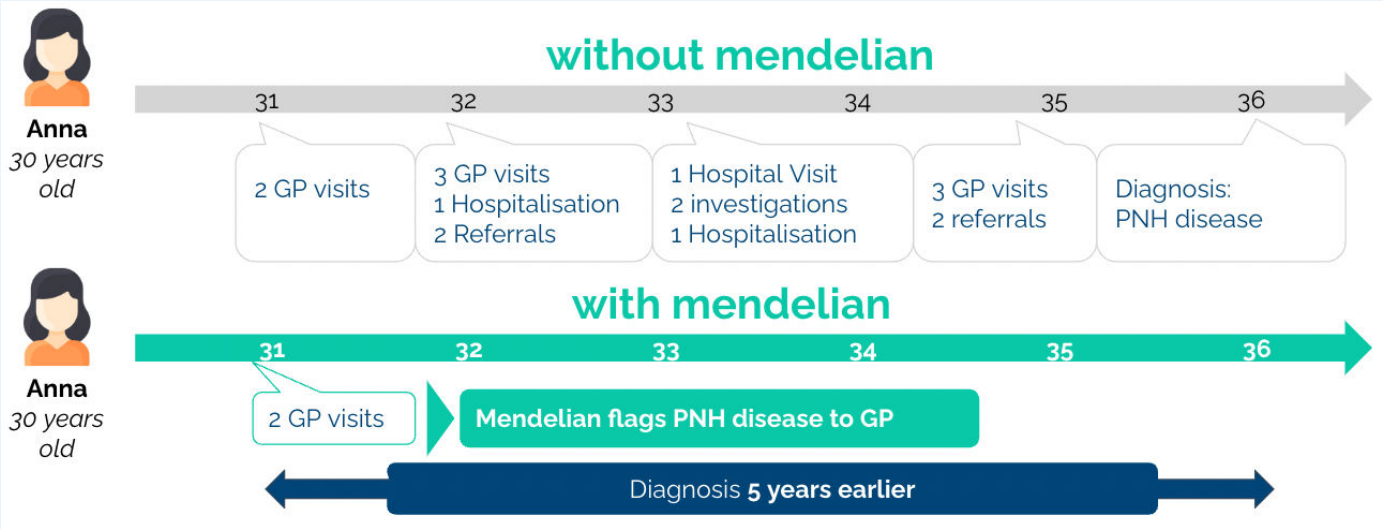
Public perception of the use of clinical decision support tools within the NHS for rare disease case finding.

Elena Marchini[1], Sarah Mason[2,3], Judith Fynn[4], Jez Stockdale[1], Hadley Mahon[1], Sarah Robinson[4], Peter Fish[1]

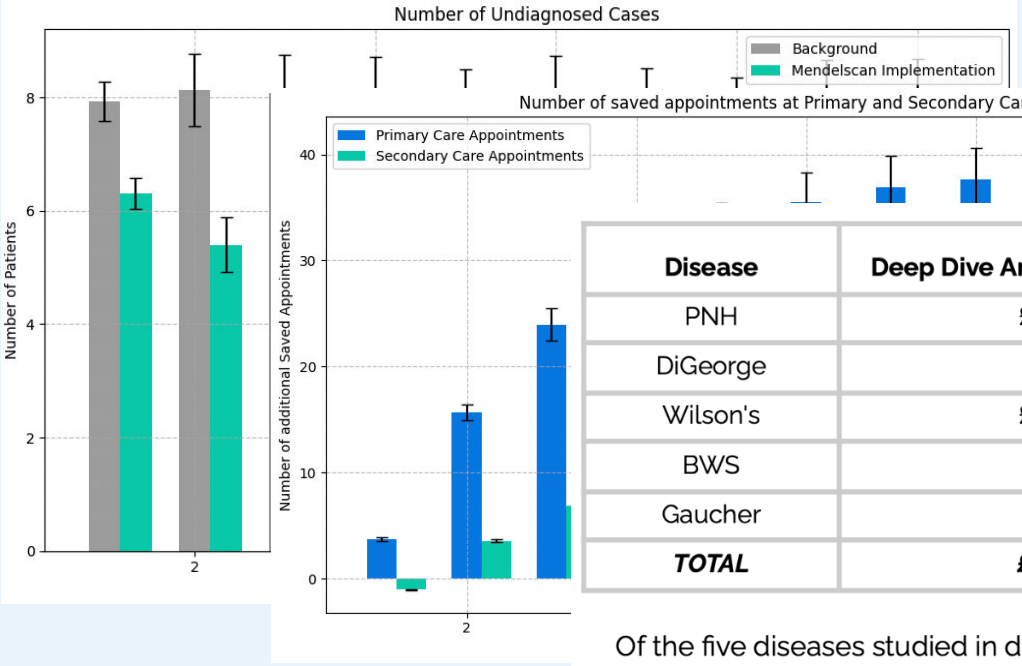
WP4: Clinical Utility and Cost Effectiveness Modelling



WP4: Clinical Utility and Cost Effectiveness Modelling



WP4: Clinical Utility and Cost Effectiveness Modelling



Disease	Deep Dive Annual Saving Potential	Savings Project in initial 5 Year Deployment
PNH	£2,550,877	£8,911,818
DiGeorge	£149,992	£476,066
Wilson's	£1,030,042	£2,407,162
BWS	£73,445	£208,585
Gaucher	£101,326	£476,066
TOTAL	***£3,905,682***	***£12,479,697***

Of the five diseases studied in depth, the average annual **pre-diagnosis saving** potential across them all is **£781,136.43**. Applying that to all 34 diseases in the AI award may give annual cost savings of **£26,558,638.69** through deployment of high performing case-finding algorithms.

WP5: Real-world deployment

- **Algorithms for 32 diseases were deployed on 720,000 primary care patients in 54 GP practices**
- **262 patients flagged, 244 reviewed**
- **1 in 2 flags received positive clinical feedback**
- **1 in 3 reports expected to lead to clinical action** (incomplete data)
- **In the reporting timeframe: 32 patients** (13%) **recontacted and referred**

End of Project Decision

- This AI Award Project produced valuable evidence, and progressed MendelScan's accordance with the NICE Evidence Framework for digital health tools
- Many disease algorithms performed highly; impressive analytical performance on research data, significant patient and NHS benefit projected (with low implementation outlay), and real world performance with positive clinical feedback and high action rates. **These disease algorithms would merit wide-scale adoption** in the NHS **and future algorithms, which perform well, should be considered under similar circumstances**.

GMSA GAIN - WP3Bi

1. AI Award Project
2. Expansion into further primary care practices / networks
3. Alternative data access
4. Phenotype-driven algorithms: IBD, Epilepsy and IRD
5. Oncology algorithms: Inherited cancer syndromes & others...

Thank you

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