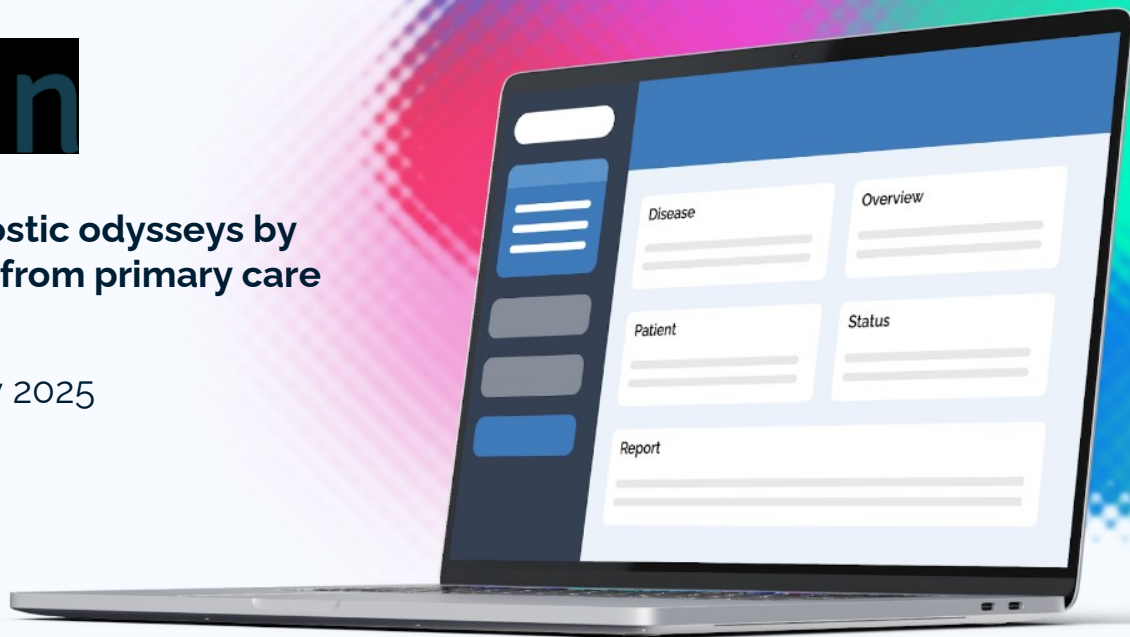


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MendelScan - shortening diagnostic odysseys by identifying rare disease at scale from primary care record

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)



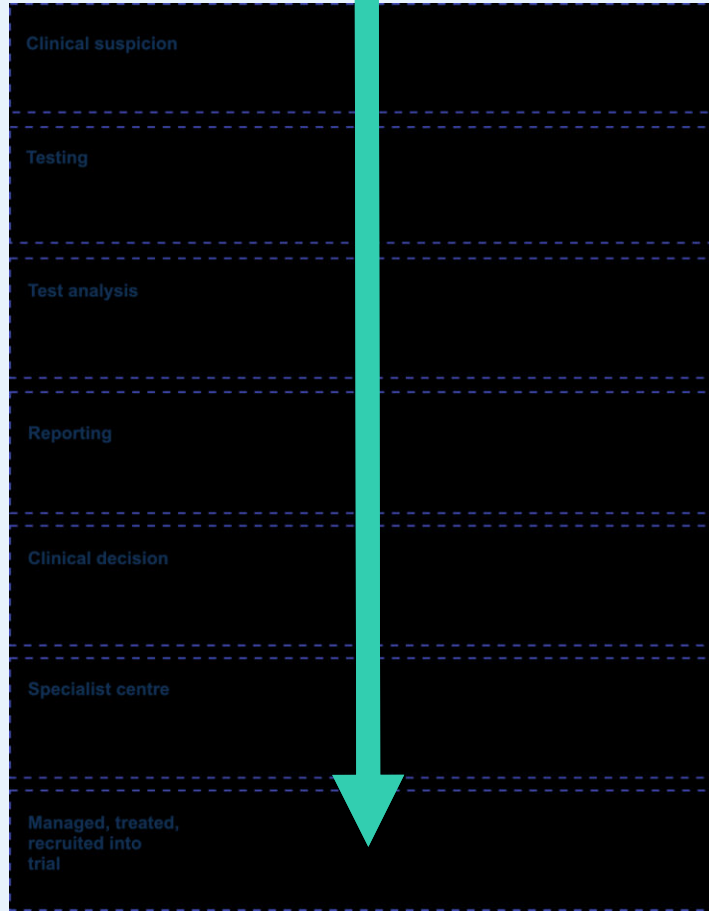
Dr Peter Fish
CEO



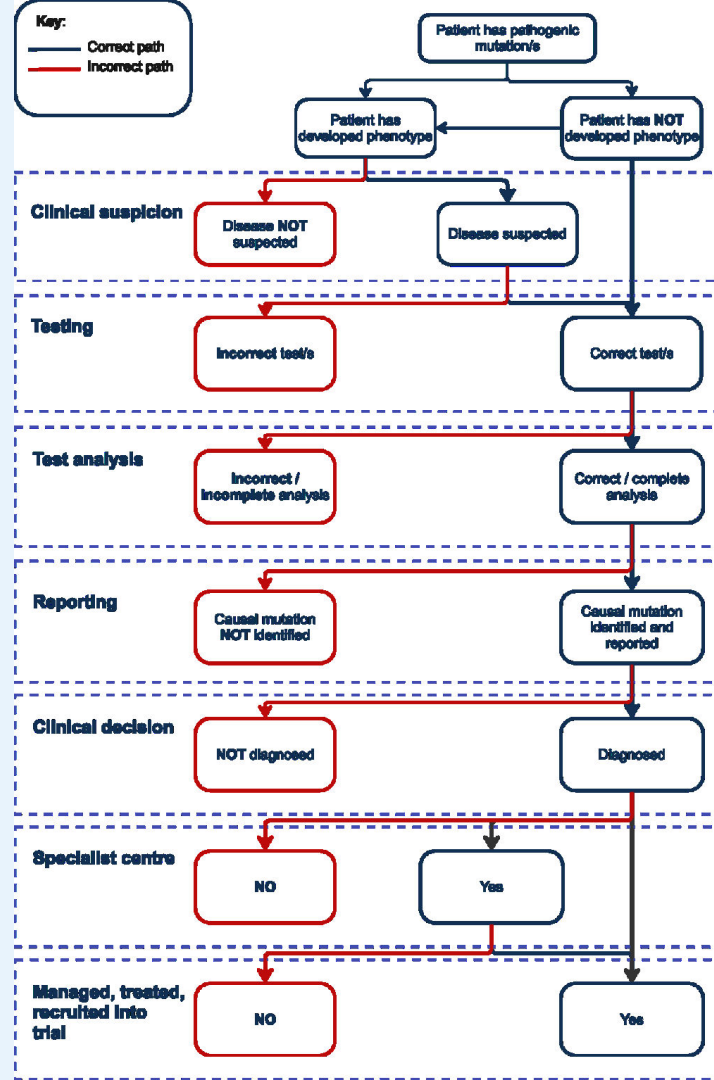
Fran Garcia
Co-founder & Non-
executive Chairman



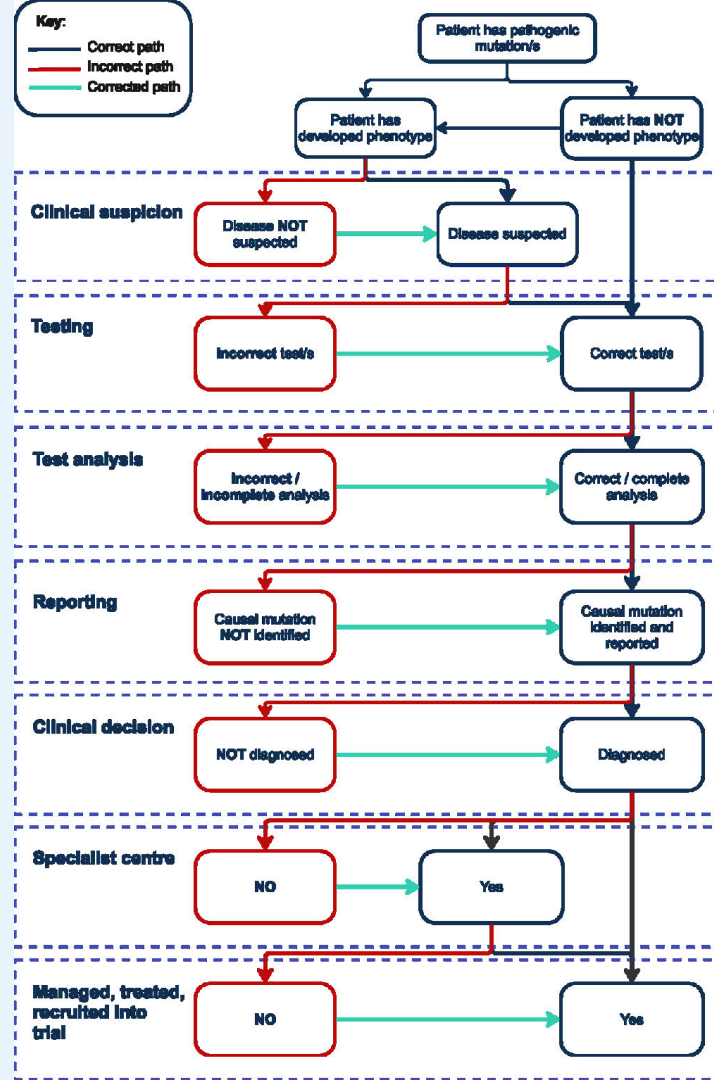
Mendelian's Approach



Mendelian's Approach



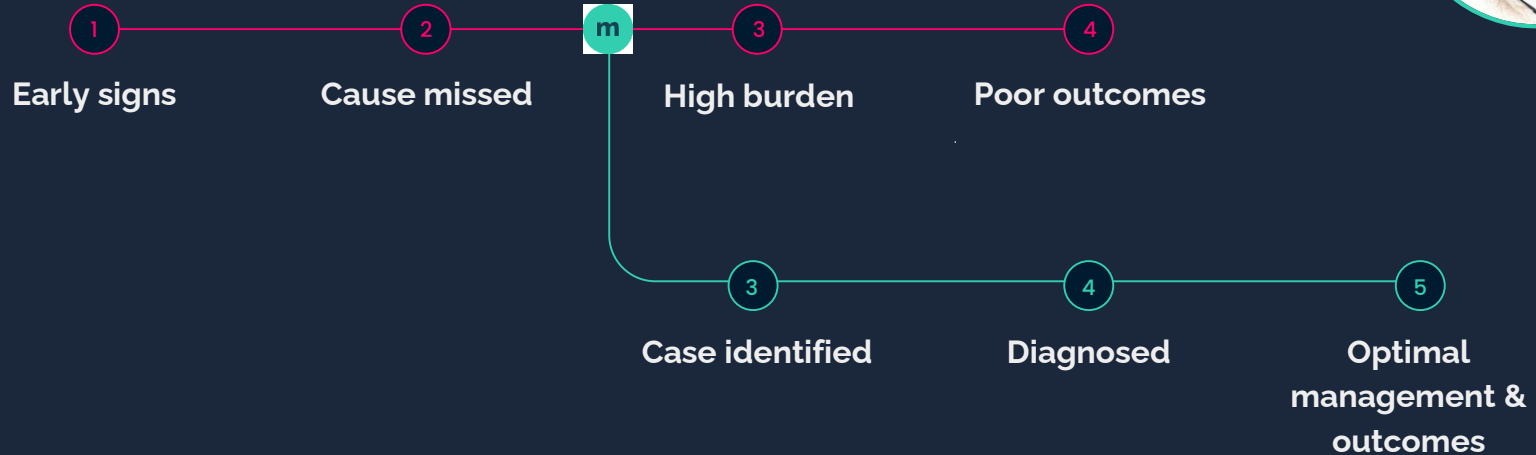
Mendelian's Approach



Clinical Suspicion is a Key Barrier to Treatment in PNH



Jenny, 38: Undiagnosed PNH (paroxysmal nocturnal haemoglobinuria)

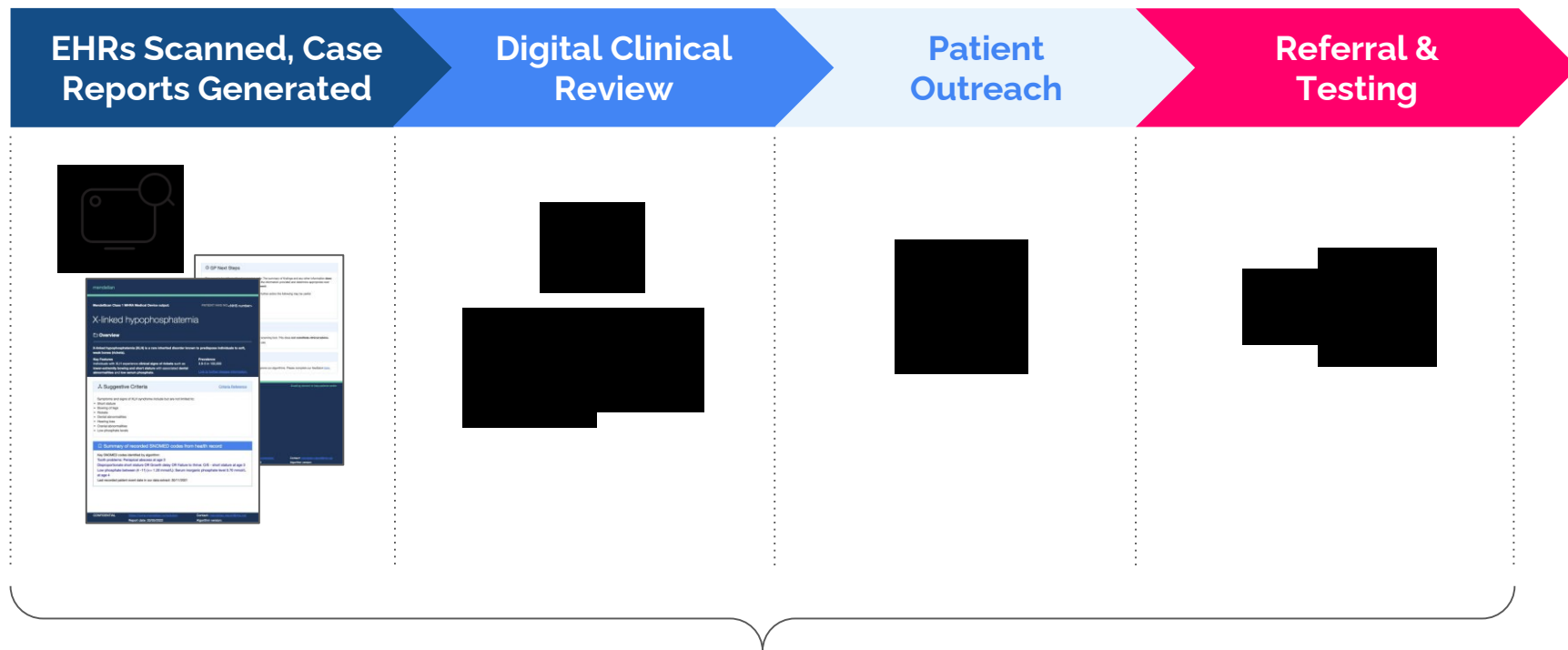


TYPICAL USE CASE: IMPROVED SPEED TO DIAGNOSIS

*Mock patient story. Based on real patient journeys.

MendelScan

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



MendelScan

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We're enabling doctors to help patients

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PATIENTS

DASHBOARDS

USERS MANAGEMENT

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

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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.](#)

LOGOUT

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

FILTER

REVIEW COMPLETE

HISTORY

REVIEW COMPLETE

HISTORY

REVIEW COMPLETE

HISTORY

REVIEW COMPLETE

HISTORY

REVIEW COMPLETE

HISTORY

s per page: 5 1-5 of 13 < >



SOLUTION OVERVIEW

CONFIDENTIAL

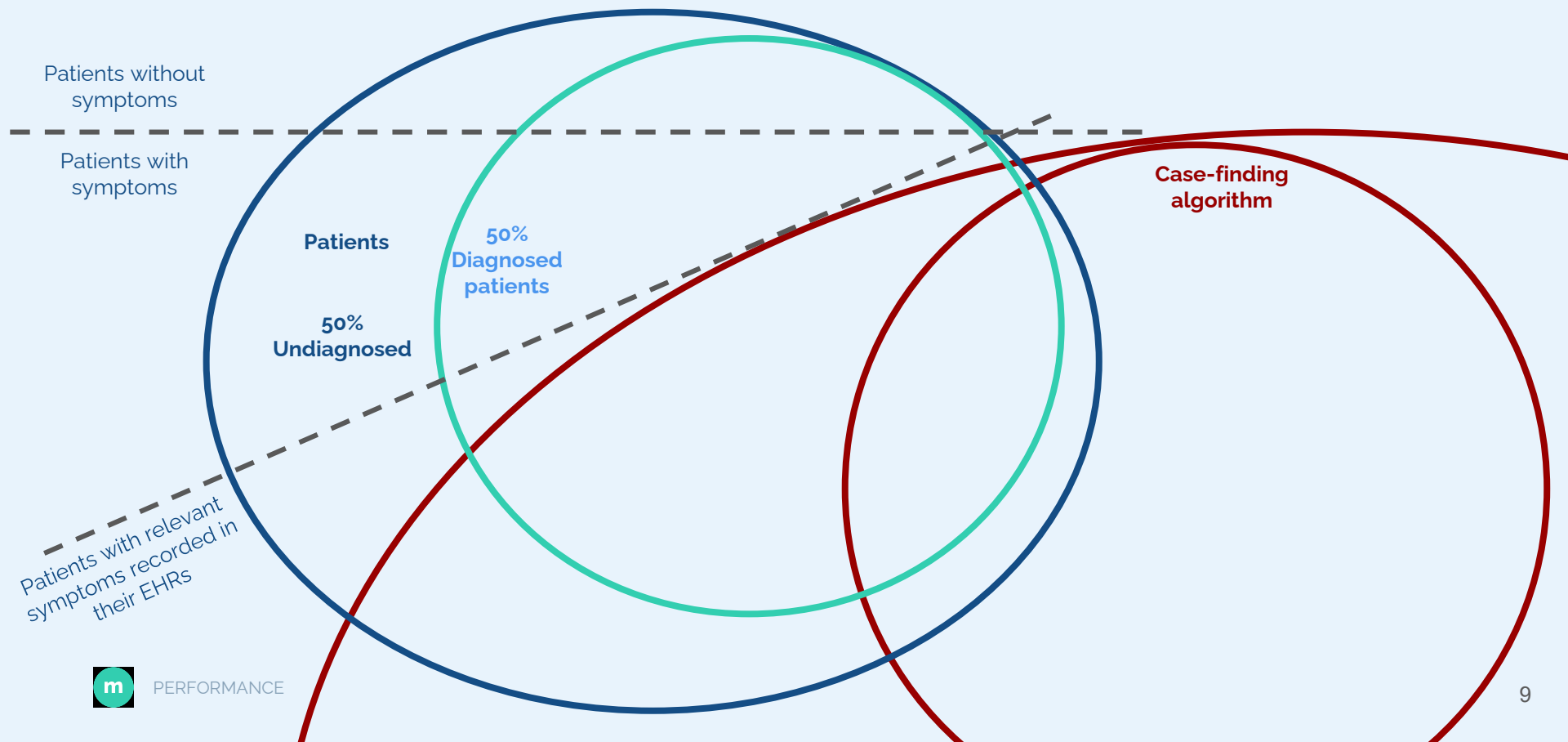
<https://www.mendelian.co/solution>

Report date: 03/05/2022

Contact: mendelian.report@nhs.net

Algorithm version:

Patient Cohorts and Algorithm Performance



NHS AI Award



NHS Accelerated Access Collaborative

What we do

How can the AAC help?

Innovation Service

Clinical Entrepreneur Programme

Small Business Resilience Initiative for Healthcare (SBRI)

Test beds

NHS Insights Prioritisation Programme

Pathway Transformation Fund

Medical technology (MedTech) funding mandate and support

Early Access to Medicines Scheme

Artificial Intelligence in Health and Care 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.

evaluation within the NHS. As part of the award, independent evaluations are being commissioned for the most mature technologies in the award programme (Phase 4 technologies) by our Evaluation Partner Group to build evidence to inform recommendations for national roll-out. [Find out more about AI Award Evaluation](#).

The Award forms a key part of the AAC's ambition to establish a globally leading testing infrastructure for innovation in the UK.

AI Award competition update

Round 3 winners

The winners of the third competition were on 3 March 2023. A total of 9 awards were made across phases 2,3 and 4. [Find out more about the winners](#).

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

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
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

\$341B
by 2027

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

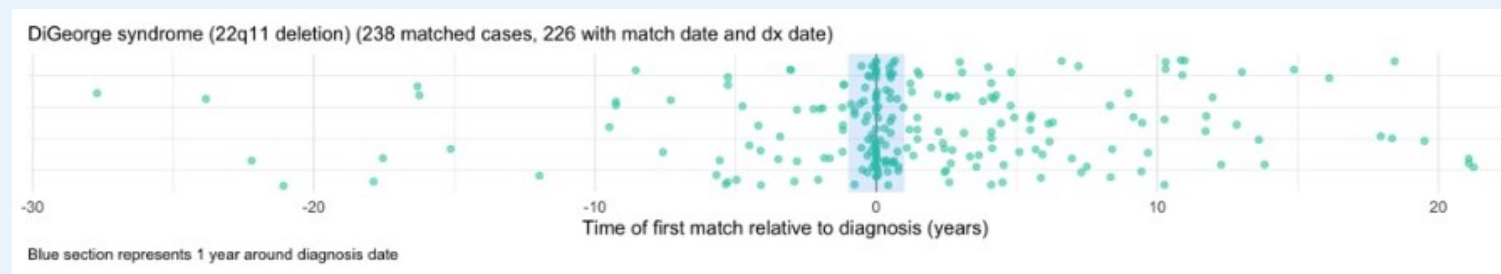
Results

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	-	-

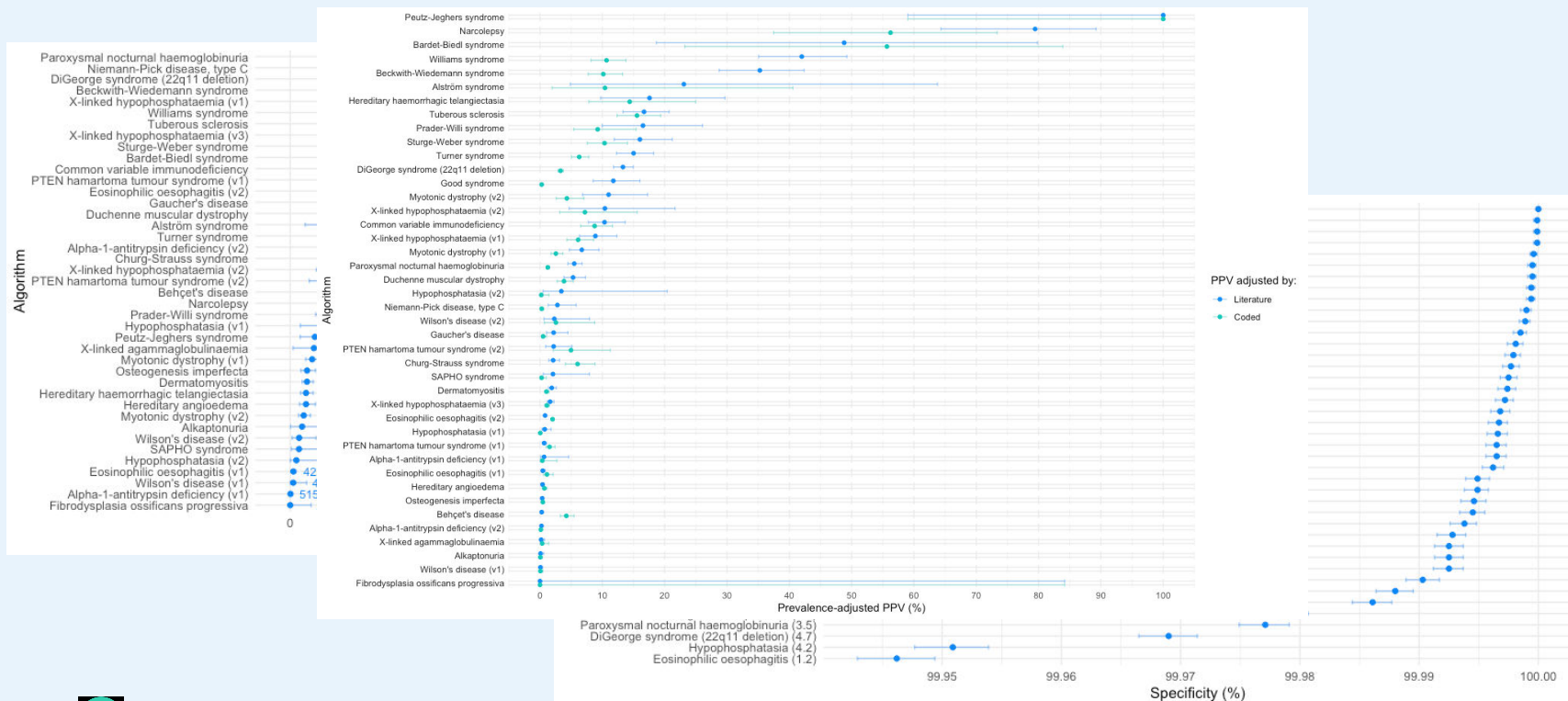
WP2: Analytical Validation

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



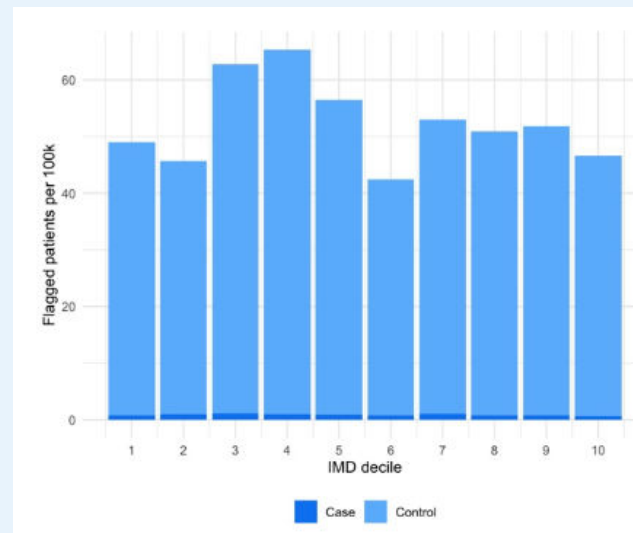
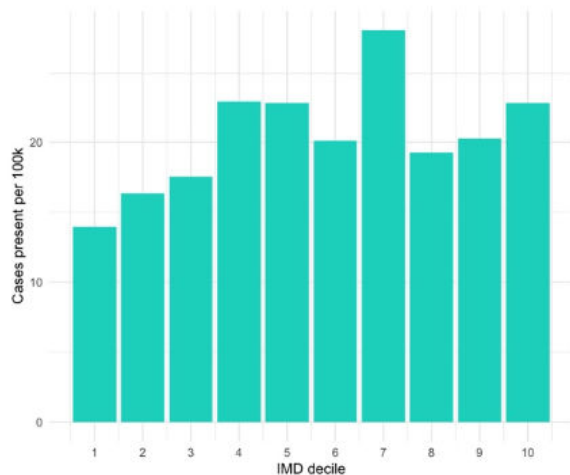
Evaluating Algorithmic Approaches to Rare Disease Case-Finding: A Retrospective Validation Study Using Electronic Health Records

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)

1. Cases across IMD deciles

Is the proportion of (coded) diagnoses different across different IMD deciles?



WP3: Public and NHS Acceptance

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



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Introduction

Thank you for taking the time to participate in this survey. The aim of this survey is to help people with undiagnosed rare diseases.

Who should complete the survey?

This survey is open to anyone who lives in the UK and is over the age of 18. If you need help completing the survey, please ask someone to assist you. Have your own point of view.

Completing the survey

- The survey consists of 36 questions and should take between 10 and 20 minutes.
- Select the box that best matches your response to each question. Please select only one box.
- All responses should be anonymous, so please do not write your name or any other identifying information.
- Questions marked with an asterisk (*) are mandatory and need to be completed.
- For every completed response, Mendelian will donate £3 to Genetic Alliance.

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4/8

50%

Technology in the Rare Disease Action Plan

The UK has developed a plan to make a significant difference in the lives of people with rare diseases. The plan has four main improvement goals: **early diagnosis, access to treatment, support for patients and their families, and research into rare diseases.**

In the rest of this survey, we would like to hear your thoughts on one specific approach and technology that is currently being trialled in the NHS to help people with undiagnosed rare diseases to get a diagnosis earlier.

This **technology can analyse health data in electronic health records** to identify people who may have undiagnosed or unsuspected rare diseases. This technology **looks for patterns in signs, symptoms, and test results that could indicate a rare disease.**

Based on the information you have just read, please select one of the options below to answer each question.

* To what extent do you agree with the following statement?

The NHS should use technology to identify rare disease patients

☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly agree

* To what extent do you agree with the following statement?

My own GP practice or hospital should use technology to identify rare disease patients

☐ Strongly disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Strongly agree

Previous

Next

Health Innovation East

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25%

-to-diagnose diseases

is less than 1 in 2,000 people, there are **over 10,000 known rare diseases** - this means **all ages are affected** by rare diseases. [Learn more](#)

re diseases is that they can be **difficult to diagnose**. This happens for several reasons:

can be **similar to those of more common diseases**;

diseases as potential causes of symptoms;

ally, it can be **challenging for doctors to "connect the dots"**.

ore a rare disease is considered, with people often going through an **extended process** **they finally get a diagnosis**.

> understand how familiar you are with rare diseases and the difficulties people can face

>lies to you to answer each question. Please note, there is no right or wrong answer.

aking this survey, to what extent do you agree with the following statement?

an most people

☐ Neutral ☐ Agree ☐ Strongly agree

aking this survey, to what extent do you agree with the following statement?

nose diseases than most people

☐ Neutral ☐ Agree ☐ Strongly agree

Previous

Next

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WP3: Public Acceptance

254

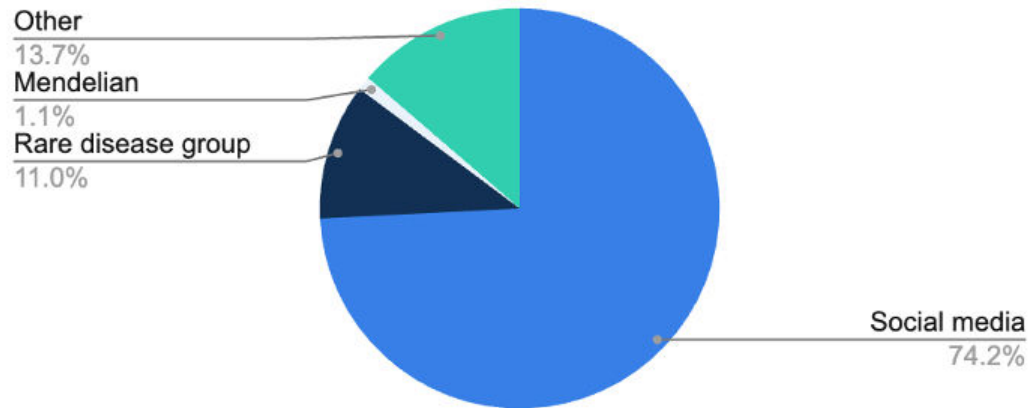
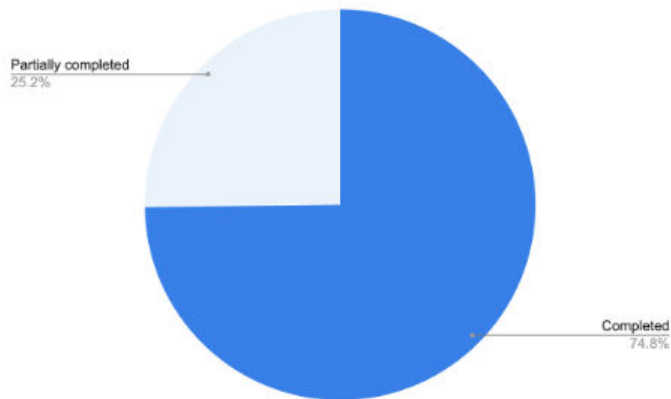
Respondents

93%

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

90%

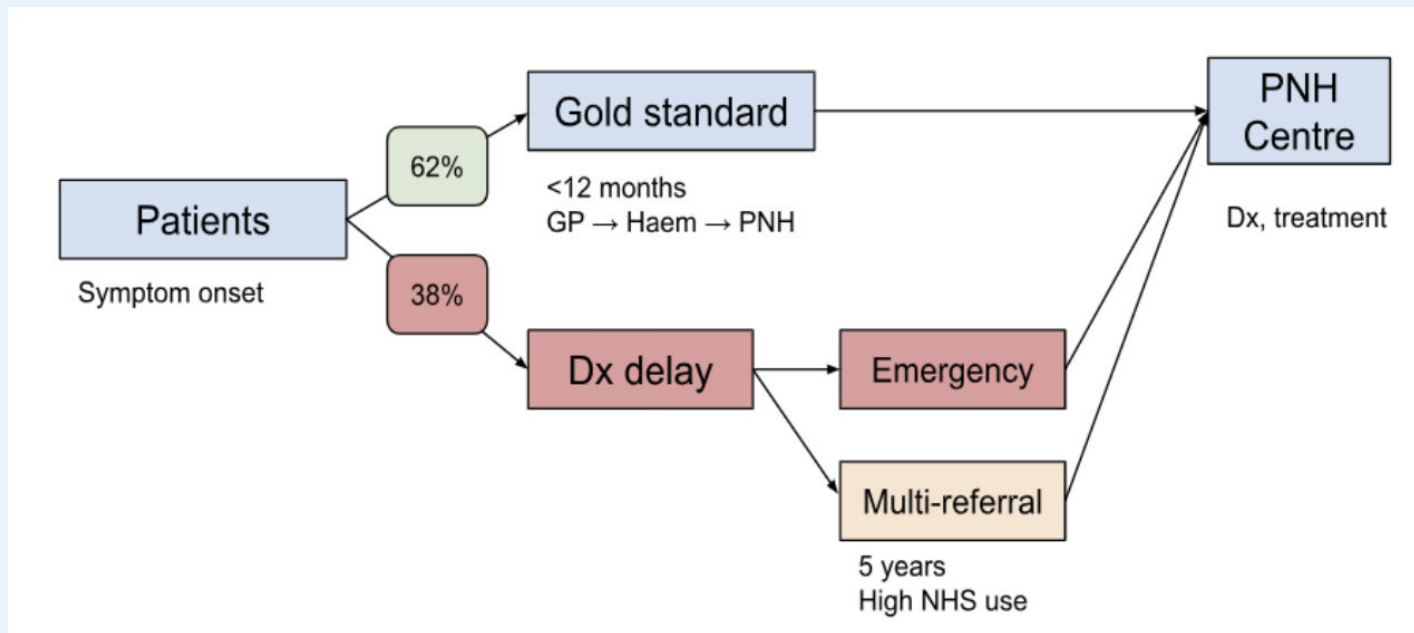
Anticipated feeling grateful that their health data had been included



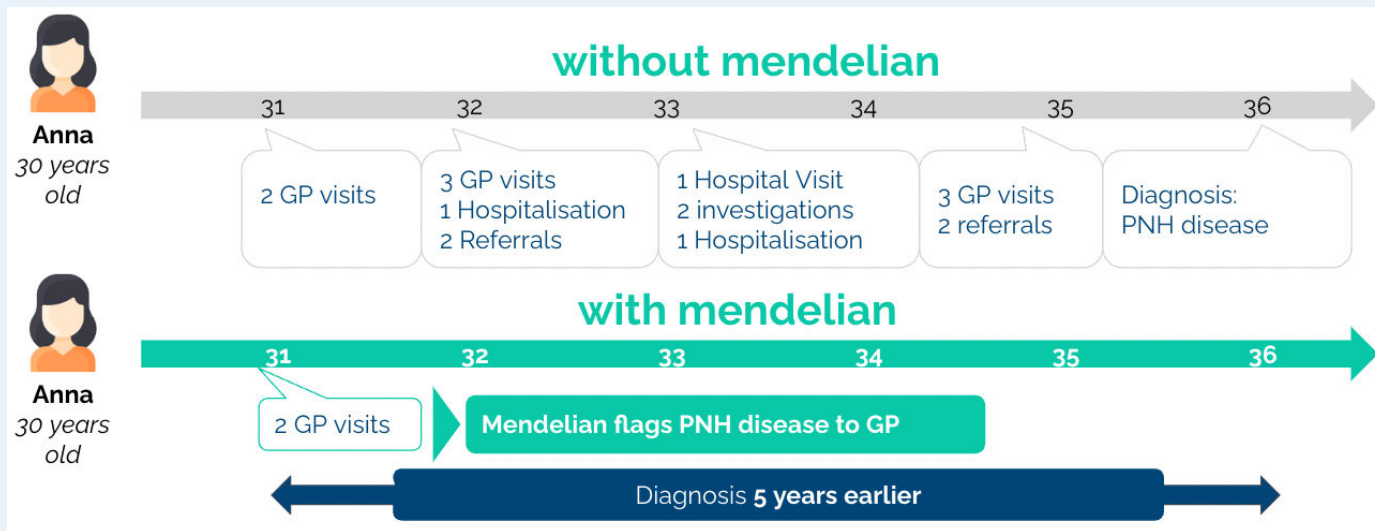
Public perception of the use of clinical decision support tools within the NHS for rare disease case finding.

Elena Marchini¹, Sarah Mason^{2,3}, Judith Fynn⁴, Jez Stockdale¹, Hadley Mahon¹, Sarah Robinson⁴, Peter Fish¹

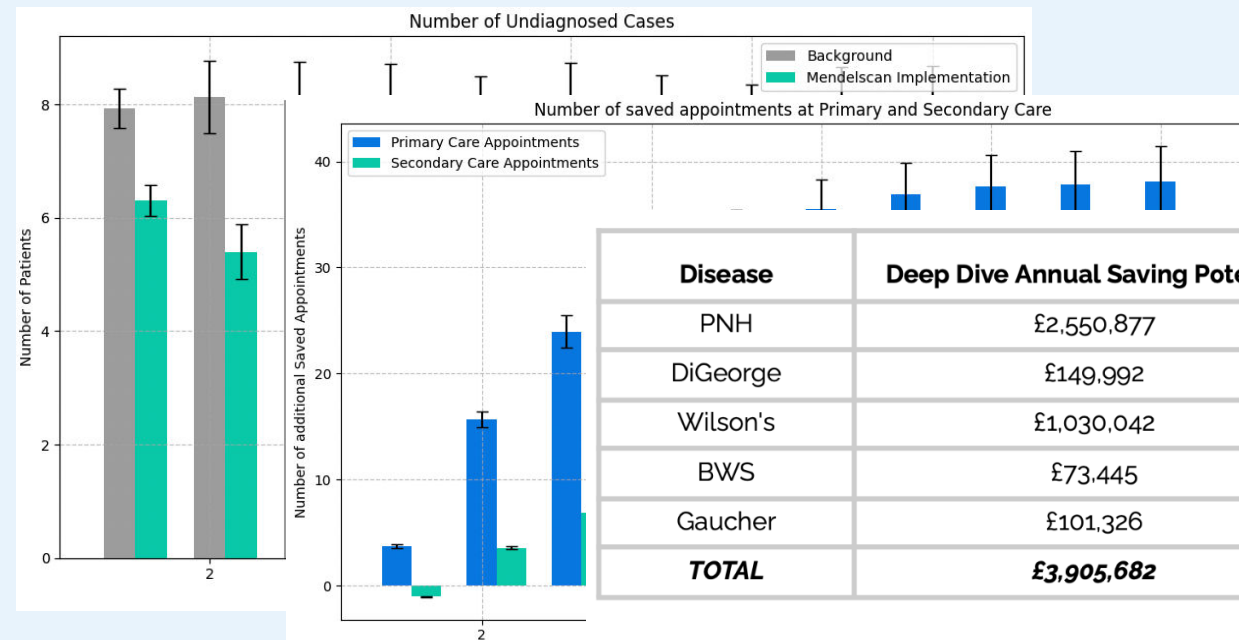
WP4: Clinical Utility and Cost Effectiveness Modelling



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



peter@mendelian.co
mendelian.co