Reimagining Patient Finding in Rare Disease

- From reactive identification → proactive population health

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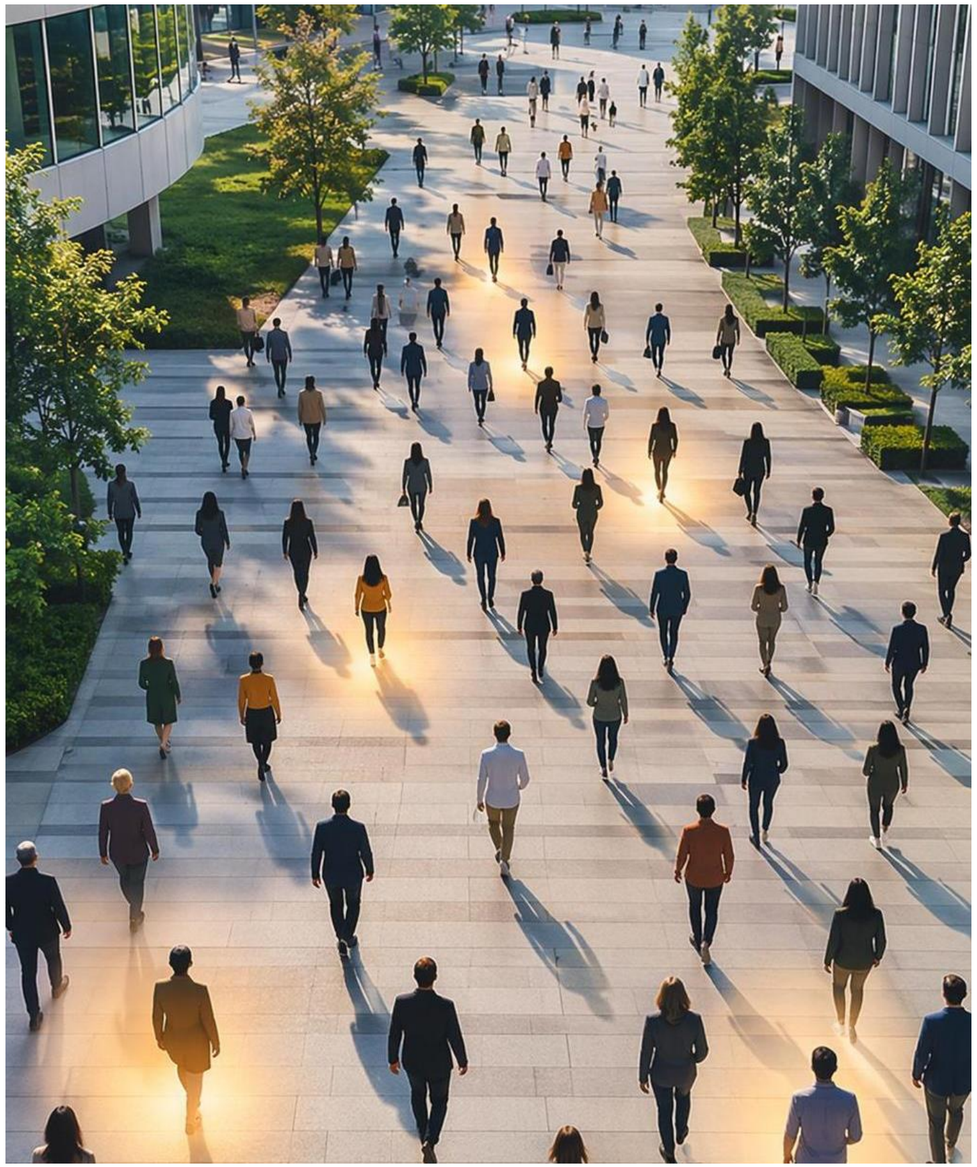
Why patient finding needs to change- - Aka ‘The Diagnostic Odyssey’ or ‘Finding the Hard to Find’

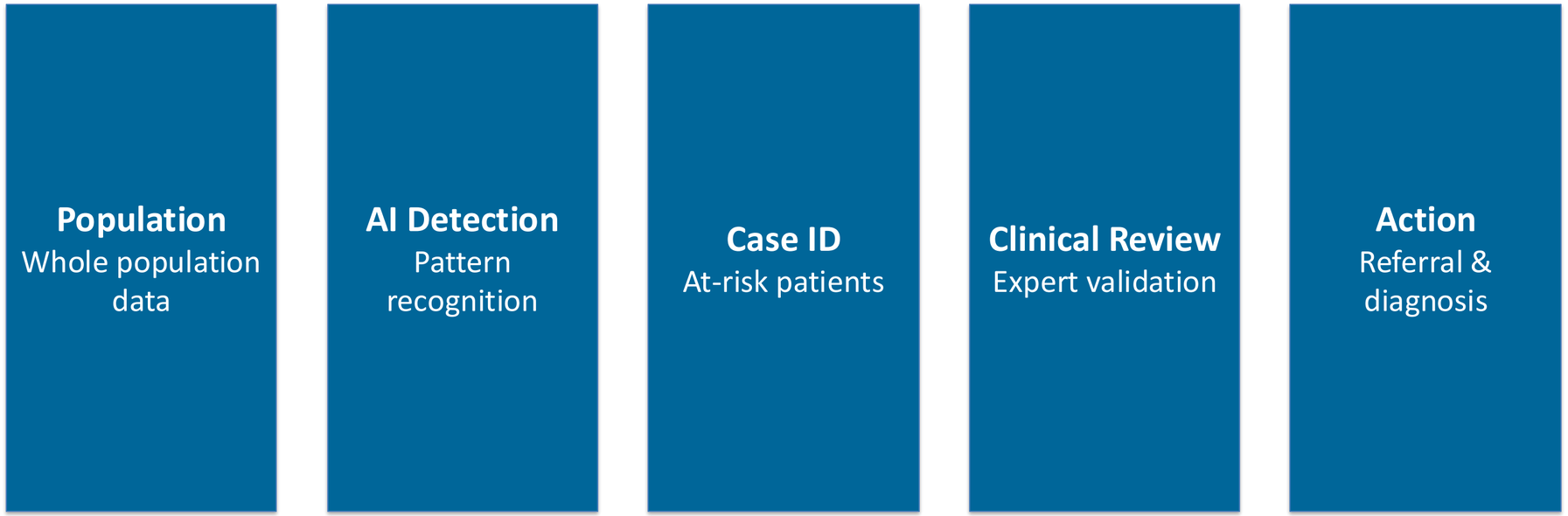
- Patients spend years navigating fragmented symptoms
- Current approach relies on already-diagnosed or visible patients
- A large populations of ‘hidden patients’ remains unidentified

A new approach:
Population-level patient finding

- Move upstream into primary care
- Screen entire patient populations
- Identify undiagnosed & misdiagnosed individuals earlier
- Enable timely diagnosis and access to care



How Biogen are Enabling Patient Finding



How Biogen are Enabling Patient Finding

Population
Whole population data

Start with whole populations, not known patients

How Biogen are Enabling Patient Finding

AI Detection
Pattern recognition

Analyse real-world health records at scale

Detect patterns across disconnected symptoms

How Biogen are Enabling Patient Finding

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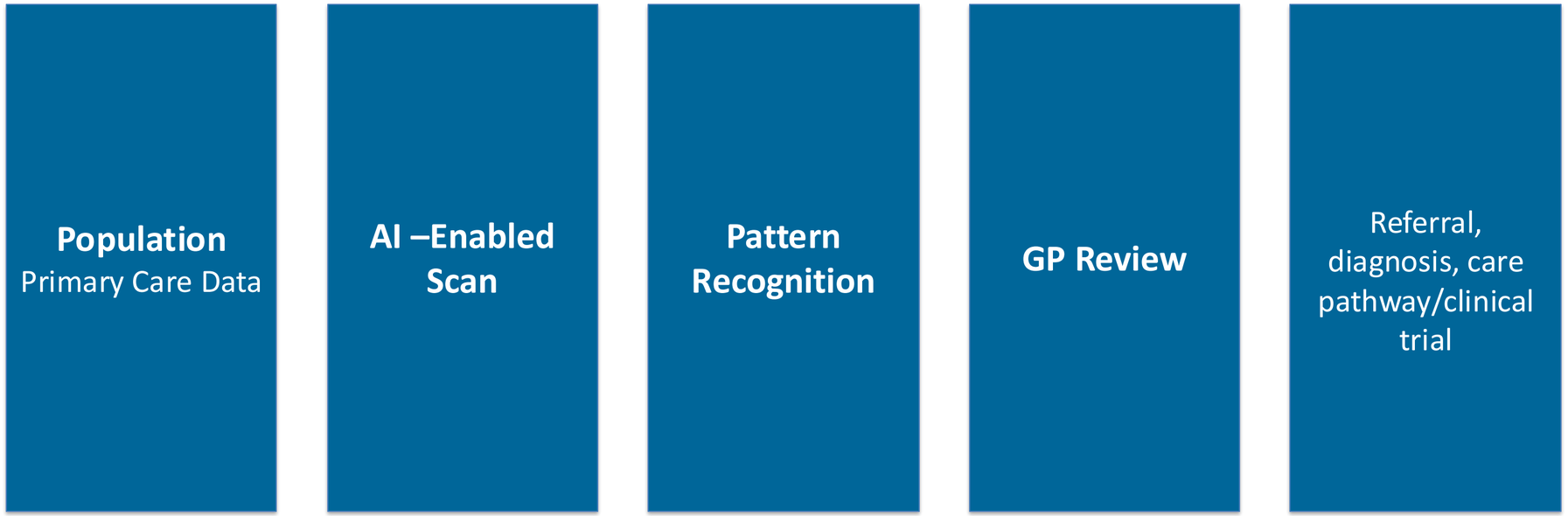
How Biogen are Enabling Patient Finding

Clinical Action	**GP's enabled to investigate, refer and diagnose**

Patient Finding In Practice



Characterising late-onse

Delayed diagnosis and missed opport

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Individuals with diagnostic codes synonymous with LOPD were id
Pompe disease

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Data source: UK OPCRD primary care records

- >1,100 UK practices
- 28,803,117 patient EHRs

Creation of the Pompe disease cohort

Individuals with a diagnostic code synonymous with LOPD based on SNOMED IDs (CTV3 codes)

- 274864009 (C3101; X40TW; X40TX)
- 722343009 (X40TY; X40TZ)
- 190741002
- 76219003
- 267424007

Patients aged ≤3 years at diagnosis were excluded as potential infantile-onset cases

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- Refer
- Clinica
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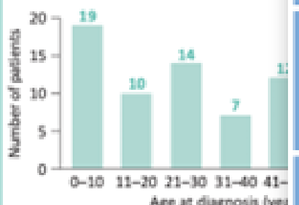
*Identified through SNOMED codes

73 unique EHRs with Pompe disease c

The age at diagnosis spanne



OR versus control cohort:

- ≤1 (no signal)
- >1–≤10 (small positive signal)
- >10–≤100 (medium positive signal)
- >100 (to infinity) (large positive signal)

Time to first appearance of clinical feature code prior to Pompe disease diagnostic code

Diagnos code

10 years | 5 years | 3 years | 2 years | 1 year

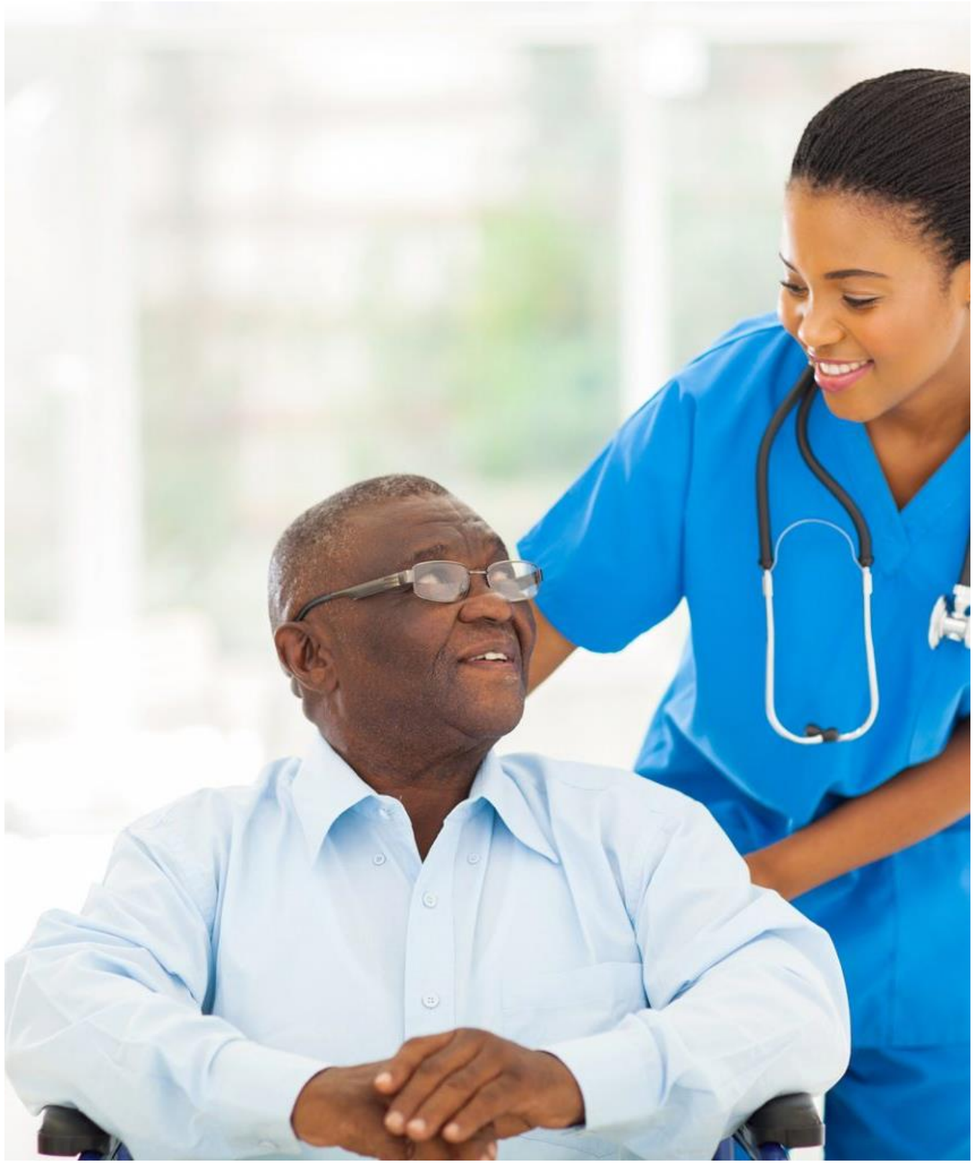
Feature category/feature		Percentage of Pompe cohort				
Bloodwork	Elevated alanine aminotransferase	36.8%	29.8%	26.3%	17.5%	12.3%
	Elevated creatine kinase	17.5%	15.8%	15.8%	12.3%	8.8%
	Elevated aspartate aminotransferase	12.3%	12.3%	10.5%	7.0%	3.5%
	Elevated lactate dehydrogenase	3.5%	3.5%	3.5%	1.8%	1.8%
Back issues	Backache	26.3%	19.3%	15.8%	14.0%	8.8%
	Spinal MRI	5.3%	3.5%	1.8%	1.8%	1.8%
Misc.	Muscle biopsy	12.3%	10.5%	10.5%	10.5%	8.8%
	Electromyography	1.8%	1.8%	1.8%	1.8%	1.8%
Salient features	Myopathy	10.5%	8.8%	8.8%	8.8%	7.0%
	Proximal myopathy	3.5%	3.5%	3.5%	3.5%	3.5%
	Sleep apnea	1.8%	0%	0%	0%	0%
Breathing pathology	Dyspnea	8.8%	7.0%	7.0%	5.3%	3.5%
	Respiratory tract infection	17.5%	8.8%	5.3%	3.5%	3.5%
	Shortness of breath on exertion	3.5%	3.5%	1.8%	0%	0%
Weakness	Lower limb weakness	1.8%	1.8%	1.8%	1.8%	1.8%
	Ptosis	1.8%	1.8%	1.8%	1.8%	1.8%
	Winged scapula	1.8%	1.8%	1.8%	1.8%	1.8%
	Difficulty climbing stairs	1.8%	1.8%	1.8%	1.8%	0%
	Hyperlordosis/scoliosis/kyphosis	1.8%	1.8%	0%	0%	0%
	Lethargy/asthenia	3.5%	1.8%	1.8%	0%	0%

What’s different

Traditional approach	Patient finding approach
Focus on visible patients	**Focus on hidden populations**
Diagnosis-dependent	**Pre-diagnosis identification**
Manual identification	**AI-enabled detection**
Reactive	**Proactive and systematic**
Limited scale	**Population-level reach**

How do we know whether we have got it right?

Specificity	Sensitivity	Positive Predictive Value (PPV)
The proportion of people without the disease that the tool correctly ignores (does not flag).	The proportion of true rare disease patients that the tool correctly identifies.	The proportion of flagged patients who actually have the disease.
scans 100 patients who do NOT have the disease, and it correctly ignores 95 of them, the specificity is 95% “How good is the tool at NOT flagging people who don’t have the disease?”	scans 100 patients who actually have a rare disease, and it correctly flags 90 of them, the sensitivity is 90%. “How good is the tool at finding the people who really have the disease?”	flags 20 patients as “possible rare disease,” and 10 of them really do have it, the PPV is 50%. “If the tool flags someone, what are the chances they really have the disease?”



In rare disease context

Because rare diseases are uncommon, PPV can be low even if sensitivity and specificity are high

So most flagged patients may not have the disease, but the tool still finds more than traditional methods

Balance is key:

- Too low sensitivity = missed patients
- Too low specificity = wasted resources on false positives
- Too low PPV = lots of unnecessary follow-up

Why this matters-
The Impact of Earlier Patient Finding

- Enables earlier diagnosis and intervention
- Identifies patients before they reach specialist care
- Improves equity of access to diagnosis and innovation
- Creates new pathways to care and research participation

A paradigm shift

- Move from waiting for patients to be identified
- → to actively finding patients within healthcare systems
- → using data, AI and clinical insight

- **Patient finding at population scale has the potential to transform how rare disease patients are identified, diagnosed and supported**