

## What is Alkaptonuria (AKU)?

- An autosomal recessive disorder with a prevalence of 1 in 500,000
- Characterised by many features but dominated by premature disabling arthritis (Fig 1)
- Due to accumulation of homogentisic acid (HGA)
- A new drug, Nitisinone, decreases production of HGA (Fig 2)
- Optimal use of Nitisinone requires effective identification of people with AKU

## Problem of AKU in the UK

- AKU is one of the orphan diseases due to its rarity
- There is no UK database of all diagnosed AKU patients
- There is no National register for disease (rare or common)

## Resources available to Identify people with AKU

- AKU Society of the UK (established in 2003)
- AKU Website (established 2003) (Fig 3)
- National Lottery Grant Award (awarded 2007)
- Manned AKU Information Centre in Royal Liverpool University Hospital (since 2007) (staffed by 2 people)

## Methodology used to Identify people with AKU

- Active Manned Interactive Website
- General Practitioner Postal Questionnaire Survey in UK (Fig 4)
- Targeted Sibling Screening
- Targeting Medical Professionals in Conferences

## Results (Table 1)

GP's survey: Over 9668 GP's were mailed (15% response rate to questionnaires) (Fig 5)

Total number of patients in UK with AKU (78)

(Fig 6. UK Map of AKU Patients)

Total Number of patients with AKU worldwide (512)

(Fig 7. World Map of AKU patients)

Numbers of Patients with AKU identified by different approaches

|                                                                            |     |
|----------------------------------------------------------------------------|-----|
| Website (including patient networks)                                       | 44  |
| GP Survey                                                                  | 23  |
| Targeted family screening                                                  | 11  |
| Medical Conference Targeting (GPs, Rheumatology, Biochemists, Orthopaedic) | 429 |

## Conclusion

In the absence of a national disease register, various strategies may be needed to identify individuals with a rare disease, some clearly more cost-effective than others

## Continuing Barriers

The full identification of an individual with AKU requires two things:

1. Knowledge of Location of Patient
2. Contact with Patient

Due to patient confidentiality concerns, contact was often incomplete

A limitation of the study is that people with access to electronic resources like the internet are more likely to be identified

## Recommendations

Our experience suggests that a dedicated manned website may be the most cost-effective way to approach the issue of identifying people with a rare disease and supporting them

## Acknowledgements

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Fig 1: Clinical features of AKU showing dark urine (a), blue pigmented ear (b), black scleral pigment (c) and ochronosis of elbow (d) and destructive arthritis of shoulder (e)

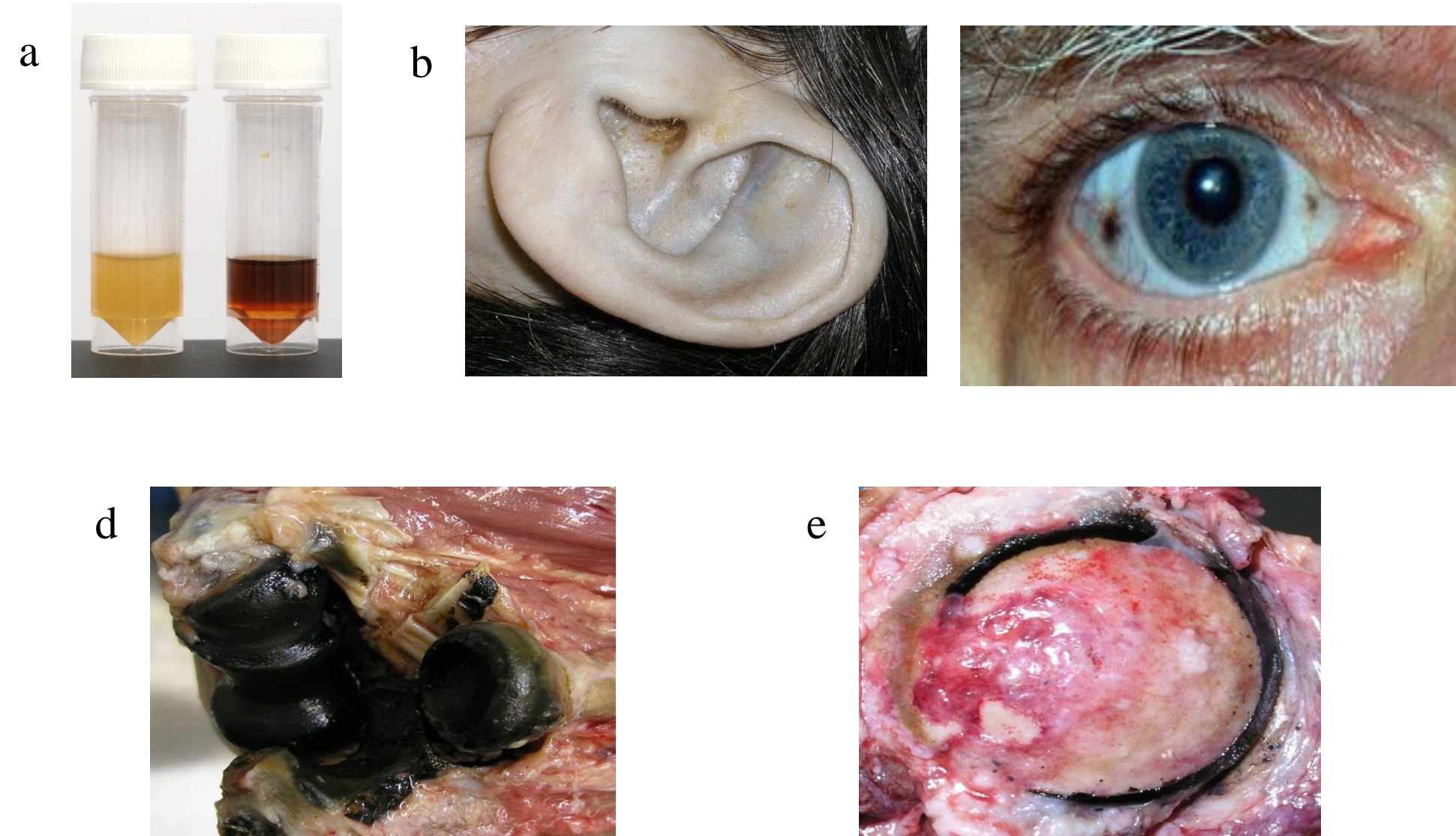


Fig 2: Metabolic Pathway showing site of defect in AKU (red line) as well as site of action of Nitisinone (blue line)

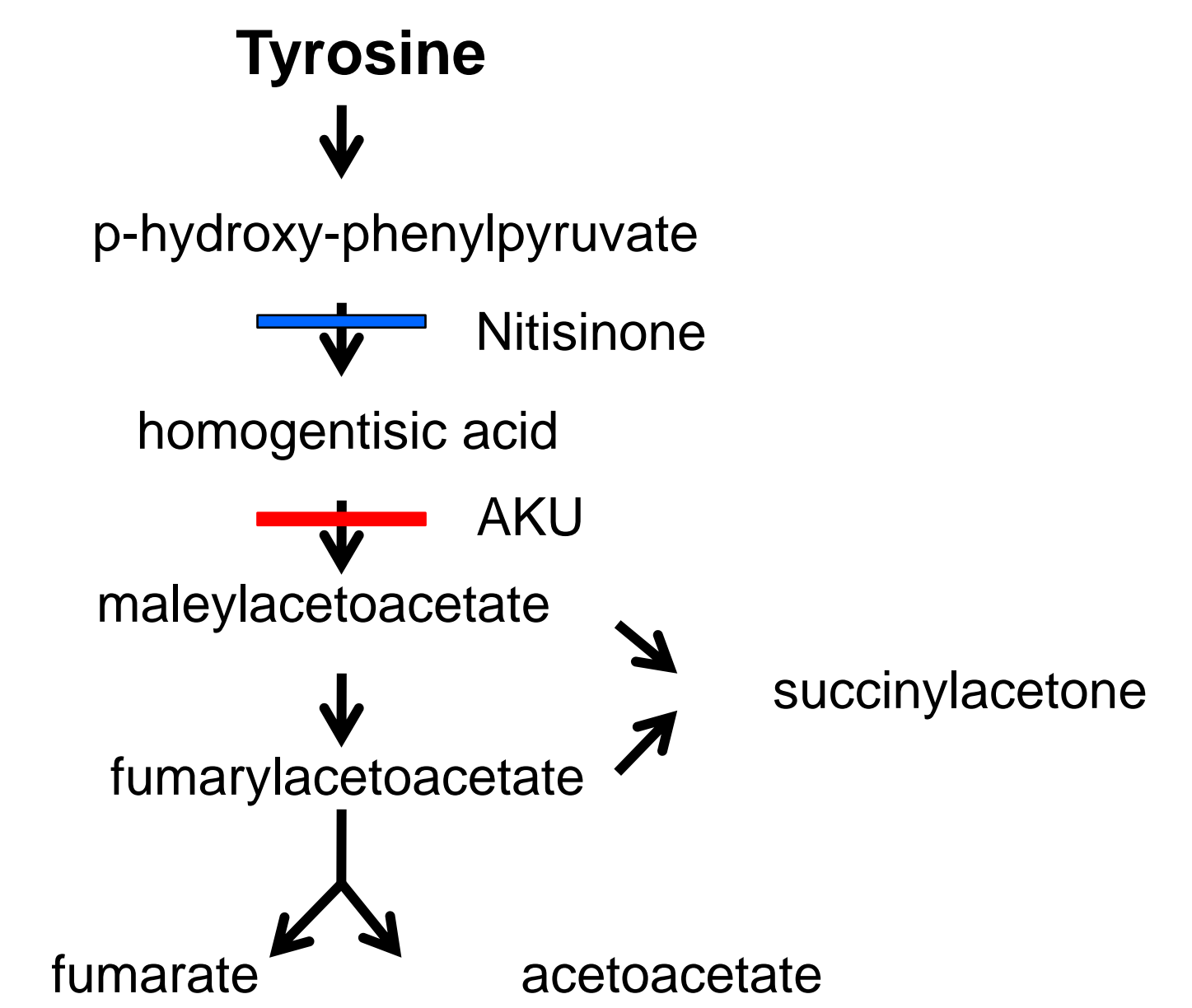
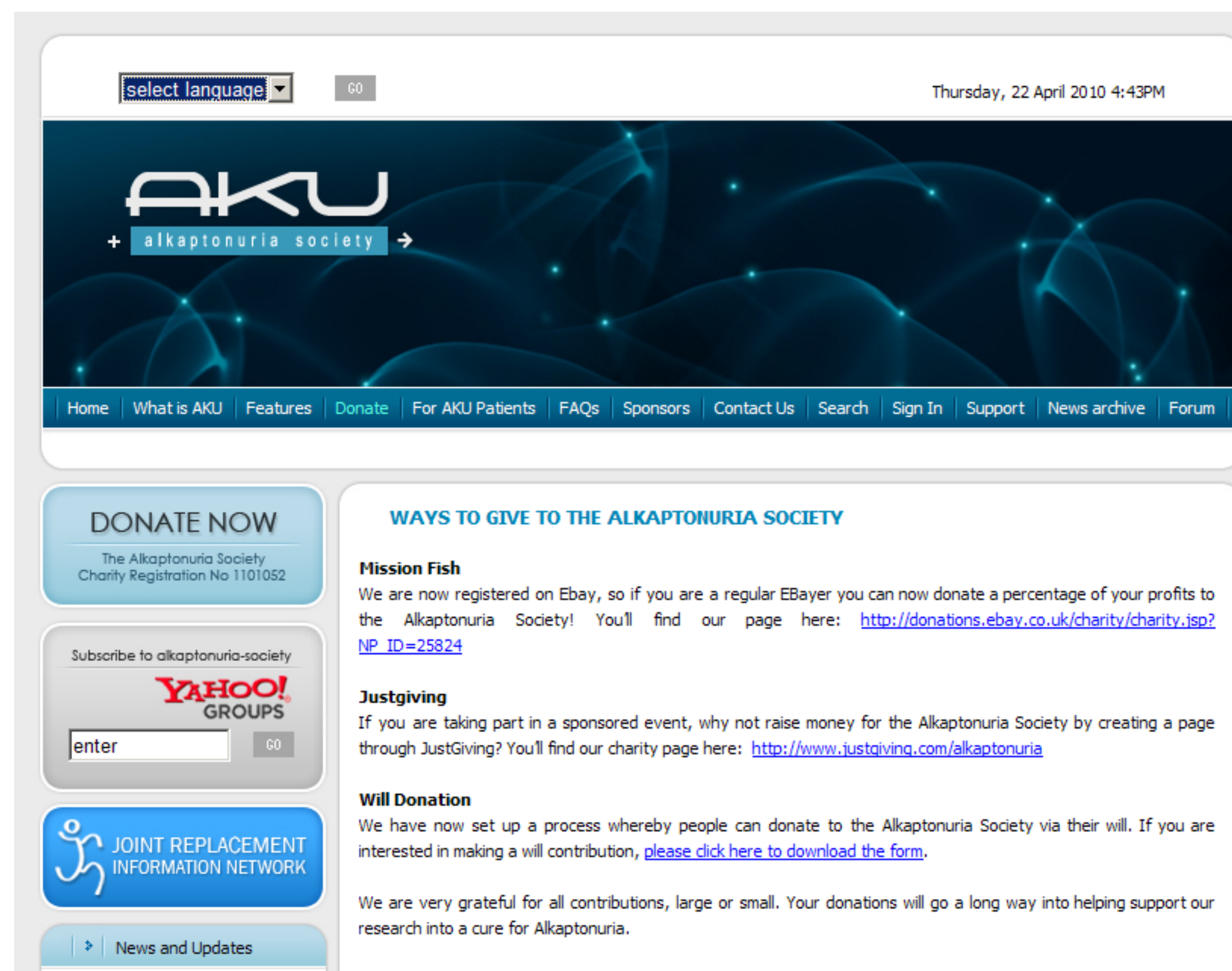


Fig 4: The GP Questionnaire used in the Survey

Fig 3: The AKU Website



A General Practitioners Questionnaire on Alkaptonuria (AKU)  
[Could you tick the **yes** or **no** in the following as appropriate?]

1. Are you aware that patients with AKU present with the following features:

a. Premature osteoarthritis Yes  No

b. A simple urine test can confirm or exclude the diagnosis of AKU Yes  No

c. Similar complaints in brothers and sisters Yes  No

d. Dark or Black urine Yes  No

e. Dark or Black discoloration of clothes Yes  No

f. Blue-Black discoloration of ears, eyes, nose and nails Yes  No

2. Do you know that the potential new treatment is available to modify the cause of disease in AKU? Yes  No

3. Do you have any patients with features described under Question 1? Yes  No

4. Do you have any patients known with AKU under your care? Yes  No

Can you indicate the number? .....

We would be grateful if you could return this Questionnaire in the pre-paid envelope provided to the address below:

FREEPOST  
BRUNNEN-UK-0007  
ALCAPTONURIA INFORMATION CENTRE  
ROOM 333B  
4<sup>TH</sup> FLOOR,  
L10 3SA  
LIVERPOOL  
TELEPHONE: 0151 706 4387  
E-MAIL: info@alkaptonuria.info  
WEBSITE: [www.alkaptonuria.info](http://www.alkaptonuria.info)

NAME OF GP: .....

Fig 5: Responses to GP questionnaire survey in UK by Strategic Health Authorities

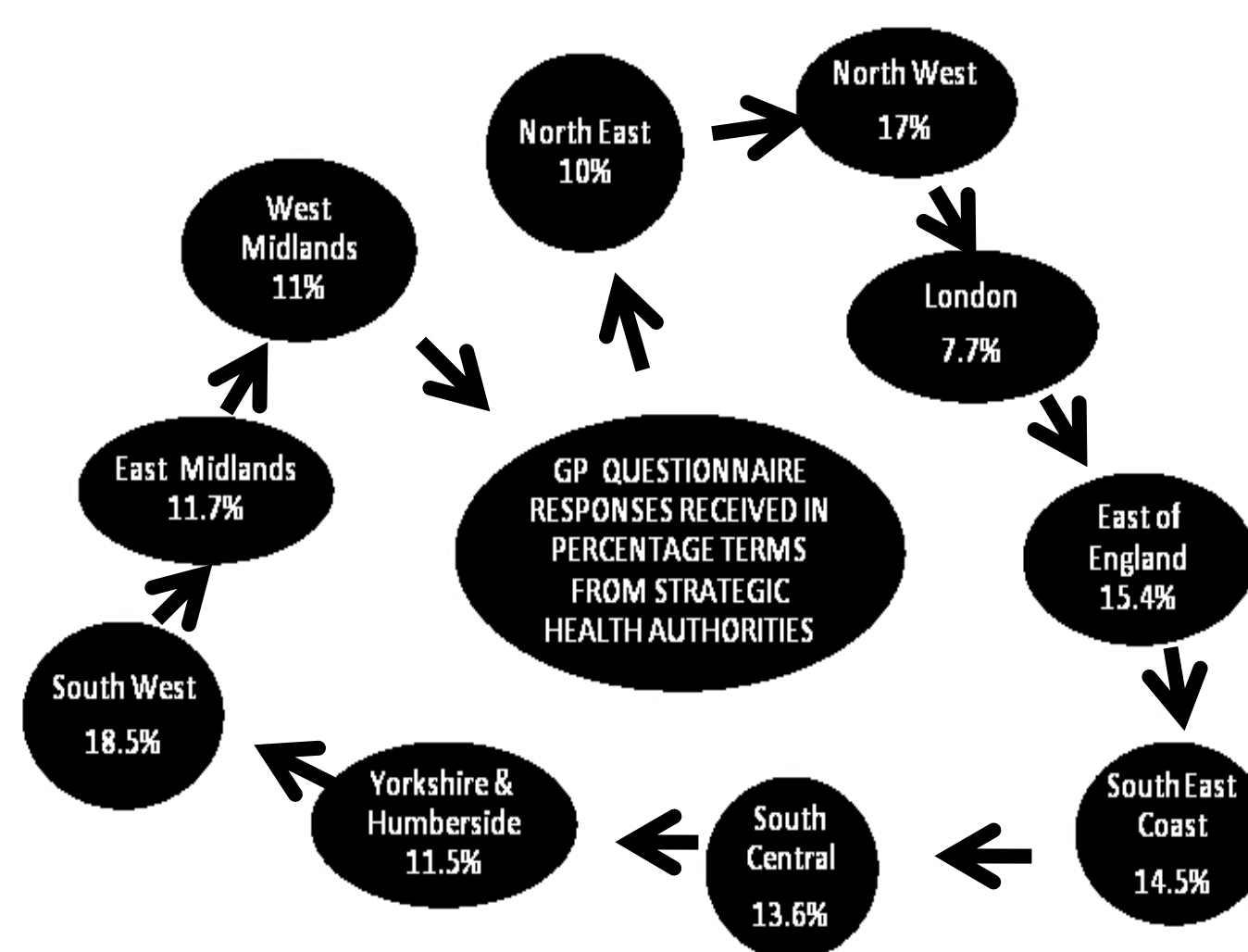


Table 1: Number of AKU Patients identified using different strategies

| Type of Strategy                                                                              | Number of Patients Identified |
|-----------------------------------------------------------------------------------------------|-------------------------------|
| Website (including patient networks)                                                          | 45                            |
| GP Questionnaire Survey                                                                       | 23                            |
| Targeted Family Screening                                                                     | 11                            |
| Medical Conference Targeting (AKU, Rare disease, GP, Rheumatology, Orthopaedics, Biochemists) | 548                           |

Fig 6: Distribution of Identified AKU Patients in UK



Fig 7: Distribution of Identified AKU Patients Worldwide

