The Rapid Expansion of the Haemoglobinopathy Patient Population in Ireland: Impact upon St. James's Hospital Transfusion Services

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Hemoglobinopathies

- Inherited disorders
- Inefficient hemoglobin manufacture
- Abnormal hemoglobin manufacture
- Anemia
- Distinct disease presentations
- All may require blood transfusion
- Regional disease prevalence

Sickle Hemoglobin

- Mutated haemoglobin tetramer with two α chains and two βS chains known as haemoglobin S

- S (HbS), where a valine residue has replaced a glutamic acid residue at the sixth position of the β-globin chain

HbS

- Great at offloading oxygen in tissues
- Not so good at maintaining shape in hypoxic, acidotic environments!

Sickle cell disease = a life of Pain

- Acute Presentations
  - Pain crises
  - Chest Syndrome
  - Stroke
- Chronic Disease
  - Renal failure
  - Pulmonary Hypertension
  - Iron Overload

Treatments: few

- Blood Transfusion, and lots of it
  - Primary and secondary prevention
- Hydroxyurea/Hydroxycarbamide
  - Patient compliance, neurocognitive issues
  - Patient fear
- Allogeneic stem cell transplantation
  - Center skills and capacity and donor availability

- *Speculative*
  - *Variety of drugs*
  - *Gene therapies*

Introduction

- When I was an SPR…
- SJH: one sickle cell patient
- Resident in London
- Presented irregularly in Dublin with crises
- Red cell exchange… but with SpR, the consultant, blood, tubes with a 3-way tap and a 50ml syringe!

Meanwhile in the Childrens hospital

ginal paper

The increasing prevalence of childhood sickle-cell disease in Ireland

C McMahon[1], CO Callaghan[1], D O'Brien[2], OP Smith[1,2]
National Children's Hospital, Tallaght[1], Central Pathology Laboratory, St James's Hospital[2], Dublin, Ireland.

Sickle-cell disease

Twenty children, aged 24 to 68 months (median 28 months) have SCD. Twelve children are from Nigeria, four from the Congo, three from Angola and one from Zaire. Their Hb level is 6.4g/dl-9.7g/dl with a median of 7.7g/dl. All have had full red cell genotyping and consistently fail to express the Duffy red cell antigen (Fya/Fyb). One child not expressing M antigen on her red cells received an M antigen positive unit of red cells and has recently developed an anti-M antibody which has made cross-matching of red cells difficult.

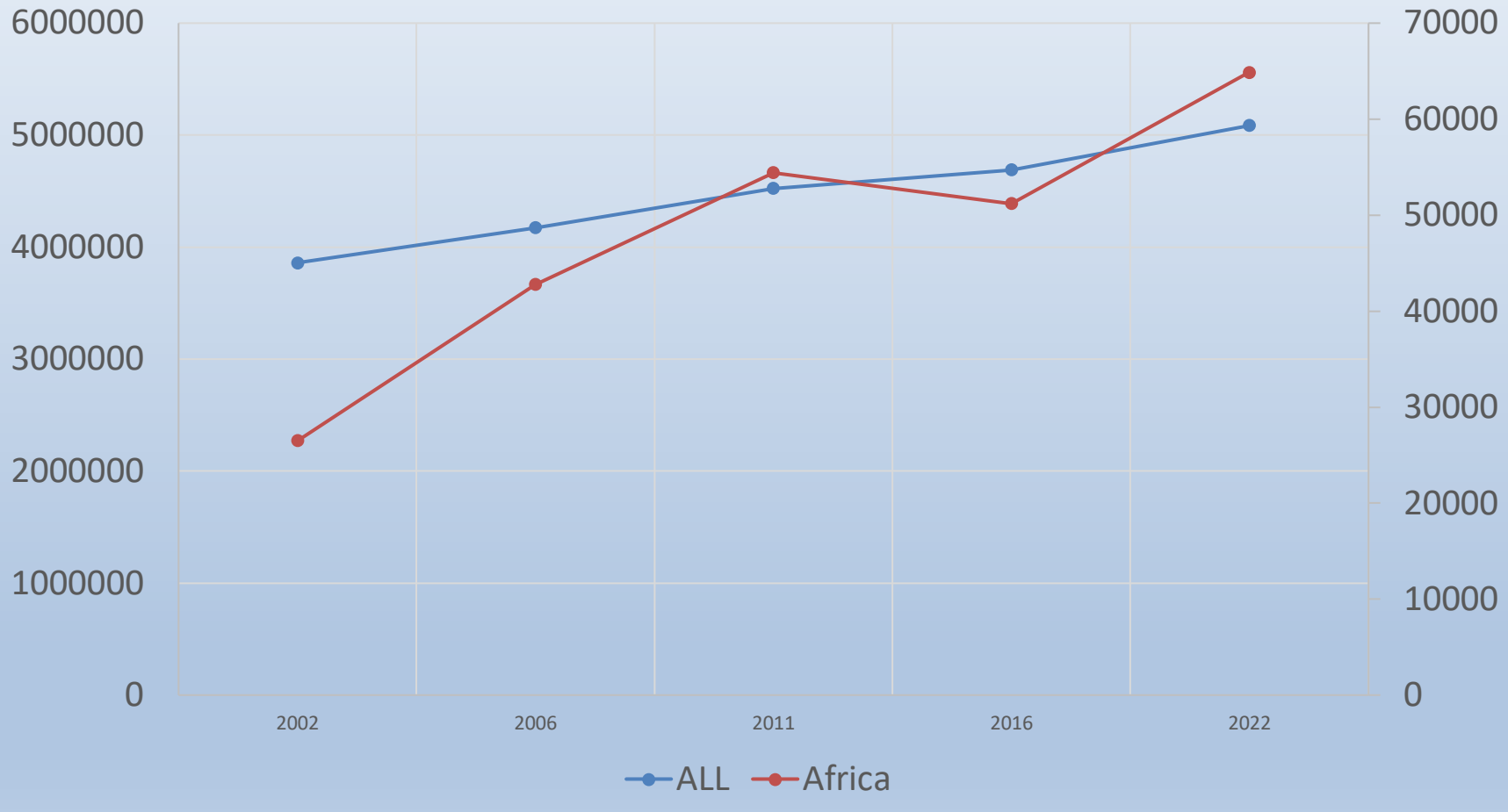
(McMahon, Callaghan et al. 2001)

4 or 5 years later

- Paediatric clinics
- Children attending for regular blood tests and adjustment of Hydroxyurea doses

- A few more years later…
- NIH, NHLBI: much older patients with complex transfusion requirements, some undergoing sibling allogenic stem cell transplantation

Population expansion and migration



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Current status

- St. James's Hospital
- 256 adult patients with haemoglobinopathies
  – 242 Sickle Cell Disease patients and 14 Thalassaemia patients
- CHI crumlin

- Nationwide
  – 700 plus

Study Aims

- Document and describe the challenges
- Demonstrate the expansion in patient numbers
- How much blood was being used
- *Fortunate to have both an interested medical scientist (Kate Murphy) and research SPR (Dr Eileen Ryan) to engage in the topic*

Methods

- Retrospective quantification of red cell usage by the adult hemoglobinopathy service (AHS) and other blood using specialties
- January 2015 to December 2022
- Age, gender and red cell genotype collected for patients within the AHS who received ≥1 red
- The National Blood Centre reviewed all red cell requests from the hospital during this period and compared these with nationwide red cell issues

Results

Variable	Result or Frequency (%)
Age	
Median	25
Minimum, Maximum	19, 58
Gender	
Male	56 (49.1)
Female	58 (50.1)
Diagnosis	
SCD	104 (91.2)
Thalassaemia	10 (8.8)

Table 1: Basic Characteristics of Transfused Haemoglobinopathy Patients

Results

- Total number of patients attending the AHS grew from 112 in 2015 to 264 in 2022.
- The number of patients transfused by the haemoglobinopathy service has also increased greatly from 15 in 2015 up to 78 in 2022.
- The haemoglobinopathy service's red cell usage accounted for 1.6% of total red cell usage in SJH in 2015 dramatically increasing to 28.9% in 2022.

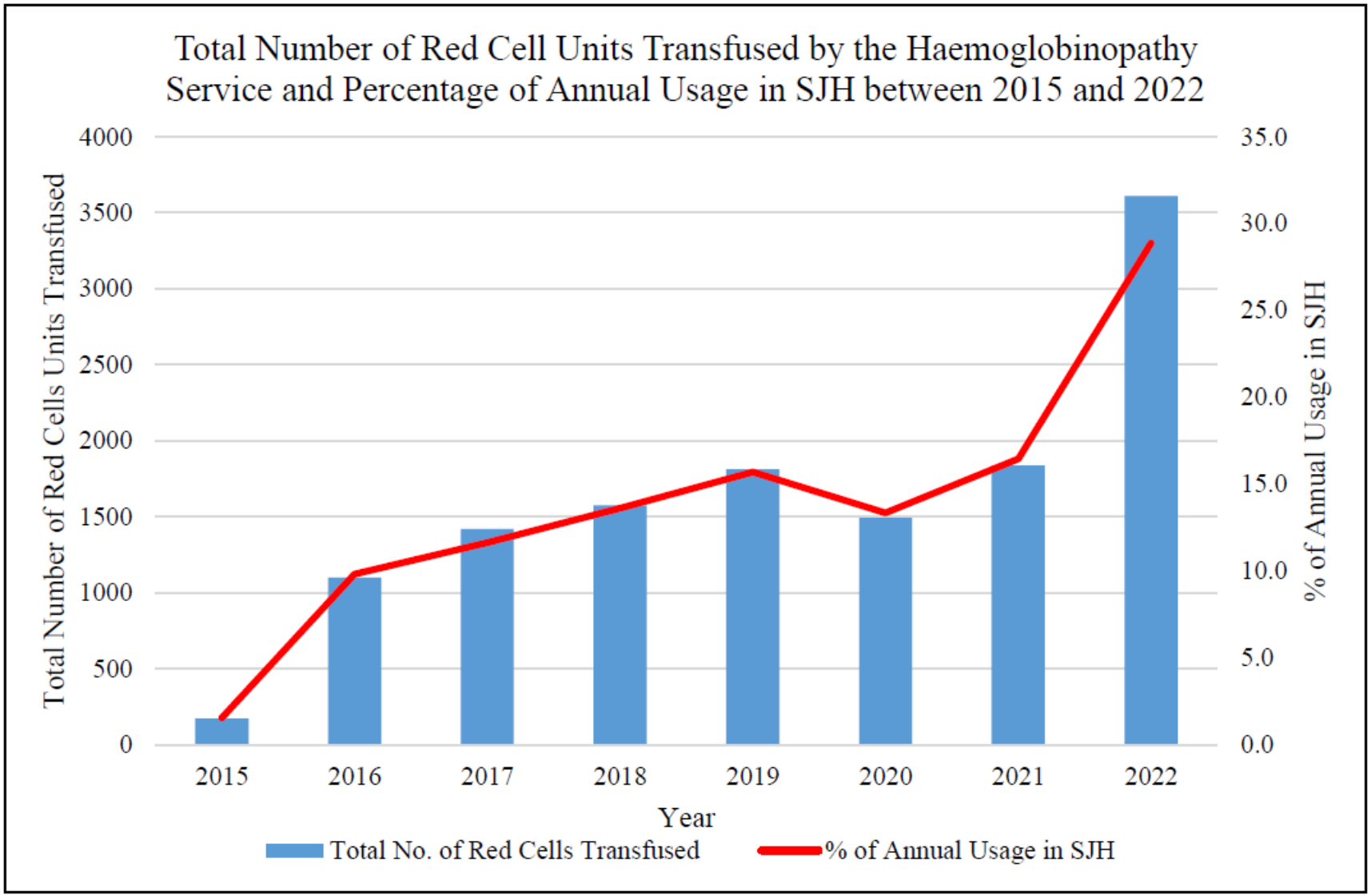
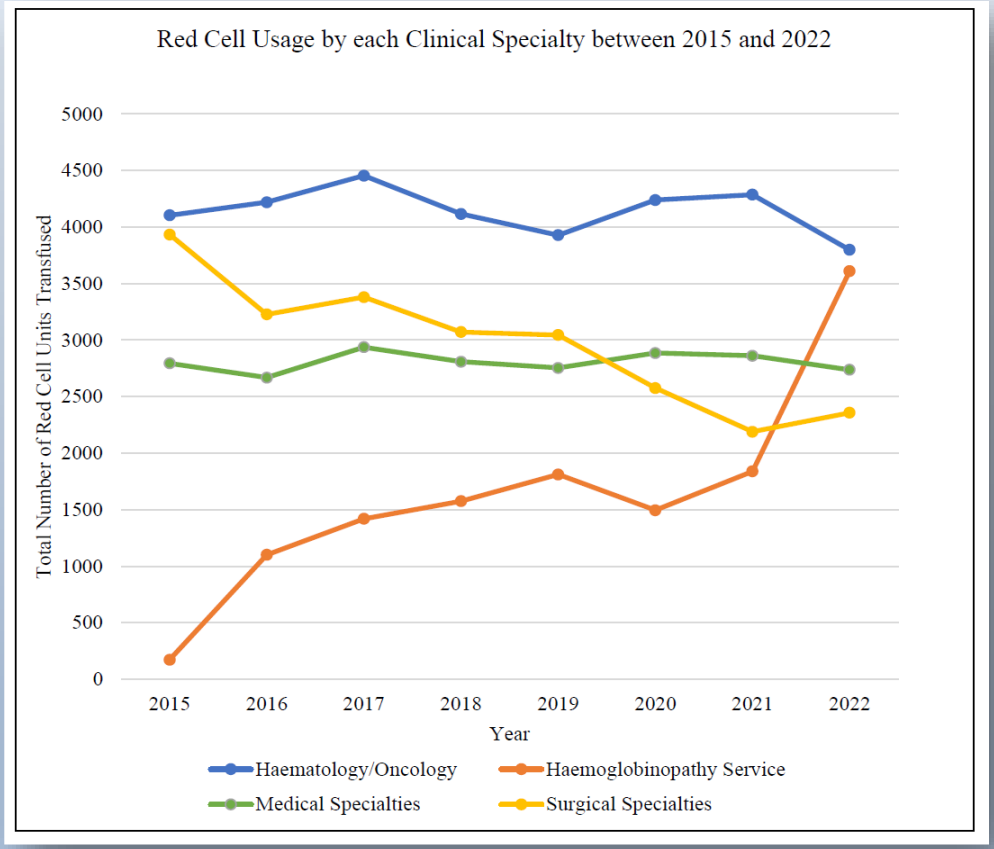


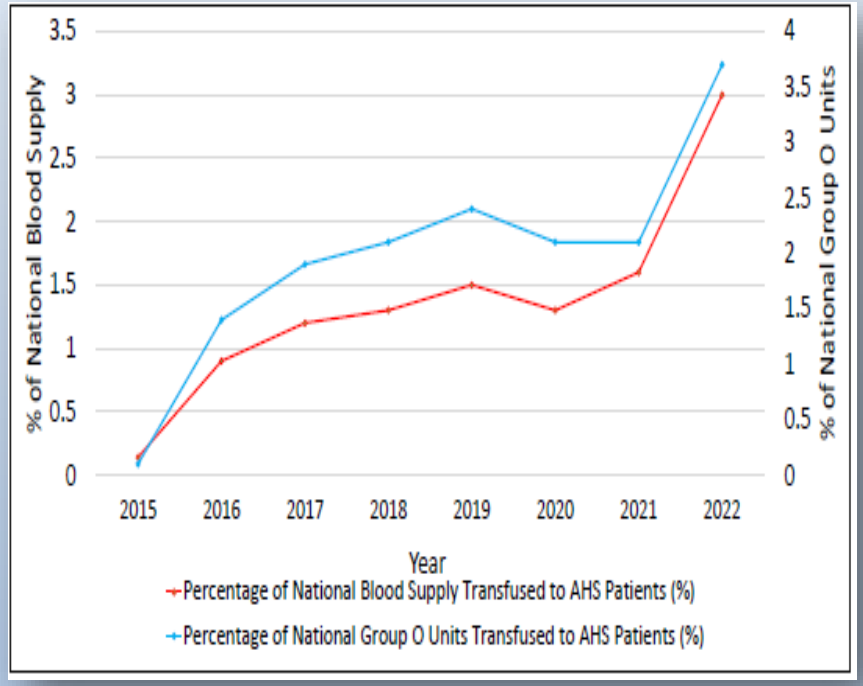
Figure 7: Graph depicting change in Total Red Cell Usage by the Haemoglobinopathy Service from 2015 to 2022

Figure 2: Red Cell Usage by each Specialty in SJH



- The service with the highest level of red cell usage consistently in SJH was the haematology/oncology service 4103 units in 2015 and 3797 units in 2022
- Red cell usage by the surgical specialties has steadily decreased 3933 units in 2015 vs 2356 units in 2022
- The red cell usage by the haemoglobinopathy service has increased dramatically 172 units in 2015 up to 3608 units in 2022

Figure 3: Impact of the AHS on the National Blood Supply



- The percentage of the national blood supply transfused to the AHS patients increased from 0.1% in 2015 to 3.7% in 2022.
- The percentage the national supply of group O units to AHS patients increased from 0.14% to 3% over the 8-year study period.

Table 2: Red Cell Antigen Expression in Transfused AHS Patients

Table 2: The most frequent Rh genotype observed in the transfused haemoglobinopathy patient cohort was R0r (this genotype occurs infrequently in the Irish donor population – 1.25%[1]).

Most Probable Genotype	AHS Patients (%)	Irish Donor Population (%)
R0r	59.60	1.25
R2r	14.00	13.07
R1r	11.40	33.35
R1R1	7.90	17.62
R1R2	3.50	13.95
rr	2.60	16.66
R2R2	0.90	2.89

Discussion

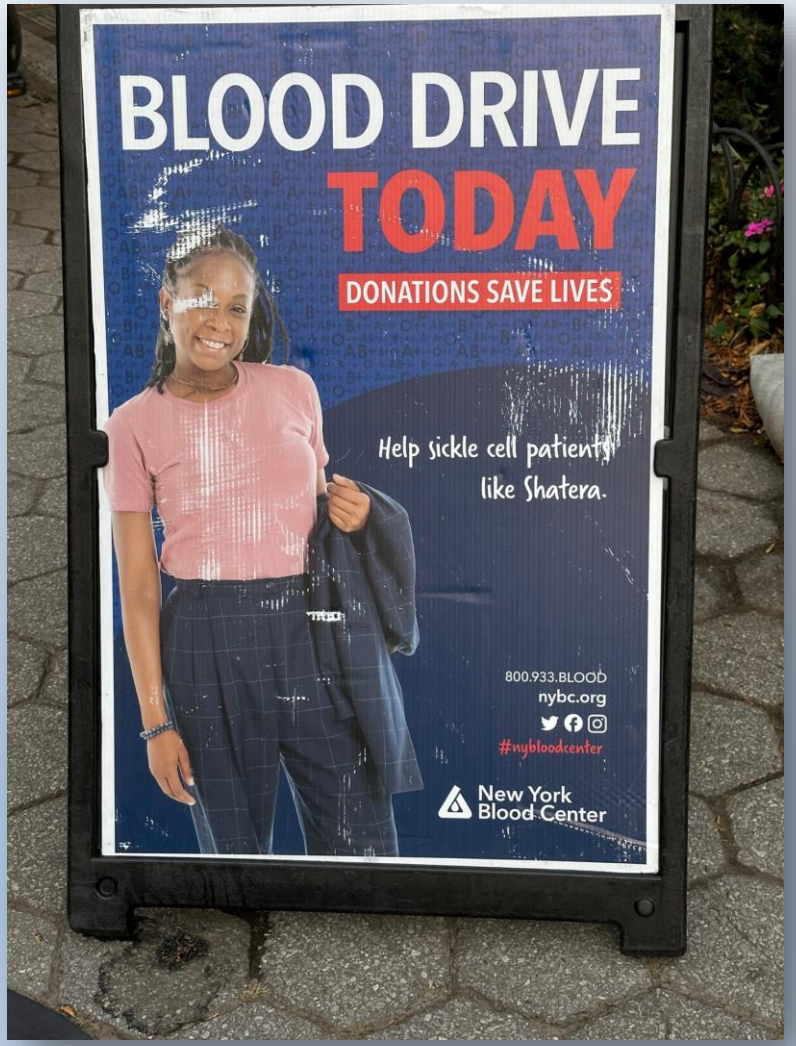
- Dramatic growth of the AHS in Ireland over the last number of years.
- It is likely that the AHS will become the chief user of red cells in the hospital in the future as the demand for the service is very high despite reaching capacity in April 2022.
- Limitation at present is service capacity
- Differences in red cell antigen expression between the transfused AHS patient cohort and the general donor population were observed.
- For example, the difference in Rh blood group antigen expression between the haemoglobinopathy patients and the Irish donor population has led to a high number of group O RhD negative units being transfused to haemoglobinopathy patients, most of whom (61%) were group O RhD positive.

Discussions

- Is there a mismatch between clinical guidance and real-world realities?
- Age of red cells, for example
- With ever-expanding populations, how do health services cope with increasing number of patients requiring HbS <30%?

Discussion

- Supply:
- Donors Recruitment strategies
- Society specific tailored messaging



Conclusion

- Blood services will continue to have to recruit donors, that reflect the population diversity
- Clinicians, naturally, will advocate for the best treatment available for their patients
- Nevertheless, changes to regional practice could improve blood availability. There is not age specific requirement for blood in the USA