Complications SCD

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19-11-25 HCC MDT teaching

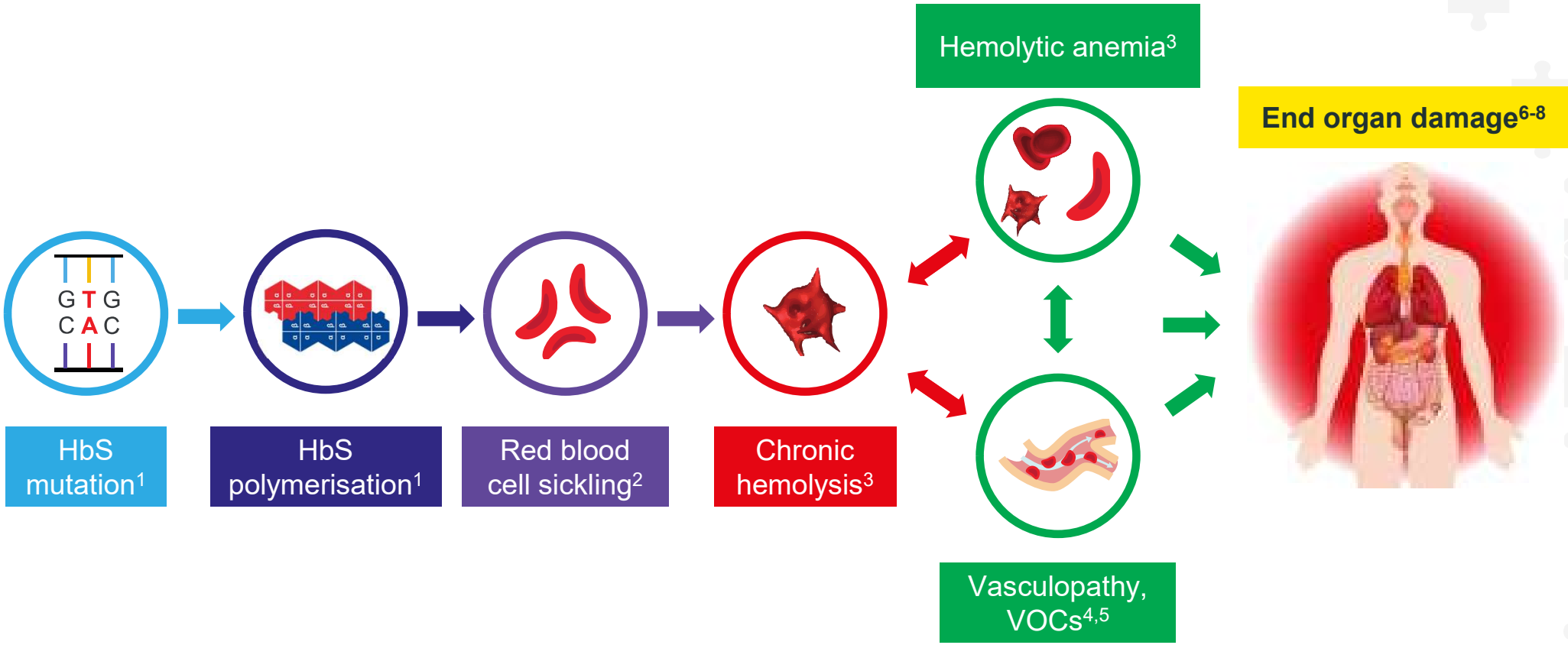
Objectives for today

Explore the pathophysiological cascade of SCD and its complications

Highlight the importance of long-term management of patients with SCD to improve outcomes

SCD, sickle cell disease.

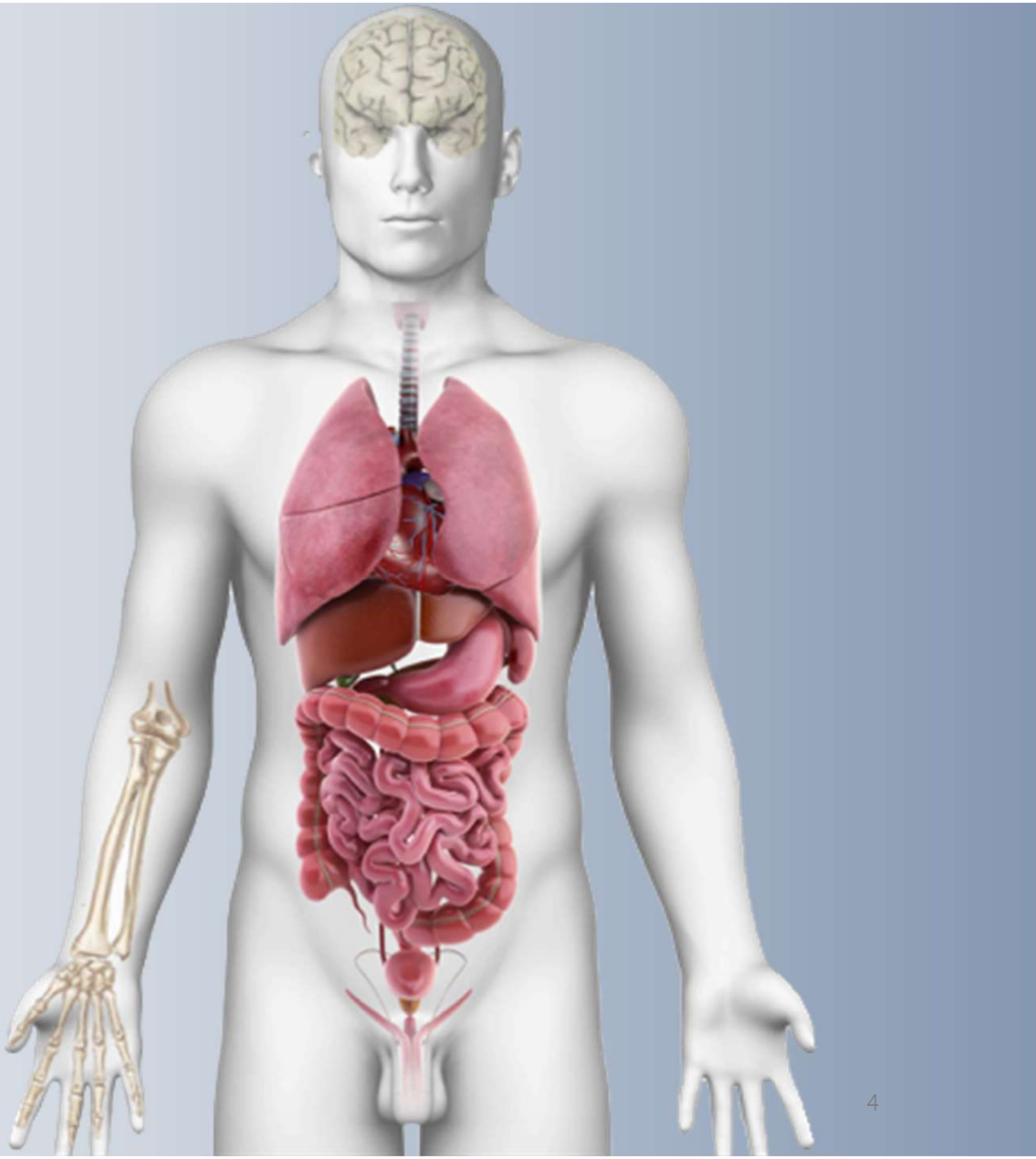
SCD is caused by the sickle hemoglobin (HbS) mutation, resulting in HbS polymerisation and red blood cell sickling[1–3]



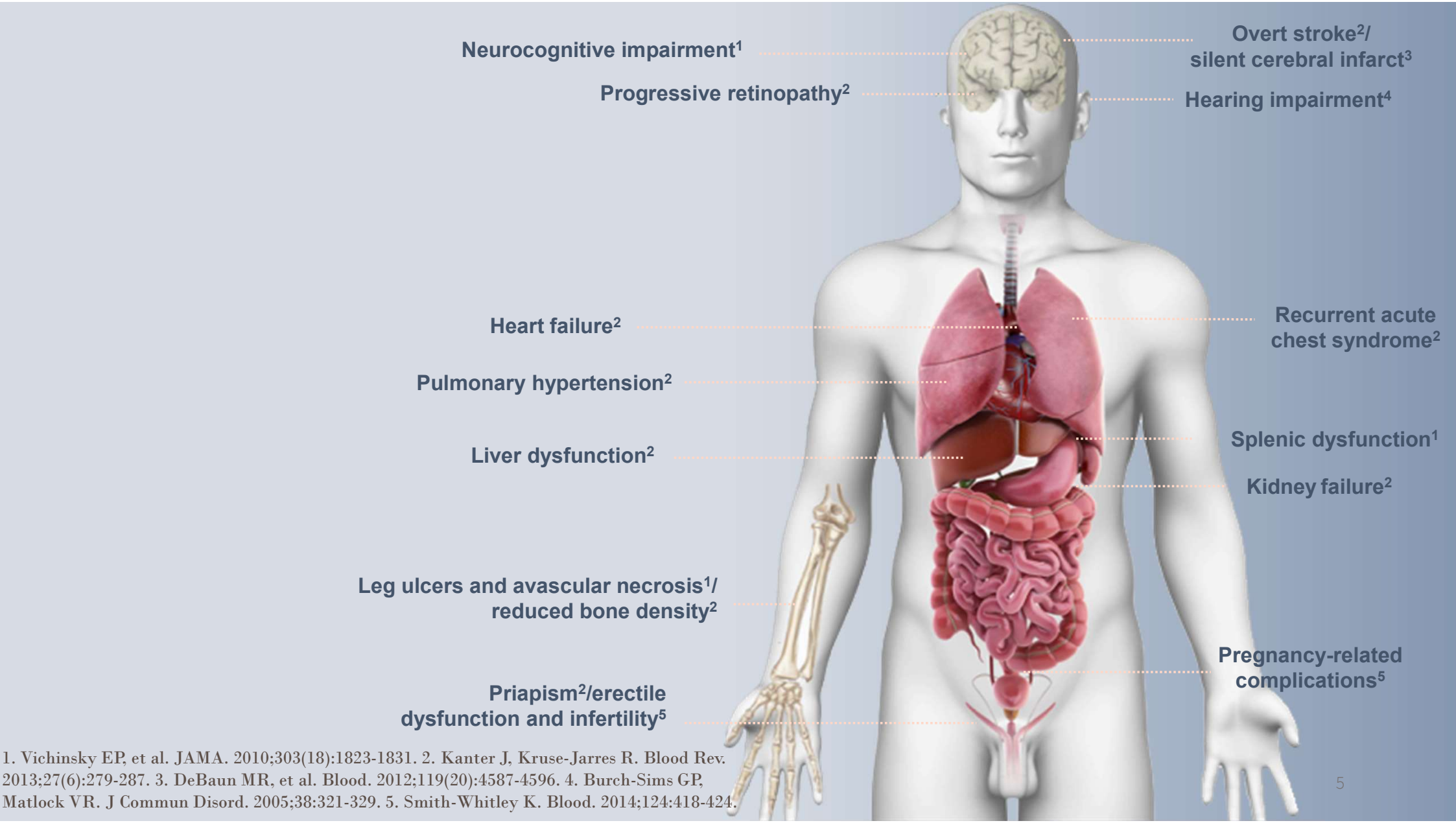
VOC, vaso-occlusive crisis.

1. Bunn HF. *N Engl J Med* 1997;337:762–769. 2. Ashley-Koch A, *et al. Am J Epidemiol* 2000;151:839–845. 3. Odièvre MH, *et al. Indian J Med Res* 2011;134:532–537. 4. Matte A, *et al. Mediterr J Hematol Infect Dis* 2019;11:e2019002. 5. Conran N, Belcher JD. *Clin Hemorheol Microcirc* 2018;68:263–299. 6. Kato GJ *et al. J Clin Invest* 2017;127:750–760. 7. Yates AM *et al. Pediatr Blood Cancer* 2019;66:e27717. 8. Gladwin MT, Kato GJ. *Hematology Am Soc Hematol Educ Program* 2005;51–57.

The effects of this pathophysiological cascade cause end-organ damage and mortality[1–4]



1. Vichinsky EP, et al. JAMA. 2010;303(18):1823-1831. 2. Kanter J, Kruse-Jarres R. Blood Rev. 2013;27(6):279-287. 3. DeBaun MR, et al. Blood. 2012;119(20):4587-4596. 4. Burch-Sims GP, Matlock VR. J Commun Disord. 2005;38:321-329. 5. Smith-Whitley K. Blood. 2014;124:418-424.



1. Vichinsky EP, et al. JAMA. 2010;303(18):1823-1831. 2. Kanter J, Kruse-Jarres R. Blood Rev. 2013;27(6):279-287. 3. DeBaun MR, et al. Blood. 2012;119(20):4587-4596. 4. Burch-Sims GP, Matlock VR. J Commun Disord. 2005;38:321-329. 5. Smith-Whitley K. Blood. 2014;124:418-424.

Life expectancy for patients with SCD has improved over the last few decades

SCD, sickle cell disease.
Gardner K, *et al. Blood* 2016;128(10):1436–1438.

As patients with SCD live longer, there is an increased prevalence of end-stage organ damage

SCD, sickle cell disease.
Powars DR, et al. Medicine (Baltimore) 2005;84:363–376.

SCD is associated with both acute and chronic effects, and significant morbidity[1,2]

SCD, sickle cell disease.

1. Pinto VM, et al. Intern Emerg Med 2019;14:1051–1064; 2. Payne AB, et al. Ann Emerg Med 2020; 76(3S):S28–S36.

Acute effects of SCD

Painful **vaso-occlusive crises** are the **hallmark of SCD**, resulting from dysfunctional Hb

Chest syndrome

Splenic or hepatic sequestration

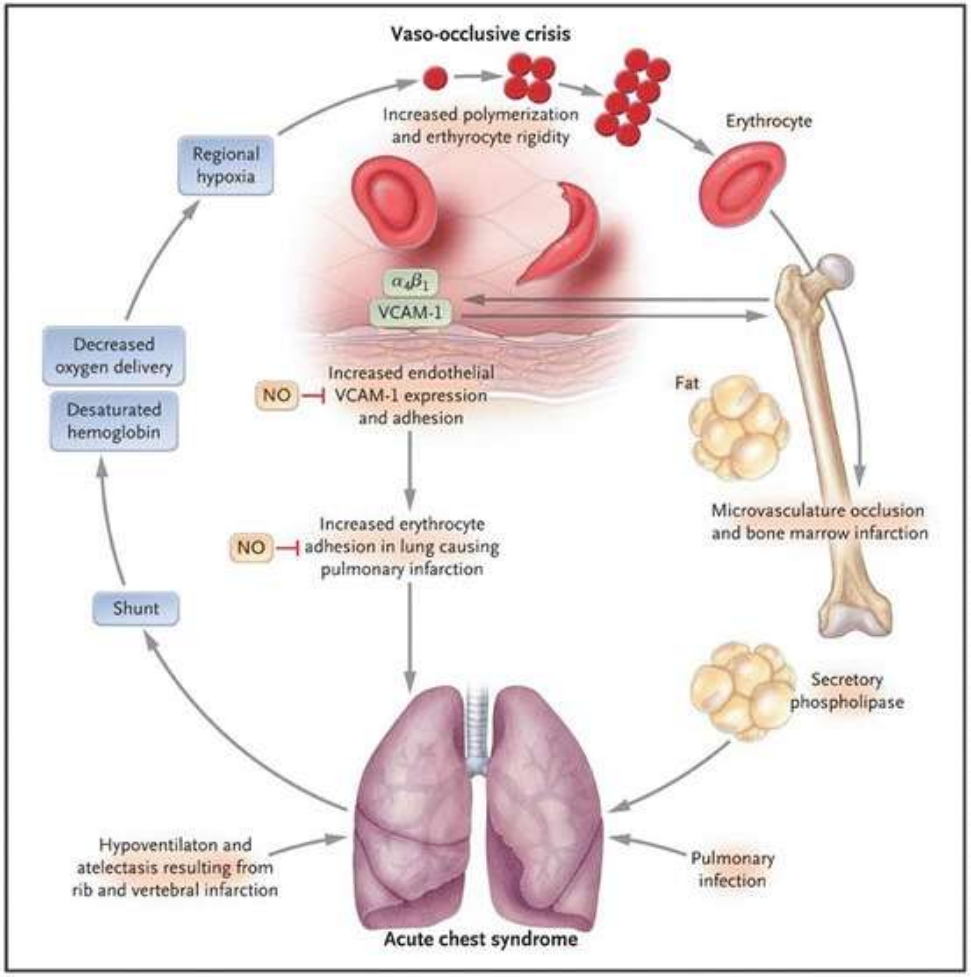
Cerebral events

Hb, hemoglobin; SCD, sickle cell disease.
Pinto VM, et al. Intern Emerg Med 2019;14:1051–1064.

Acute Chest Syndrome

- Defined as the development of a new pulmonary infiltrate, involving at least one complete lung segment, that is accompanied by fever, chest pain, tachypnea, wheezing, or cough

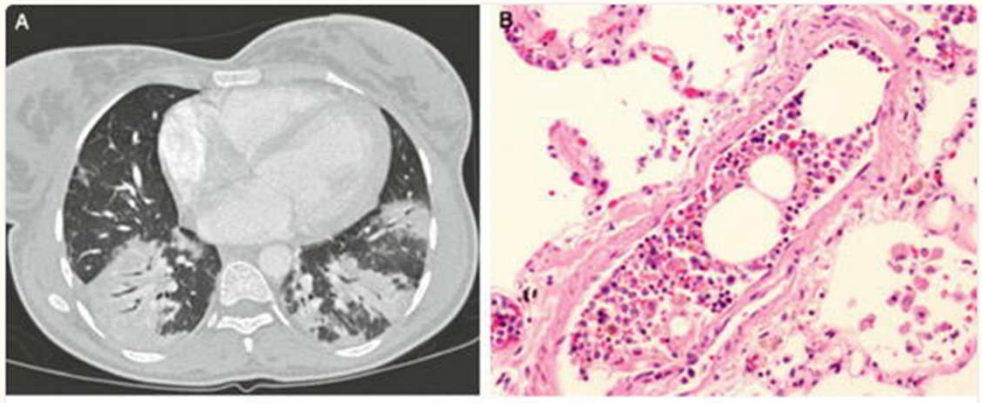
- 29 % of all SCD patients will have at least one episode of ACS, and approximately half of those patients will have more than one ACS episode.
  HbSS>HbSbeta0Thal>HbSC>HbSbeta+Thal



Sysol JR, Machado R. Sickle Cell Disease and Acute Chest Syndrome: Epidemiology, Diagnosis, Management, Outcomes. Hematologic Abnormalities and Acute Lung Syndromes. 2016 Jun 11:67–87. doi: 10.1007/978-3-319-41912-1_4. PMCID: PMC7120070.

Clinical presentation - Epidemiology

- 17 % prevalence of pulmonary thrombosis without associated peripheral venous thrombosis
- Pulmonary pressures can rise during episodes of ACS, leading to the development of acute right heart failure and increased mortality following the ACS event
- 10-20 % of patients admitted with acute VOC develop ACS in the first 3 days of hospitalization.
- The mean duration of hospitalization for patients with ACS is 10.5 days.
- Overall mortality is 3 % in all ACS patients and 9 % in adults.



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PMC7120070.

Management ACS

- Oxygen if SaO2<90%
- Monitor fluid intake, provide IV fluid, but prevent over-hydration
- Incentive Spirometry
- Antibiotics depending on local microbiology policy

- The need for transfusion and the modality of simple versus exchange transfusion should be individualized based on ACS severity and the risk for developing acute respiratory failure

- In patients with multiple moderate to severe ACS episodes despite maximal hydroxyurea therapy, the use of chronic transfusion therapy to maintain a low percentage of RBCs containing HbS has been shown to decrease the rate of ACS and vaso-occlusive pain crises in SCD.

Infectious pathogens isolated in 671 episodes of the acute chest syndrome[a]

Pathogen	No. of episodes
Chlamydia pneumoniae	71
Mycoplasma pneumoniae	51
Respiratory syncytial virus	26
Coagulase-positive *Staphylococcus aureus*	12
Streptococcus pneumoniae	11
Mycoplasma hominis	10
Parvovirus	10
Rhinovirus	8
Parainfluenza virus	6
Haemophilus influenzae	5

Sysol JR, Machado R. Sickle Cell Disease and Acute Chest Syndrome: Epidemiology, Diagnosis, Management, Outcomes. Hematologic Abnormalities and Acute Lung Syndromes. 2016 Jun 11:67–87. doi: 10.1007/978-3-319-41912-1_4. PMCID: PMC7120070.

Chronic effects of SCD highlight the need for a long-term vision

Pulmonary hypertension[1]

Cardiovascular disease[2]

Kidney disease[1]

Cognitive dysfunction[1]

Hepatopathy[1]

Bone-joint diseases[1]

Eye disease[1]

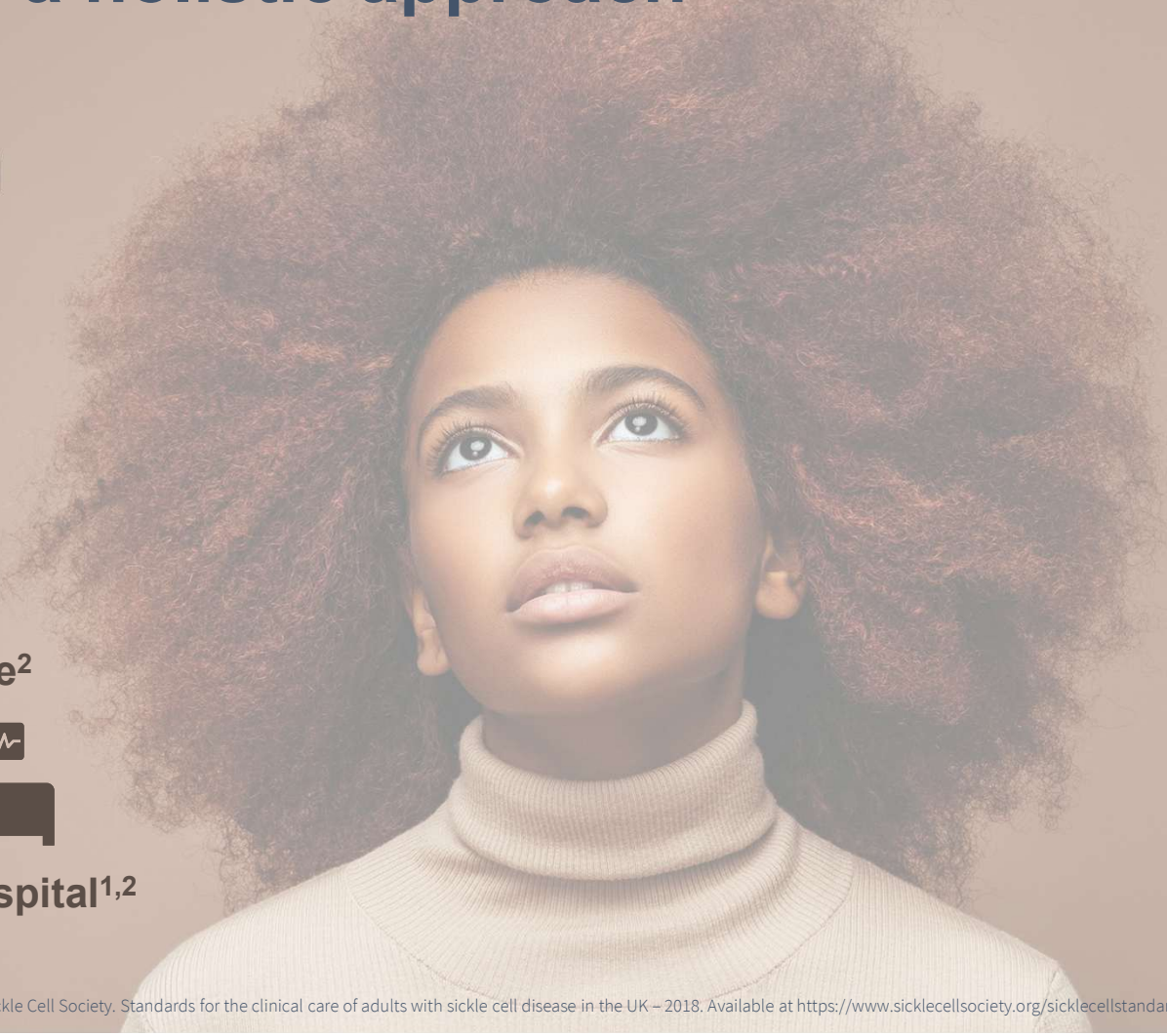
SCD, sickle cell disease.

1. Pinto VM, *et al. Intern Emerg Med* 2019;14:1051–1064; 2. Payne AB, *et al. Ann Emerg Med* 2020; 76(3S):S28–S36.

It’s time to expand our focus from managing acute pain events to a long-term approach[1,2]

1. Brennan-Cook J, *et al. Prof Case Manag* 2018;23:213–219; 2. Okpala I, *et al. Eur J Haematol* 2002;68:157–162.

The long-term management of patients with SCD requires a holistic approach



Community care[1,2]

Education[1,2]

Specialised centre[2]

Local hospital[1,2]

Home[1,2]

Social integration[2]

Workplace[1,2]

Family life[2]

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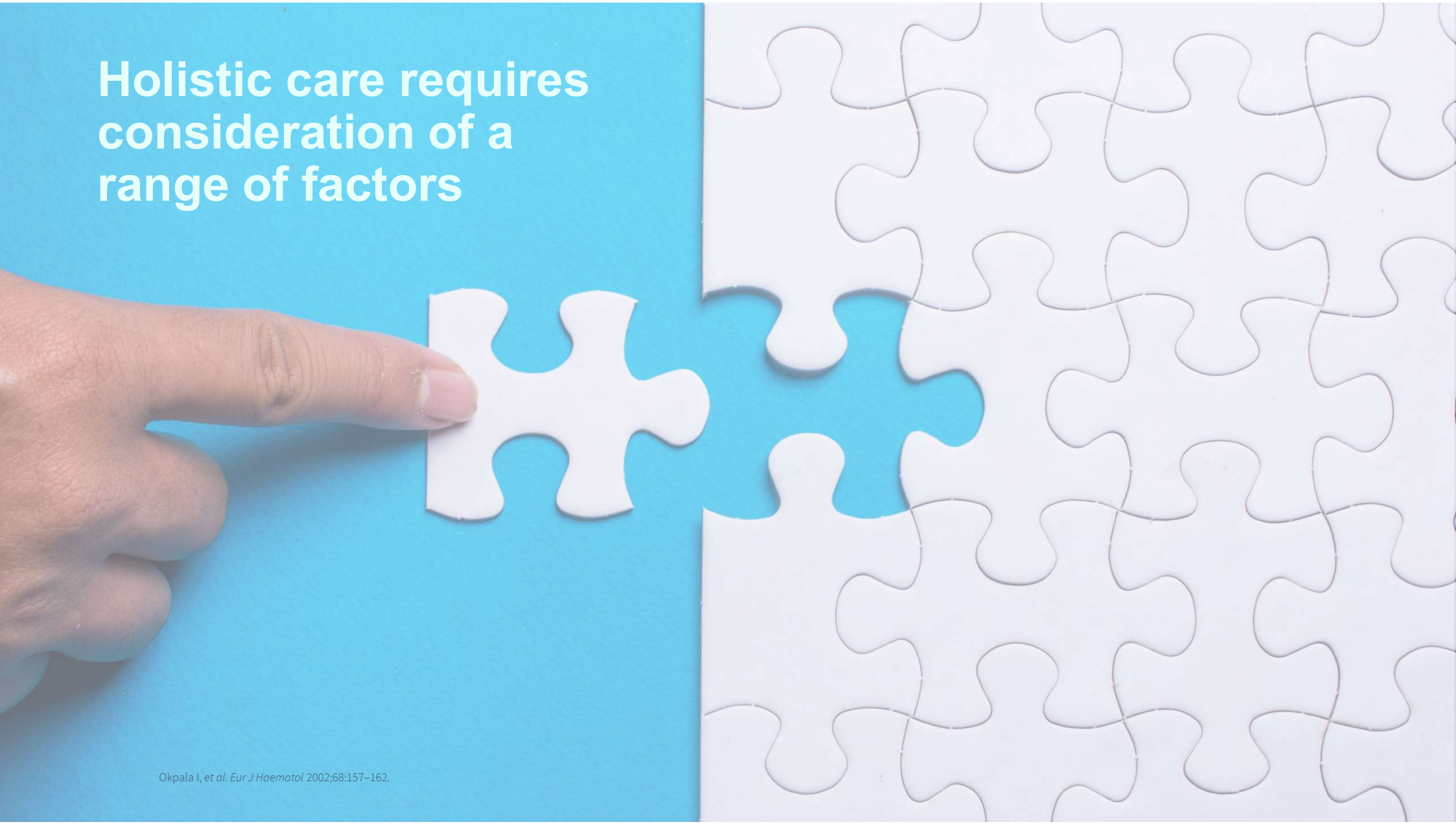
1. Okpala I, et al. Eur J Haematol 2002;68:157–162; 2. Sickle Cell Society. Standards for the clinical care of adults with sickle cell disease in the UK – 2018. Available at https://www.sicklecellsociety.org/sicklecellstandards/. (last accessed March 2022).

Holistic care requires consideration of a range of factors



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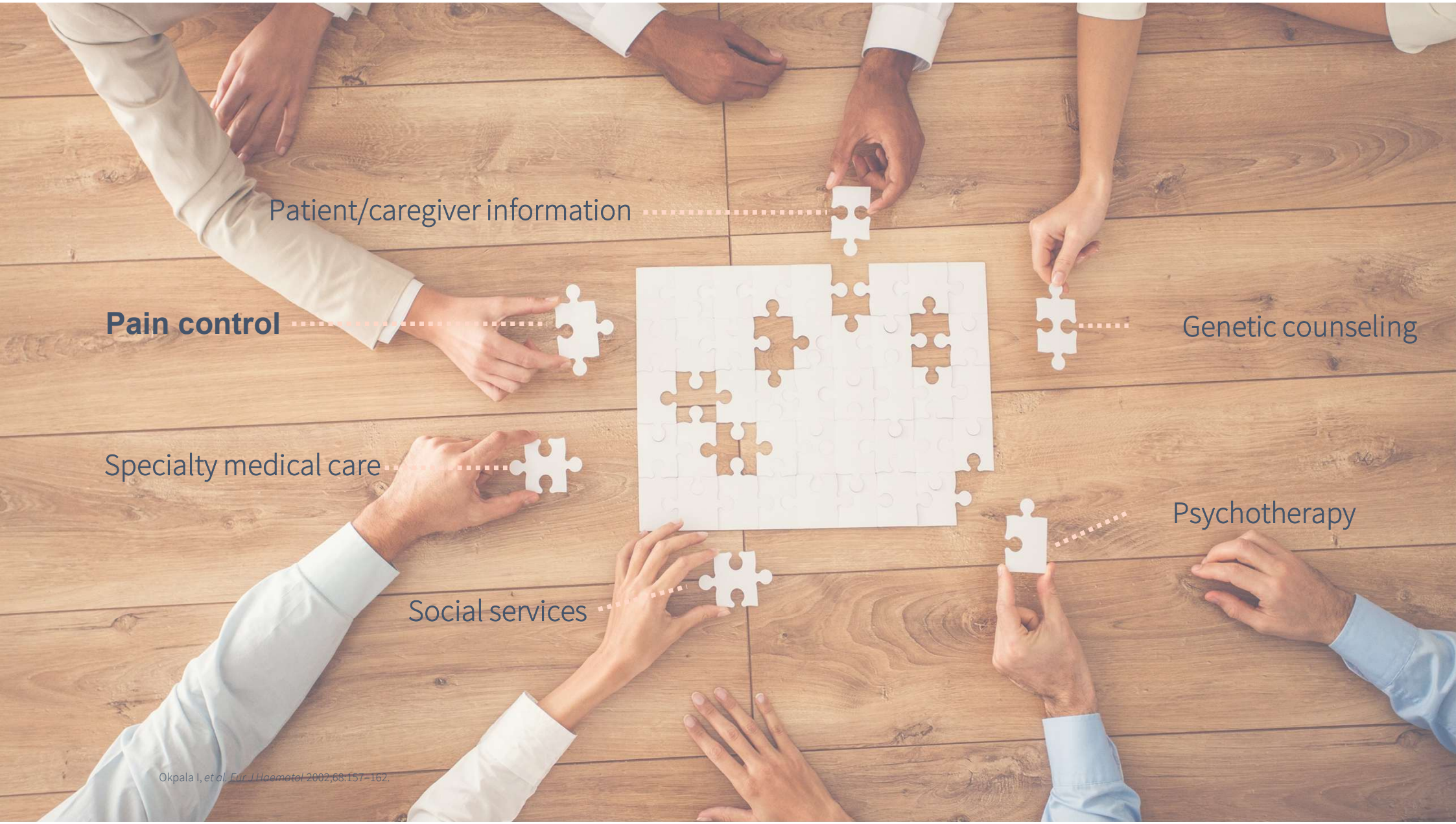


Okpala I, *et al. Eur J Haematol* 2002;68:157–162.

The multidisciplinary team are integral in the long-term management of patients with SCD[1,2]

1. Okpala I, *et al. Eur J Haematol* 2002;68:157–162; 2. Sickle Cell Society. Standards for the clinical care of adults with sickle cell disease in the UK – 2018. Available at https://www.sicklecellsociety.org/sicklecellstandards/. (last accessed March 2022).

Case study 1 – male in his twenties with HbSS

- Social: Adopted from the Gambia and moved to England at the age of 5 years
- During childhood: he experienced no major VOCs, no admissions or transfusions
- Transitioned to adult services at age 16

- Recent annual review (2024)
- Ophthalmology: did not attend his appointments
- Renal: normal eGFR
- Cardiac: normal ECHO (2022)
- Resp: normal lung function test
- Bone: normal VitD level with VitD tablets
- Lab: Hb 90, WBC 8, Plt 616, ferritin 183, HbS 80%, HbF 6%, retic 332, bili 62, LDH 662, eGFR > 90, creat 79

Clinical case study provided based on speaker's personal clinical experience. Individuals have consented to the sharing of information.
*The voxelotor marketing authorisation was recommended for suspension in the EU by the EMA on 25/09/2024. EMA Press release. Available at: https://www.ema.europa.eu/en/news/ema-recommends-suspension-sickle-cell-disease-medicine-oxbryta. Accessed October 2024. ACS, acute chest syndrome; DMT, disease-modifying therapies; haplo, haploidentical; HbSS, homozygous sickle haemoglobin; HC, hydroxycarbamide; HLA, human leukocyte antigen; HSCT, haematopoietic stem cell transplantation; MSD, matched sibling donor; MTD, maximum tolerated dose; PDE9, phosphodiesterase 9; PRN, *pro re nata* (as needed); RCT, randomised clinical trial; VOC, vaso-occlusive crisis.

Case study 1 continued

- Frequent admissions with acute VOCs from age 19yo
- Severe complications such as acute chest syndrome
- Despite disease modifying treatment his SCD phenotype remains severe
- Change of behaviour in 2022 when patient stopped all medication

2018 (aged 19)	2019	2020	2021	2022	2023
Frequent VOCs needing top-up transfusions	ACS requiring urgent red-cell exchange	Frequent VOCs, requiring more analgesia on admission	EMA approval of a HbS polymerisation inhibitor*	Stopped all his DMTs, switched to herbal substances (orders online)	Family was HLA-typed
4 admissions/year	5 admissions/year	6 admissions/year	6 admissions/year (2021–2024)		No MSD, sister was a haploidentical donor
Started with HC 1.5g (MTD)	Declined regular red cell exchanges	Took part in a Phase 2 RCT (PDE9 inhibitor)	Taking oxycodone 10mg PRN at home		Refused a RCT which allows 50% chance of access to a haplo-HSCT

- Since 2023, continuous frequent admissions (4x/year) and recurrent chest crises needing red cell exchange

Case study 1 continued

Chronic pain problem

- Reports daily bone pain; takes oxycodone 10mg up to 4–6x/day
- Requests repeat prescriptions with his GP
- GP limits the prescriptions
- Patients frequently attends the day-unit with pain
- Unwilling to engage with chronic pain service, but meets with psychology occasionally
- Feels disappointed in the health care system

"I always have pain"

"I am used to this"

"This is normal for me"

Social impact

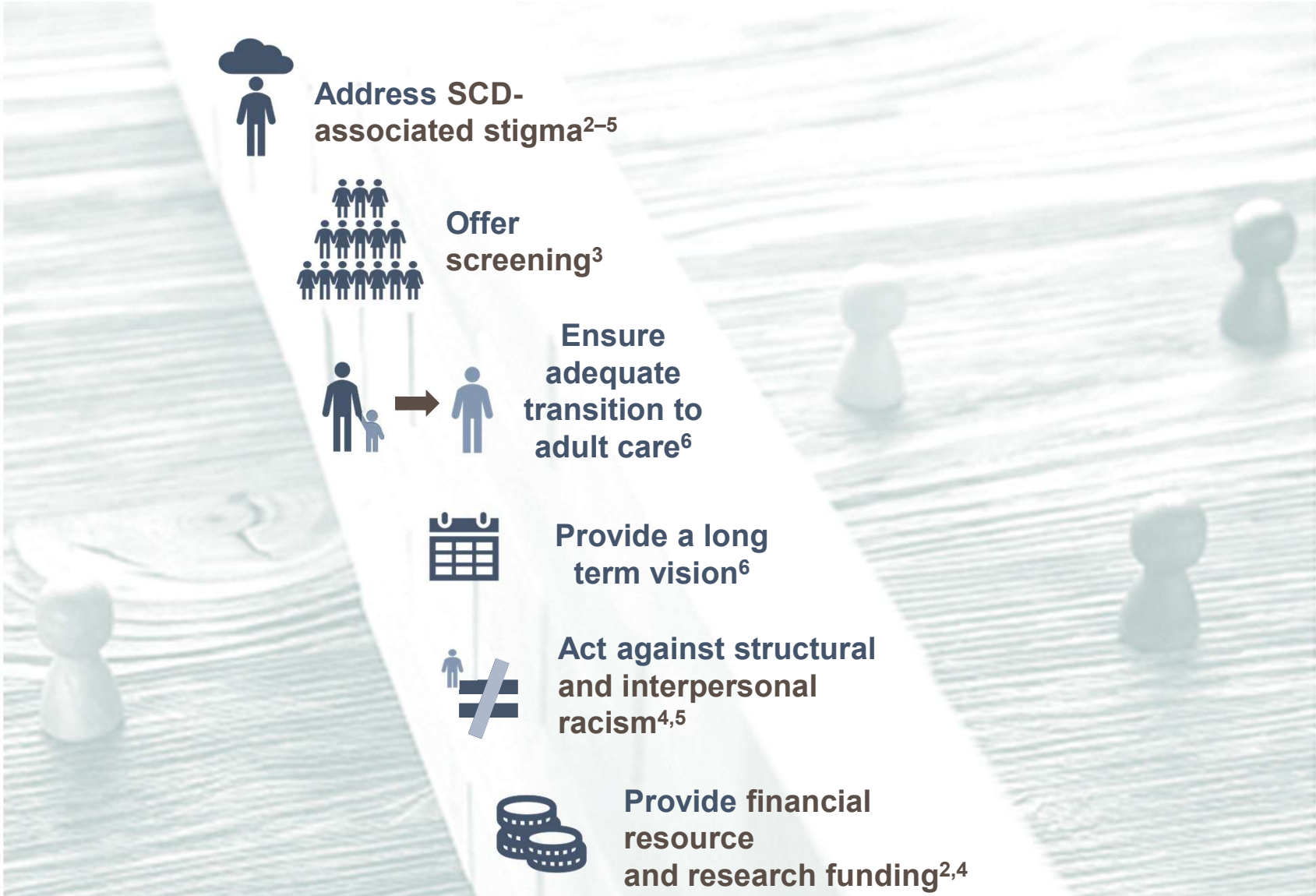
- Due to pains, dropped out of college in 2018
- Unable to hold jobs for due to admissions, failed an apprenticeship, tried to start-up his own business
- Currently on benefits and lives with his mother

Conclusion

- Young male patient with HbSS, with a severe phenotype
- Would meet criteria for curative therapies, as no clear end organ damage (yet), mostly affected by daily chronic pains
- Refused to proceed with curative treatment due to fear of TRM

Clinical case study provided based on speaker's personal clinical experience. Individuals have consented to the sharing of information.
GP, general practitioner; HbSS, homozygous sickle haemoglobin; TRM, transplant-related mortality.

Numerous actions are required to improve access to appropriate care[1]



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Thank you for your attention

Special thanks to our SW Haemoglobinopathy team for their help and support

We are happy to take questions

Please note we offer 24/7 urgent medical haemoglobinopathy support
Non-urgent advice and guidance – we ask you to submit your case for MDT discussion
We are not always able to respond to your email queries urgently


Have a good day