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Owusu-Ofori S, Remmington T

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[Intervention Review]

Splenectomy versus conservative management for acute sequestration crises in people with sickle cell disease

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ABSTRACT

Background

Acute splenic sequestration crises are a complication of sickle cell disease, with high mortality rates and frequent recurrence in survivors of first attacks. Splenectomy and blood transfusion, with their consequences, are the mainstay of long-term management used in different parts of the world. This is a 2017 update of a Cochrane Review first published in 2002, and previously updated, most recently in 2015.

Objectives

To assess whether splenectomy (total or partial), to prevent acute splenic sequestration crises in people with sickle cell disease, improved survival and decreased morbidity in people with sickle cell disease, as compared with regular blood transfusions.

Search methods

We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group Haemoglobinopathies Trials Register, which comprises of references identified from comprehensive electronic database searches and handsearching relevant journals and abstract books of conference proceedings. We also searched clinical trial registries. Additional trials were sought from the reference lists of the trials and reviews identified by the search strategy.

Date of the most recent search: 14 August 2017.

Selection criteria

All randomized or quasi-randomized controlled trials comparing splenectomy (total or partial) to prevent recurrence of acute splenic sequestration crises with no treatment or blood transfusions in people with sickle cell disease.

Data collection and analysis

No trials of splenectomy for acute splenic sequestration were found.

Main results

No trials of splenectomy for acute splenic sequestration were found.

Authors' conclusions

Splenectomy, if full, will prevent further sequestration and if partial, may reduce the recurrence of acute splenic sequestration crises. However, there is a lack of evidence from trials showing that splenectomy improves survival and decreases morbidity in people with sickle cell disease. There is a need for a well-designed, adequately-powered, randomized controlled trial to assess the benefits and risks

of splenectomy compared to transfusion programmes, as a means of improving survival and decreasing mortality from acute splenic sequestration in people with sickle cell disease.

There are no trials included in the review and we have not identified any relevant trials up to August 2017. We will continue to run searches to identify any potentially relevant trials; however, we do not plan to update other sections of the review until new trials are published.

PLAIN LANGUAGE SUMMARY

Removing spleens from people with sickle cell disease after a splenic sequestration compared to blood transfusions to prevent further attacks

Review question

We reviewed the evidence to see whether removing all, of part of, the spleen to prevent acute splenic sequestration improved survival and decreased illness in people with sickle cell disease, as compared with regular blood transfusion. This is a 2017 update of a Cochrane Review first published in 2002, and previously updated, most recently in 2015.

Background

In some people with sickle cell disease, red blood cells become trapped and destroyed in the spleen. This damages the spleen, which may become enlarged leading to splenic sequestration crises. These crises consist of abdominal pain, rapid heart rate and other symptoms. Such an attack can be fatal without prompt treatment. All or part of the spleen (splenectomy) is often removed after a person has survived such a crisis to try and prevent another one. This surgery may leave the individual at a higher risk of infection. We looked for trials which compared surgery to blood transfusions.

Search date

The evidence is current to: 14 August 2017.

Key results

We found no trials to provide reliable evidence about the risks or benefits of splenectomy for people with sickle cell disease after splenic sequestration. There is a need for a trial to assess the benefits and risks of splenectomy compared to transfusion programmes.

There are no trials included in the review and we have not identified any relevant trials up to August 2017. We will continue to run searches to identify any potentially relevant trials; however, we do not plan to update other sections of the review until new trials are published.

BACKGROUND

Description of the condition

Sickle cell disease (SCD) is a generic term for a group of inherited genetic disorders of haemoglobin, the oxygen-carrying protein contained in red blood cells. Under low oxygen tension the abnormal haemoglobin polymerises, distorting the red blood cells into a sickle shape. This sickling has two effects; firstly the sickled cells block small blood vessels resulting in tissue damage; and secondly the sickled cells are easily removed from circulation, resulting in anaemia. Common complications of SCD include increased severity of infections, pain episodes, stroke, kidney failure, chest infections and lung damage (acute sickle chest syndrome). In addition, growth and development may be delayed (Platt 1984).

Sickle cell disease was originally a disease of African, Indian, and Middle Eastern heritage because the carrier state affords protection against severe malaria; but migration has now made it a global problem (Davies 1989). The inheritance is in an autosomal recessive pattern, so individuals with SCD have inherited abnormal genes from both parents. The inheritance of the gene for sickle haemoglobin may be combined with those for other structurally abnormal haemoglobins, such as haemoglobin C, and also with abnormalities of haemoglobin production, such as beta thalassaemia.

Splenic sequestration occurs when red blood cells become entrapped in the spleen, which enlarges, pooling and then destroying the red blood cells. It is defined clinically as a fall of two grams per decilitre (g/dL) or more in blood haemoglobin concentration from the persons' normal levels, and an enlarging spleen (Topley 1981). Splenic sequestration crisis can be either acute or chronic. An acute splenic sequestration (ASS) is when splenic sequestration occurs rapidly. It manifests clinically as abdominal pain and distension, pallor, weakness, breathlessness, and rapid heart rate (Al-Salem 1999). Chronic sequestration (hypersplenism) has a gradual onset and can follow an attack of ASS (Topley 1981).

The incidence of ASS in homozygous SCD is highest in young children, ranging from 7% to 30% in children up to two years of age (Powell 1992; Topley 1981). After infection, ASS is the second most common cause of death in the first decade of life accounting for between 15% to 44% of deaths in this period (Emond 1985; Powell 1992; Topley 1981). The first attack can occur in infants as young as five weeks (Airede 1992), but attacks are uncommon after puberty. Most cases are seen in individuals with homozygous (SS) sickle cell anaemia, but have also been reported in S beta thalassaemia and sickle haemoglobin C (SC). Mortality can be reduced by the early detection of SCD by neonatal screening, followed by parental education (to detect splenic enlargement and pallor) and by early clinical intervention (Emond 1985; Powell 1992).

Acute splenic sequestration crisis is a medical emergency that requires the immediate restoration of blood volume, usually with red cell transfusions. ASS recurs in about 50% of survivors of the first attack with diminishing intervals between subsequent crises (Emond 1985). The mortality rate of the survivors who suffer a recurrence is approximately 20% (Topley 1981). Due to the frequency of recurrences, both long-term blood transfusion therapy and the surgical removal of the spleen (splenectomy) have been used as methods to prevent further ASS and death (Grover 1990).

Although transfusions have been used to reduce the frequency of attacks of ASS, they are expensive, time-consuming, and are associated with adverse effects including development of antibodies to red blood cells (alloimmunization), iron overload, transmission of blood-borne infections such as hepatitis and HIV, and allergic reactions (Rao 1985).

Description of the intervention

Splenectomy (full, partial, and embolisation) is also used to prevent ASS. The advantages of having a splenectomy include stopping blood transfusions and the absence of discomfort from mechanical pressure of the enlarged spleen (Al-Salem 1999). The main objection to performing a splenectomy in young children with SCD is the increased risk of infection. The risk of septicaemia after splenectomy is approximately 2% overall, 4% in children less than four years of age, and can be 30% or more in children in the first year of life (Idowu 1998). Current UK guidelines recommend that people who have had a splenectomy should receive lifelong prophylactic penicillin, and be given pneumococcal vaccine before surgery with boosters every three years after splenectomy. *Haemophilus influenzae* (*H influenzae*) type b and meningococcal vaccines have also been recommended (WPBCSH 1996). There is also concern that children living in malaria endemic regions have an increased risk of malarial attacks following a splenectomy (Evans 1945). The fear of loss of the immune protection the spleen gives to the body and of having to undergo surgery are disincentives for splenectomy. Partial splenectomies are performed as an alternative in children in order to try and retain some immune competence, which would otherwise have been lost (Idowu 1998). Other problems associated with partial or full splenectomy include: the risk of having recurrences of ASS in the remnant spleen; and anaesthetic and surgical complications, such as left lower lung collapse.

Why it is important to do this review

As there is continuing debate over the risks and benefits of splenectomy compared to repeated exchange transfusion as strategies to avoid recurrent attacks of ASS, we have reviewed the advantages and disadvantages of both full and partial splenectomy to prevent recurrence of ASS in people with SCD.

This is an update of a Cochrane Review first published in 2002, and most recently updated in 2015 (Owusu-Ofori 2002; Owusu-Ofori 2015).

OBJECTIVES

To determine whether a full or partial splenectomy, by whatever means, performed to prevent acute splenic sequestration improved survival and decreased morbidity in people with SCD, as compared with regular blood transfusion.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized (RCT) or quasi-randomized trials. Trials in which quasi-randomized methods, such as alternation, were to be

included if there was sufficient evidence that the treatment and control groups were similar at baseline.

Types of participants

All people with confirmed SCD (including SS, SC, SβO, Sβ+ proven by haemoglobin electrophoresis) who had experienced at least one ASS crisis.

In this review we defined an ASS crisis as a fall in haemoglobin of at least 2 g/dL from steady-state levels, an acutely enlarging spleen, and evidence of reticulocytosis indicating an increased bone marrow response (Topley 1981).

Types of interventions

Full or partial splenectomy to prevent an ASS compared to conservative management (no treatment or a regimen of regular blood transfusions e.g. four-weekly) to prevent an ASS.

Types of outcome measures

Primary outcomes

1. Death
2. Episodes of ASS (in individuals who either had a partial splenectomy or conservative management)

Secondary outcomes

1. Pneumococcal infections
2. Other infections including malaria
3. Blood transfusions
4. Number of days as a hospital inpatient
5. People experiencing sickle-related events (pain episodes, stroke, kidney failure, and chest syndrome)
6. People developing chronic hypersplenism
7. Adverse effects of interventions including development of alloantibodies, blood-borne infections, iron overload, surgical complications, or any other adverse effects

Search methods for identification of studies

A comprehensive search strategy was formulated in an attempt to identify all relevant trials regardless of language or publication status (published, unpublished, in press, and in progress).

Electronic searches

Relevant trials were identified from the Group's Haemoglobinopathies Trials Register using the terms: (sickle cell OR (haemoglobinopathies AND general)) AND (sple* OR pneumococcal).

The Haemoglobinopathies Trials Register is compiled from electronic searches of the Cochrane Central Register of Controlled Trials (CENTRAL) (updated each new issue of the Cochrane Library) and weekly searches of MEDLINE. Unpublished work is identified by searching the abstract books of five major conferences: the European Haematology Association conference; the American Society of Hematology conference; the British Society for Haematology Annual Scientific Meeting; the Caribbean Public Health Agency Annual Scientific Meeting (formerly the Caribbean Health Research Council Meeting); and the National Sickle Cell Disease Program Annual Meeting. For full details of all searching activities for the register, please see the relevant section of the Cochrane Cystic Fibrosis and Genetic Disorders Group's website.

Date of the most recent search of the Group's Haemoglobinopathies Trials Register: 14 August 2017.

In addition to the above, we carried out further searches of the following clinical trial registers:

- ClinicalTrials.gov (www.ClinicalTrials.gov);
- World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) Search Portal (apps.who.int/trialsearch/).

The following databases were searched for a previous version of the review:

- MEDLINE (Ovid, 1966 to June 2003);
- Embase (Ovid, 1988 to June 2003).

See the appendices section for the full search strategies (Appendix 1).

Searching other resources

The reference lists of all included articles and relevant systematic reviews were reviewed to identify any additional studies.

Data collection and analysis

Selection of studies

We did not apply the process described below, as we were not able to identify any trials eligible for inclusion. However, if we include any trials in future updates of this review, we will apply the following methods.

The two authors will independently screen the titles of references found to identify potentially relevant trials from the results of the searches. Both authors will independently apply an eligibility form to these potentially relevant trials. The form will take into account the inclusion criteria as described in the 'Criteria for considering studies for this review'. We will resolve disagreements by discussion, or if necessary by consulting a third party. The reasons for excluding trials will then be stated in the review.

Data extraction and management

Each author will independently extract data on trial information including methods, participants, interventions and outcomes. We will check any discrepancies that occur in data extraction by referring to the original paper. One author (SOO) will enter data into Review Manager software (Review Manager 2011).

We planned to group outcome data into those measured at one week and one, three, six and 12 months and annually thereafter. If outcome data were recorded at other time periods consideration would be given to examining those as well.

Assessment of risk of bias in included studies

Each review author will independently assess trials following the domain-based evaluation as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). The assessments will be compared and any inconsistencies between the review authors will be discussed and resolved.

Assessment will be made of the following domains, each will be assessed as having either a low, unclear or high risk of bias.

1. Generation of the allocation sequence
2. Concealment of allocation
3. Blinding (of participants, personnel and outcome assessors)
4. Incomplete outcome data
5. Selective outcome reporting

Measures of treatment effect

Where appropriate, we will analyze data using Review Manager software (Review Manager 2011). We will combine binary data using the Mantel-Haenszel odds ratio or risk ratio where appropriate. We will use mean difference for continuous data, which has been reported using means and standard deviations. Any skewed data found, will be analyzed using the most appropriate method available, e.g. transforming data or summary statistics. We will present continuous data, reported using medians and ranges, in tables only. With event counts, though it would be preferable to state beforehand how data will be analyzed, we will analyze such data in one of several ways based on the format of the data available. We will decide to make the outcome being considered either dichotomous, continuous, time-to-event or a rate, and then extract counts accordingly.

Dealing with missing data

Where the trials have been published in abstract form, presented at meetings, or reported to the authors, we will seek full reports from the trial authors. We will contact the primary investigator if information is missing or unclear.

Assessment of heterogeneity

We will measure the degree of heterogeneity between trials using the I^2 statistic from the meta-analysis. The I^2 quantifies the effect of heterogeneity by providing a measure of the degree of inconsistency in the trial results (Higgins 2003).

Assessment of reporting biases

We will examine funnel plots for asymmetry. Selection biases, e.g. publication and location biases, poor methodological quality of studies and heterogeneity may be some causes of funnel plot asymmetry.

Data synthesis

In the absence of homogeneity of treatment effects, we will use a random-effect approach, otherwise, we will use the fixed-effect model.

Subgroup analysis and investigation of heterogeneity

If there are a sufficient number of trials, we will explore the following sources of heterogeneity:

1. type of SCD;
2. age;
3. partial or complete splenectomy or embolisation;
4. transfusion regimens i.e. either at four-weekly intervals or periods more than four-weekly intervals, top up transfusions or exchange, or transfusions when HbS mean less than 40% or more than 40%;
5. developed versus developing countries.

RESULTS

Description of studies

We found no trials that were eligible for inclusion in the review.

Risk of bias in included studies

No trials were included in the review.

Effects of interventions

No trials were eligible for inclusion in the review.

DISCUSSION

There is a paucity of evidence to support splenectomy, by whatever means, performed to improve survival and decrease morbidity from ASS.

Common practice for the initial management of ASS is red cell transfusion to manage shock (hypovolaemia) and to alleviate symptoms of anaemia. After this, the long-term management options are a splenectomy; a transfusion programme; or careful observation for early signs of ASS until the spleen gradually becomes non-functional (splenic atrophy). In certain places, the choice of treatment depends on the severity of the initial episode of ASS and the age of individual. In developing countries, where the regular supply of 'zero-risk' blood may not be constant, chronic transfusion programmes are hardly considered as part of management of ASS. Chronic transfusions have been advocated by some, to protect susceptible children from recurrent attacks of ASS until splenic atrophy has occurred (Topley 1981).

Splenectomies have also been suggested for children with a variety of presentations (Grover 1990; Topley 1981; Wright 1999). The obvious advantage of having the spleen removed is that it prevents recurrent events, but the counter arguments are that splenectomy compromises their already impaired immune status and the operation being unnecessary in a condition in which the spleen is likely to become non-functional. Another debatable point is whether the spleen, after an attack of ASS, or in established hypersplenism (i.e. chronic enlargement of spleen with a persistent reduction in haemoglobin level), makes any contribution to the immune status of the individual. It is also prudent to bear in mind that the child with sickle cell anaemia after surgical splenectomy may have a similar risk as one in whom the natural phenomenon of 'autosplenectomy' (nature's own physiological spleen removal) has occurred.

Few people with SCD in high-income countries, who are known to have received prophylactic penicillin and pneumococcal and *H influenzae* vaccines after splenectomy, go on to suffer overwhelming infection (Emond 1984; Kinney 1990). In the UK, guidelines for the prevention and treatment of infection in people with an absent or dysfunctional spleen (asplenia) recommend pneumococcal and *H influenzae* type b immunization, as well as life-long prophylactic antibiotics (WPBCSH 1996). The above prophylactic measures may reduce the risk of septicaemia but may not guarantee protection from penicillin-resistant organisms. Asplenic individuals are at risk of severe falciparum malaria and

thus adherence to antimalarial prophylaxis in malaria endemic regions cannot be overemphasised (Evans 1945).

Different forms of splenectomy (such as partial splenectomy, splenic embolisation, and splenic irradiation) are employed in the management of chronic splenic enlargement in order to preserve splenic tissue and function (Idowu 1998; Pinca 1992). The advantages of less invasive procedures include avoidance of large scars, and the absence of high platelet counts normally resulting from splenectomy. Disadvantages such as infections and the reappearance of hypersplenism could result. Laparoscopic splenectomy is also another described alternative (Hendricks 2000).

Clinicians must, however, bear in mind that the risks of splenectomy should be compared with those of potential therapies such as blood transfusion and weighed against the dangers of their complications. It should also be considered that the natural history of ASS shows recurrence after the age of five years to be less likely.

AUTHORS' CONCLUSIONS

Implications for practice

No randomized controlled trials (RCTs) of splenectomy for splenic sequestration were found for inclusion in this review. Therefore, the research evidence on which to base clinical decisions is limited to case series and other less robust trials.

There are no trials included in the review and we have not identified any relevant trials up to August 2017. We will continue to run searches to identify any potentially relevant trials; however, we do not plan to update other sections of the review until new trials are published.

Implications for research

This systematic review has identified the need for a well-designed, adequately-powered RCT to assess the benefits and risks of splenectomy compared to transfusion programmes, as a means of improving survival and decreasing mortality from acute splenic sequestration in people with sickle cell disease.

ACKNOWLEDGEMENTS

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APPENDICES

Appendix 1. Search strategies

Database/ Resource	Strategy
www.ClinicalTrials.gov (searched 31 August 2017)	Condition/ Disease: sickle Other terms: splenectomy OR splenic OR spleen OR spleens OR hypersplenism OR splenomegaly
WHO International Clinical Trials Registry Platform (ICTRP) (searched 31 August 2017)	[Advanced Search Form] Title: splenectomy OR splenic OR spleen OR spleens OR hypersplenism OR splenomegaly Condition: sickle OR anaemia OR anemia Recruitment Status: All
MEDLINE (Ovid, searched 1966 to June 2003)	1. exp hemoglobinopathies/ 2. sickle cell.tw. 3. (hemoglobin ss or hemoglobin sc or hemoglobin c).ti,ab. 4. (haemoglobin ss or haemoglobin sc or haemoglobin c).ti,ab. 5. meniscocytosis.tw. 6. hemoglobinopath$.tw.

(Continued)

	7. haemoglobinopath$.tw.
	8. drepanocyt$.tw.
	9. thalassemia.tw.
	10.'splenic sequestration'.ti,ab.
	11. 'acute splenic sequestration cris$'.ti,ab.
	12. assc.tw.
	13. hypersplenism.tw.
	14. hypersplenism/
	15. splenomegaly/
	16. splenomegaly.tw.
	17. spleen.tw.
	18. or/1-17
	19. splenectomy/
	20. splenectomy.tw.
	21. blood transfusion/
	22. blood transfusion.tw.
	23. red cell transfusion.tw.
	24. 19 or 20 or 21 or 22 or 23
	25. 18 and 24
	26. limit 25 to human
Embase (Ovid, searched 1988 to June 2003)	1. exp hemoglobinopathies/
	2. sickle cell.tw.
	3. (hemoglobin ss or hemoglobin sc or hemoglobin c).ti,ab.
	4. (haemoglobin ss or haemoglobin sc or haemoglobin c).ti,ab.
	5. meniscocytosis.tw.
	6. hemoglobinopath$.tw.
	7. haemoglobinopath$.tw.
	8. drepanocyt$.tw.
	9. thalassemia.tw.
	10.'splenic sequestration'.ti,ab.
	11. 'acute splenic sequestration cris$'.ti,ab.
	12. assc.tw.
	13. hypersplenism.tw.
	14. hypersplenism/

(Continued)

15. splenomegaly/
16. splenomegaly.tw.
17. spleen.tw.
18. or/1-17
19. splenectomy/
20. splenectomy.tw.
21. blood transfusion/
22. blood transfusion.tw.
23. red cell transfusion.tw.
24. 19 or 20 or 21 or 22 or 23
25. 18 and 24
26. limit 25 to human

WHAT'S NEW

Date	Event	Description
8 April 2021	Review declared as stable	A search for relevant studies was undertaken on 14 August 2017. None of the identified trials were eligible for inclusion in any section of the review. No new studies are expected in this area, therefore, we are no longer planning on updating this review.

HISTORY

Protocol first published: Issue 1, 2002
Review first published: Issue 4, 2002

Date	Event	Description
12 October 2017	New citation required but conclusions have not changed	There are no trials included in the review and we have not identified any relevant trials up to August 2017. We will continue to run searches to identify any potentially relevant trials; however, we do not plan to update other sections of the review until new trials are published.
12 October 2017	New search has been performed	A search of the Cochrane Cystic Fibrosis and Genetic Disorders Haemoglobinopathies Trials Register did not identify any potentially eligible references for inclusion in any section of the review. A search of clinicaltrials.gov https://clinicaltrials.gov/ and WHO ICTRP http://apps.who.int/trialsearch/ identified 29 potentially-relevant references, which were assessed on title only and were clearly not eligible for any section of the review.
15 July 2015	New search has been performed	A search of the Cochrane Cystic Fibrosis and Genetic Disorders Haemoglobinopathies Trials Register identified six references,

Date	Event	Description
		none of which were eligible for inclusion in any section of the review. The 'Plain language summary' has been updated in line with the most recent guidelines.
15 July 2015	New citation required but conclusions have not changed	There are no trials included in the review and we have not identified any relevant trials up to June 2015. We will continue to run searches to identify any potentially relevant trals; however, we do not plan to update other sections of the review until new trials are published.
11 February 2015	Amended	Contact details updated.
11 September 2013	Review declared as stable	This review was first published in 2002 in which no trials were included. We have not identified any relevant trials up to May 2013. We therefore do not plan to update this review until new trials are published, although we will search the Group's Cystic Fibrosis Trials Register on a two-yearly cycle.
19 April 2013	New search has been performed	A search of the Cystic Fibrosis and Genetic Disorders Haemoglobinopathies Trials Register did not identify any potentially eligible trials.
19 April 2013	New citation required but conclusions have not changed	The review has been updated with minor changes made throughout.
8 October 2010	New search has been performed	A search of the Group's Haemoglobinopathies Trials Register identified no trials potentially eligible for inclusion in the review.
26 April 2010	Amended	Contact details updated.
7 November 2008	Amended	Converted to new review format.
29 August 2008	New search has been performed	A search of the Group's Haemoglobinopathies Trials Register did not identify any potentially eligible trials.
1 February 2008	New search has been performed	A search of the Group's Trials Register identified no additional trials eligible for inclusion in this review.
1 February 2008	Amended	The original 'Synopsis' has been updated with a new 'Plain language summary' in line with guidance from The Cochrane Collaboration.
1 February 2007	New search has been performed	A search of the Group's Trials Register identified no additional trials eligible for inclusion in this review.
1 December 2005	New search has been performed	A search of the Group's Trials Register identified no additional trials eligible for inclusion in this review.
1 October 2004	New search has been performed	A search of the Group's Trials Register identified no additional trials eligible for inclusion in this review.
1 July 2003	New search has been performed	No new studies were identified for inclusion in this review.

CONTRIBUTIONS OF AUTHORS

This review was conceived by the Cochrane Cystic Fibrosis and Genetic Disorders Group and designed by Dr Owusu-Ofori.

Versions up to and including 2013

Dr Owusu-Ofori, Dr Riddington and the Cochrane Cystic Fibrosis and Genetic Disorders Group conducted searches for relevant trials.

Dr Owusu-Ofori and Dr Hirst (née Riddingotn) planned to screen, appraise and abstract data for the review.

Dr Owusu-Ofori and Dr Hirst will seek additional information from authors, where necessary.

Dr Owusu-Ofori will perform data entry for future updates. Dr Owusu-Ofori and Dr Hirst will interpret the data with advice from the Cochrane Cystic Fibrosis and Genetic Disorders Group.

Dr Owusu-Ofori took the lead in the write up of the original review and the updated reviews.

Versions from 2015

Dr Owusu-Ofori took the lead in the write up of the updated reviews with input from Tracey Remmington.

DECLARATIONS OF INTEREST

Dr Shirley Owusu-Ofori: none known.

Tracey Remmington: I am the Managing Editor of the Cochrane Cystic Fibrosis and Genetic Disorders Group and work for the University of Liverpool and am funded by a grant from the National Institute for Health Research (UK).

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- No sources of support supplied

External sources

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- National Institute for Health Research, UK

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INDEX TERMS

Medical Subject Headings (MeSH)

Acute Disease; Anemia, Sickle Cell [*complications]; *Blood Transfusion; *Conservative Treatment; Recurrence; Secondary Prevention; *Splenectomy; Splenic Diseases [surgery] [*therapy]

MeSH check words

Humans