

Can Transfusion Practice in Paediatric Acute Lymphoblastic Leukaemia be Changed – A case involving a Jehovah's Witness

Dr Andrew Fletcher

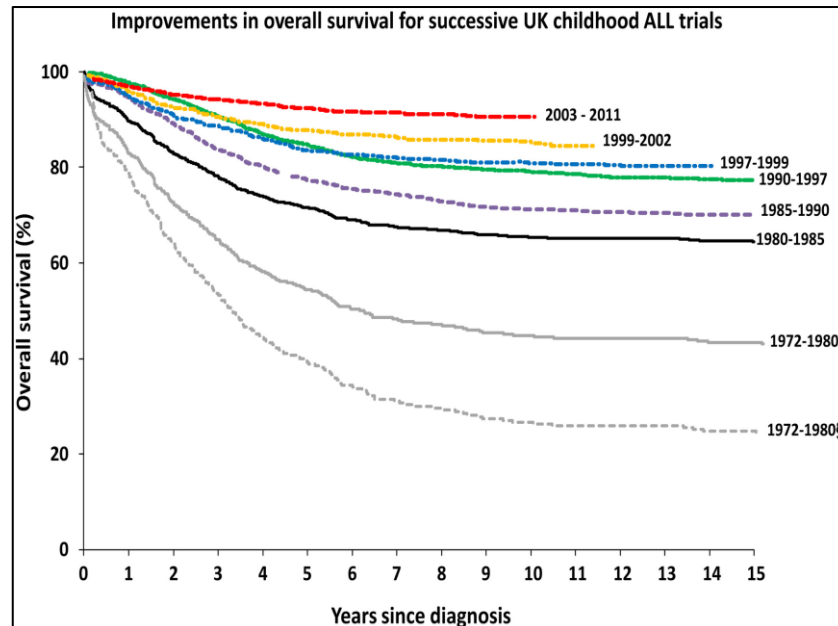
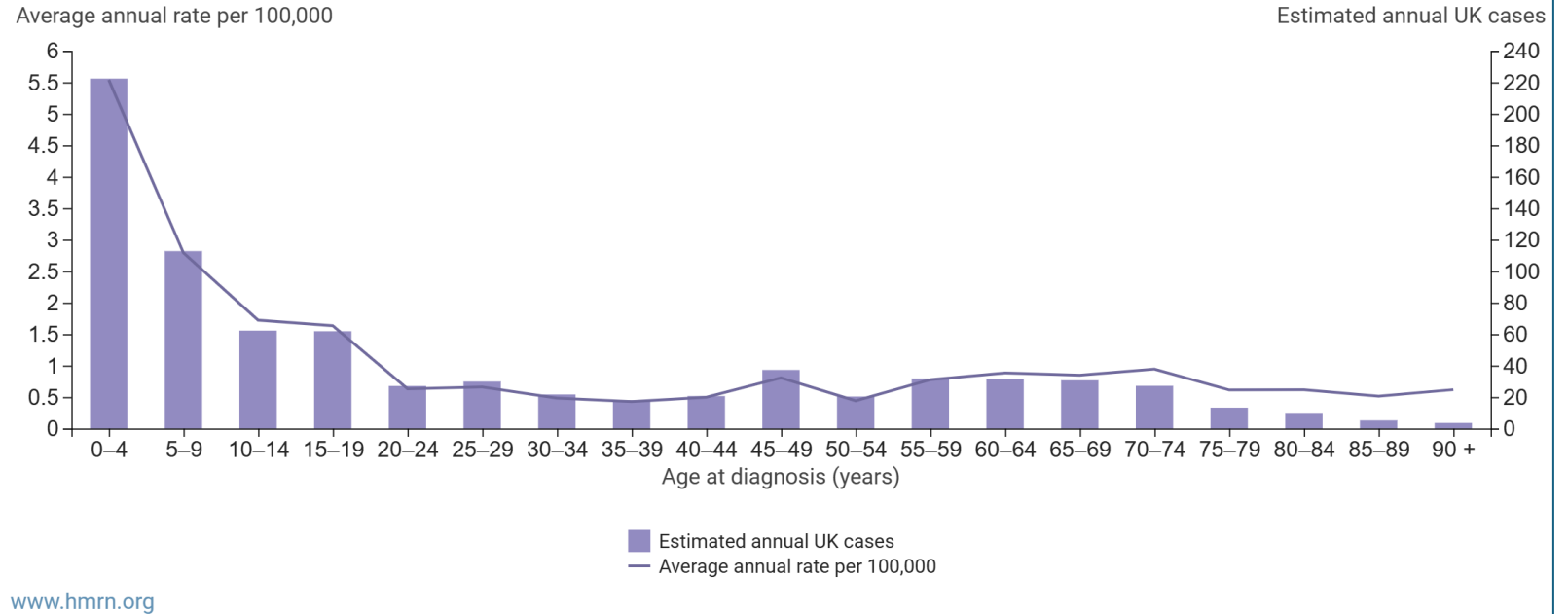
Associate Medical Director for Blood Donors and Plasma for
Medicine, NHSBT

Previously Consultant Paediatric Haematologist, NUTH

ALL

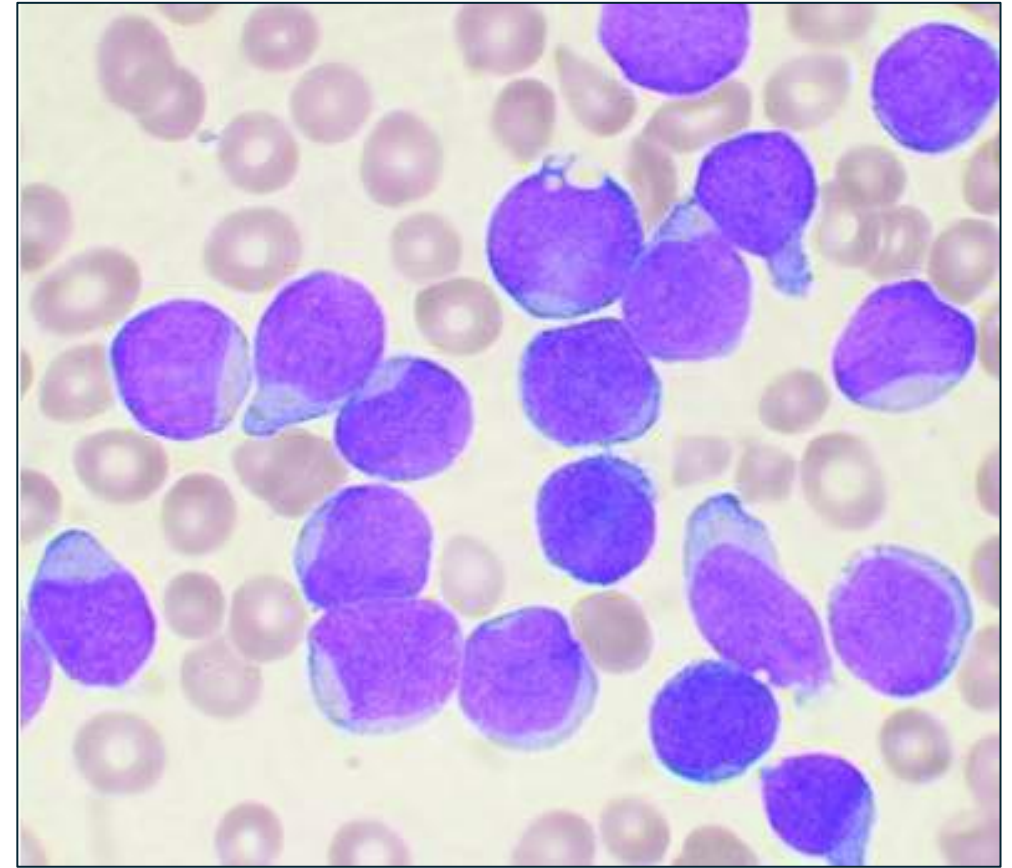
- Commonest UK Childhood Cancer
- Peak Incidence 1-10 year olds
- 3.4 per 100,000
- Survival defined by age at diagnosis, disease genetics and response to treatment
- 96% OS with chemotherapy alone

Incidence by age group



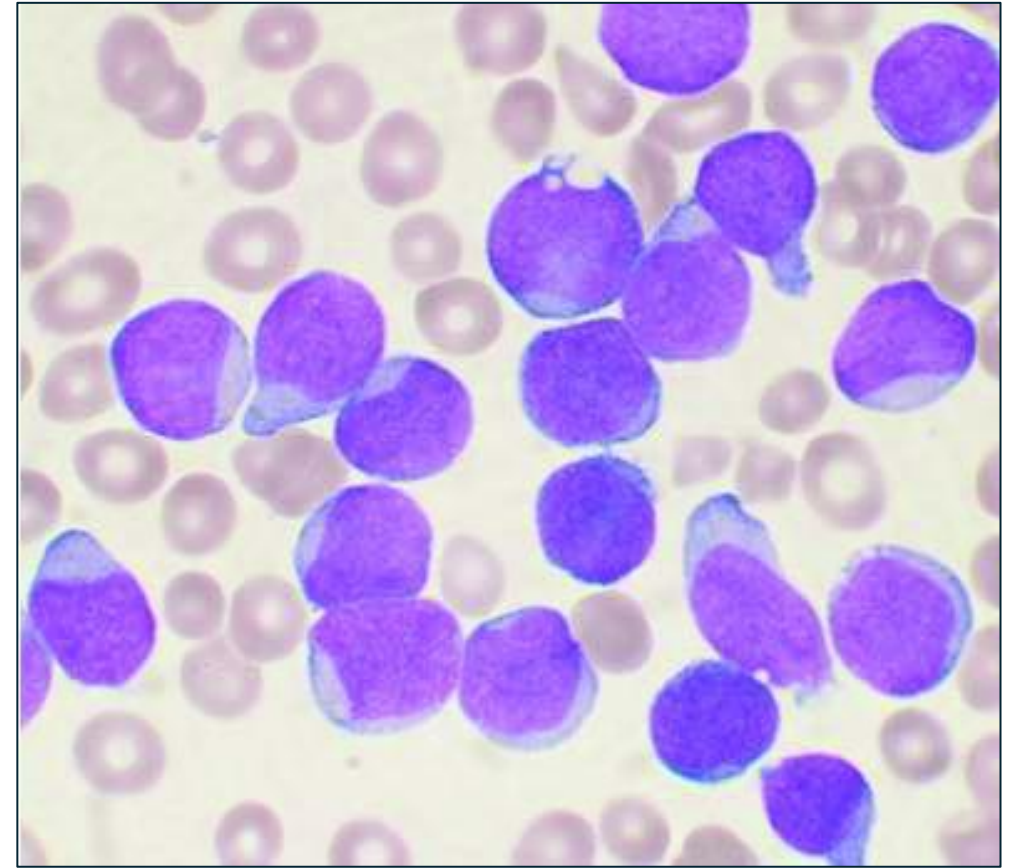
Patient

- 12 year old
- Presented with features of bone marrow failure:
 - Symptomatic anaemia, Bleeding – low platelets, febrile neutropenia
- Peripheral Blood showed circulating blasts
- Bone Marrow confirmed B-cell ALL
- Mum and Dad with child's Uncle when told about her diagnosis



Patient

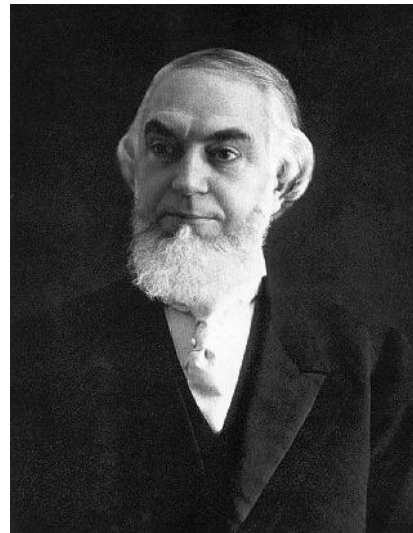
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“Before you start Dr Fletcher...We are Jehovah's Witnesses.”
Uncle was member of the local Hospital Liaison Team

Jehovah's Witnesses

- Christian denomination founded in 1881 by Charles Taze Russell
- Believe Armageddon is imminent and to prevent this God's Kingdom should be created on Earth
- Have their own Bible, the 'New World Translation'
- 9 million members in 2024, in 120,000 congregations
- Do not celebrate Christmas, Easter or Birthdays with these festivals have pagan origins



Jehovah's Witnesses – Declining Blood Products

- Genesis 9:3–4. Jehovah's rules includes:
“Every moving animal that is alive may serve as food for you...Only flesh with its life, its blood - you must not eat”
- Leviticus 17:10–15. In laying down his rule to Moses, Jehovah stated in his rules for man:
“If any man...eats any sort of blood, I will set my face against the one who is eating the blood, and I will cut him off from among his people. For the life of flesh is in the blood...because it is the blood that makes atonement by means of the life in it. That is why I have said to the Israelites: ‘None of you should eat blood.’”
- Acts 15:28–29. The Apostle James presented to the others and their followers:
“We ourselves have favoured adding no further burden to you except these necessary things: to keep abstaining from things sacrificed to idols, from blood, from what is strangles and from sexual immorality. If you carefully keep yourselves from these things, you will prosper.”

Jehovah's Witnesses

- US Study of 35 paediatric patient's families refusing blood products at diagnosis (Stevenson et al 2022):
 - 60% of those patients needing transfusion support had haematological malignancy. Of those with haematological malignancy 72% received red cells and 61% platelets
 - 18% of parents initially declined transfusion but changed their mind.
 - 36% of patients were transfused after legal intervention
- 10-12% of JWs will accept blood products (Crowe, 2019)
- 40% of paediatric cases and <25% of adult cases in literature have prolonged survival with conventional chemotherapy treatments, many having struggled through multiple lines of treatment (11 papers found so far)
- New treatments, Blinatumomab, have been effective in giving multiply relapsed patients long term survival (Nguyen, 2022)
- JW patients with ALL treated without blood products have an inferior outcome to matched controls. (Carson, 2016)
- Standard treatment in children and young adults gives 96% OS
 - Aim is to cure with first line therapy

Assumptions of Haematology Team

- You cannot get patients successfully through ALL patients without transfusions
- This young adult will get more symptomatic than younger patients
- Older patients have a higher transfusion requirement than younger/smaller ones
- Everyone needs red cell and platelet transfusions through ALL treatment
- Paediatric haematology teams will be good at patient blood management because of the risk of transfusion to patients and the volume of products they use

PBM definition from AABB

‘Patient blood management (PBM) is an evidence-based, multidisciplinary approach to caring for patients who might need a blood transfusion. PBM encompasses all aspects of the transfusion decision-making process, beginning with the initial patient evaluation and continuing through clinical management. These techniques are designed to ensure optimal patient outcomes, while maintaining the blood supply to guarantee that blood components are available for patients when they are needed.’

Proposal to MDT and Family

Standard treatment gives best options for long-term cure and minimises risk of refractory disease or relapse and need for more intensive treatment.

Administering this without transfusion support will be very difficult

Normal practice:

- Transfuse RBCs if Hb falling towards or <70 , or concerns about symptoms
- Transfuse platelets if PLT <10 and not febrile, <20 if febrile, <50 and needing procedure (line insertion), <100 and bleeding, or at any threshold and symptomatic

Proposal

- To meet family and hospital liaison team wishes to minimise transfusion in a young adult with ALL who is a JW without compromising her potential outcome of cure with first line treatment
- Only transfuse RBCs if symptomatic with anaemia
- Only transfuse platelets if symptomatic with bleeding/bruising/petechiae

Retrospective Assessment of Similar Patients

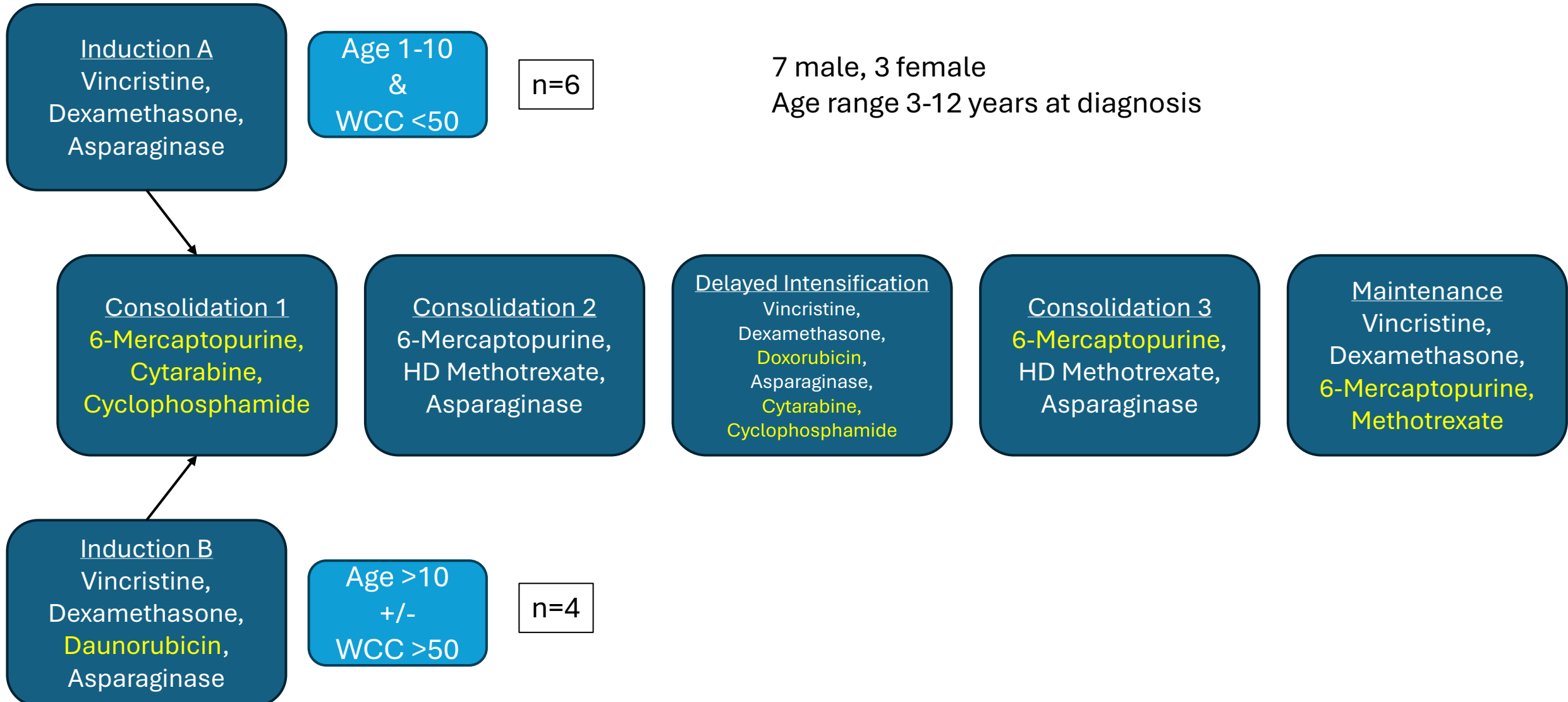
Aims

- To assess if a restrictive transfusion practice can support a patient through ALL treatment
- To assess if a restrictive transfusion practice can be adhered to
- To compare differences in total transfusion numbers and volume/kg is different using a restrictive practice compared to normal liberal practice

Method

- Compare all children treated on the ALLtogether 01 Trial receiving the same intensity treatment following induction

Patient Group



Patient Group

Induction A
Vincristine,
Dexamethasone,
Asparaginase

Age 1-10
&
WCC <50

Consolidation 1
6-Mercaptopurine,
Cytarabine,
Cyclophosphamide

Consolidation 2
6-Mercaptopurine,
HD Methotrexate,
Asparaginase

Induction B
Vincristine,
Dexamethasone,
Daunorubicin,
Asparaginase

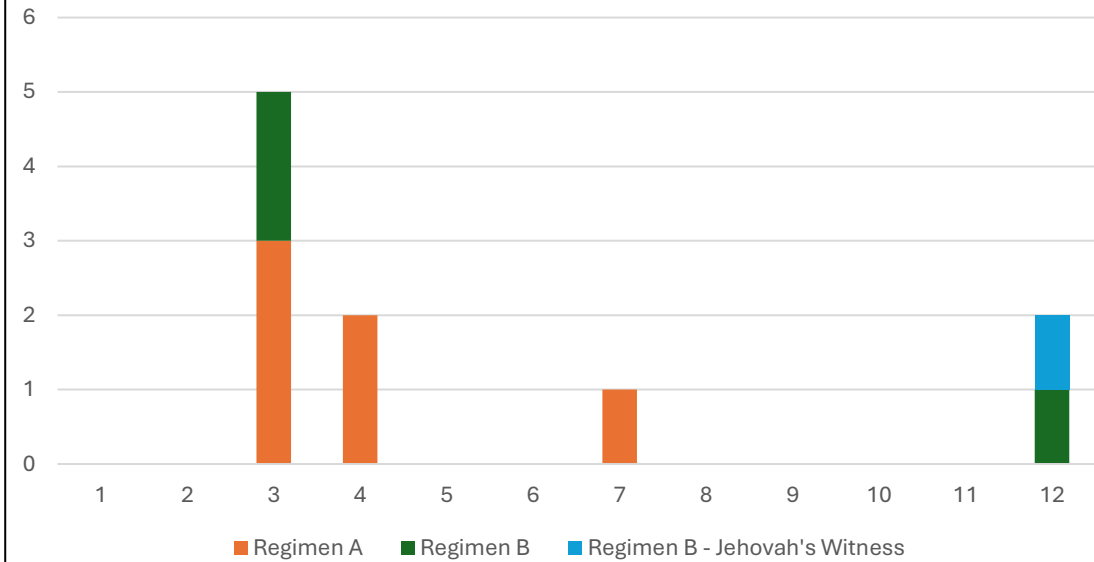
Age >10
+/-
WCC >50

Delayed Intensification
Vincristine,
Dexamethasone,
Doxorubicin,
Asparaginase,
Cytarabine,
Cyclophosphamide

Consolidation 3
6-Mercaptopurine,
HD Methotrexate,
Asparaginase

Maintenance
Vincristine,
Dexamethasone,
6-Mercaptopurine,
Methotrexate

Age at Diagnosis and Induction Regimen



Results

Induction A
Vincristine,
Dexamethasone,
Asparaginase

Age 1-10
&
WCC <50

n=6

Consolidation 1
6-Mercaptopurine,
Cytarabine,
Cyclophosphamide

Consolidation 2
6-Mercaptopurine,
HD Methotrexate,
Asparaginase

Induction B
Vincristine,
Dexamethasone,
Daunorubicin,
Asparaginase

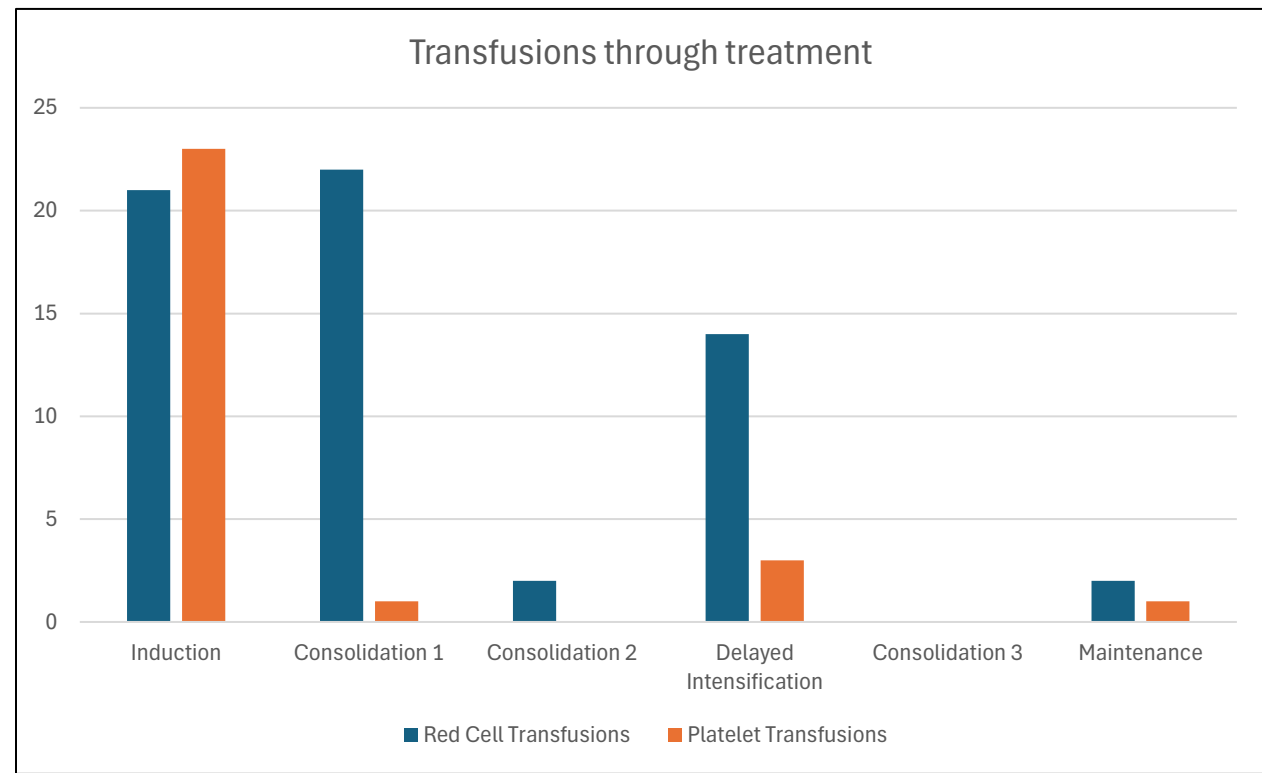
Age >10
+/-
WCC >50

n=4

Delayed Intensification
Vincristine,
Dexamethasone,
Doxorubicin,
Asparaginase,
Cytarabine,
Cyclophosphamide

Consolidation 3
6-Mercaptopurine,
HD Methotrexate,
Asparaginase

Maintenance
Vincristine,
Dexamethasone,
6-Mercaptopurine,
Methotrexate



Results

Induction A
Vincristine,
Dexamethasone,
Asparaginase

Induction B
Vincristine,
Dexamethasone,
Daunorubicin,
Asparaginase

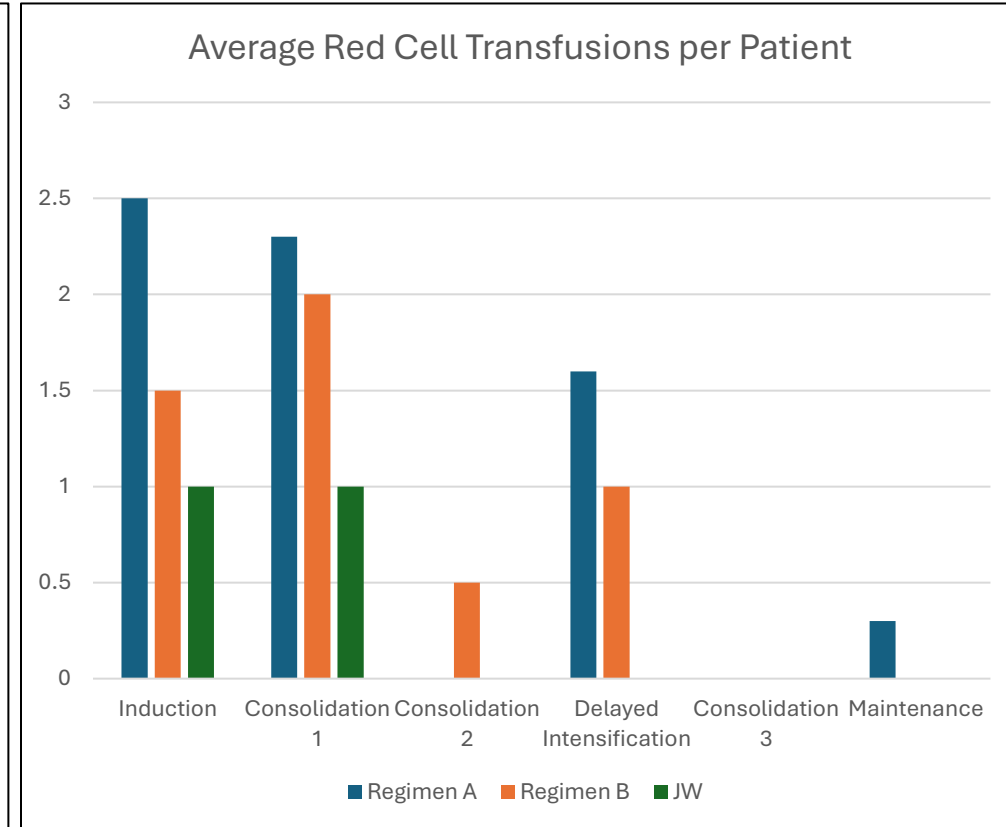
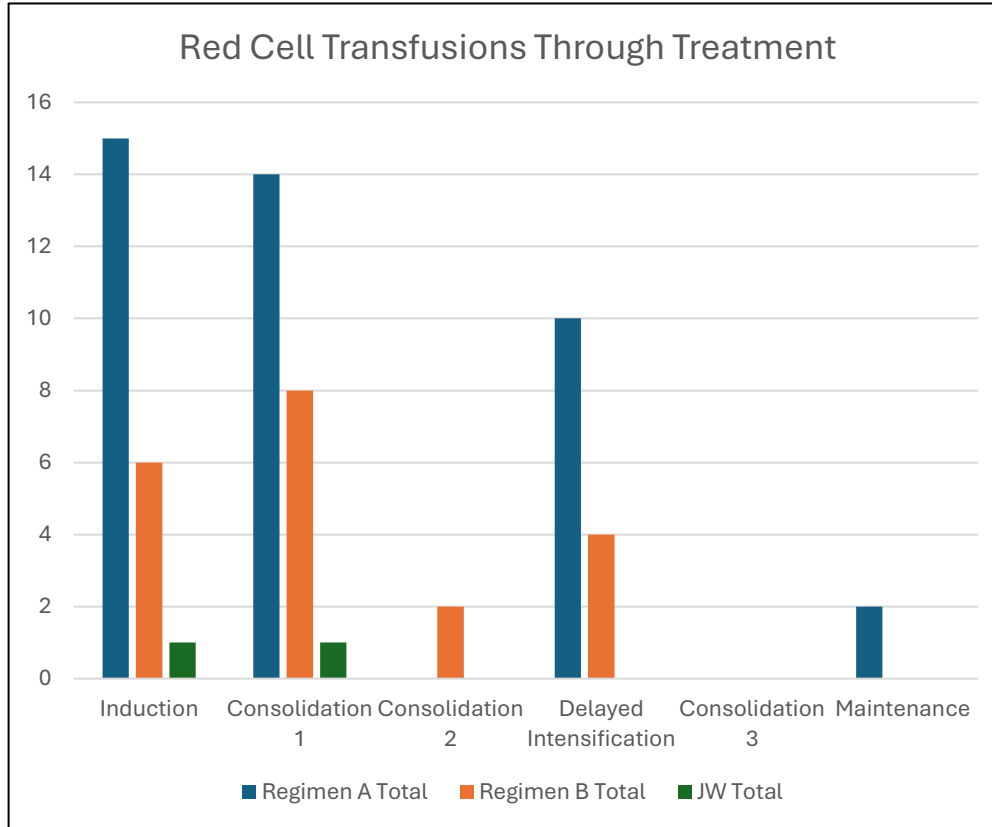
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Asparaginase

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Vincristine,
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Cyclophosphamide

Consolidation 3
6-Mercaptopurine,
HD Methotrexate,
Asparaginase

Maintenance
Vincristine,
Dexamethasone,
6-Mercaptopurine,
Methotrexate



Results

Induction A
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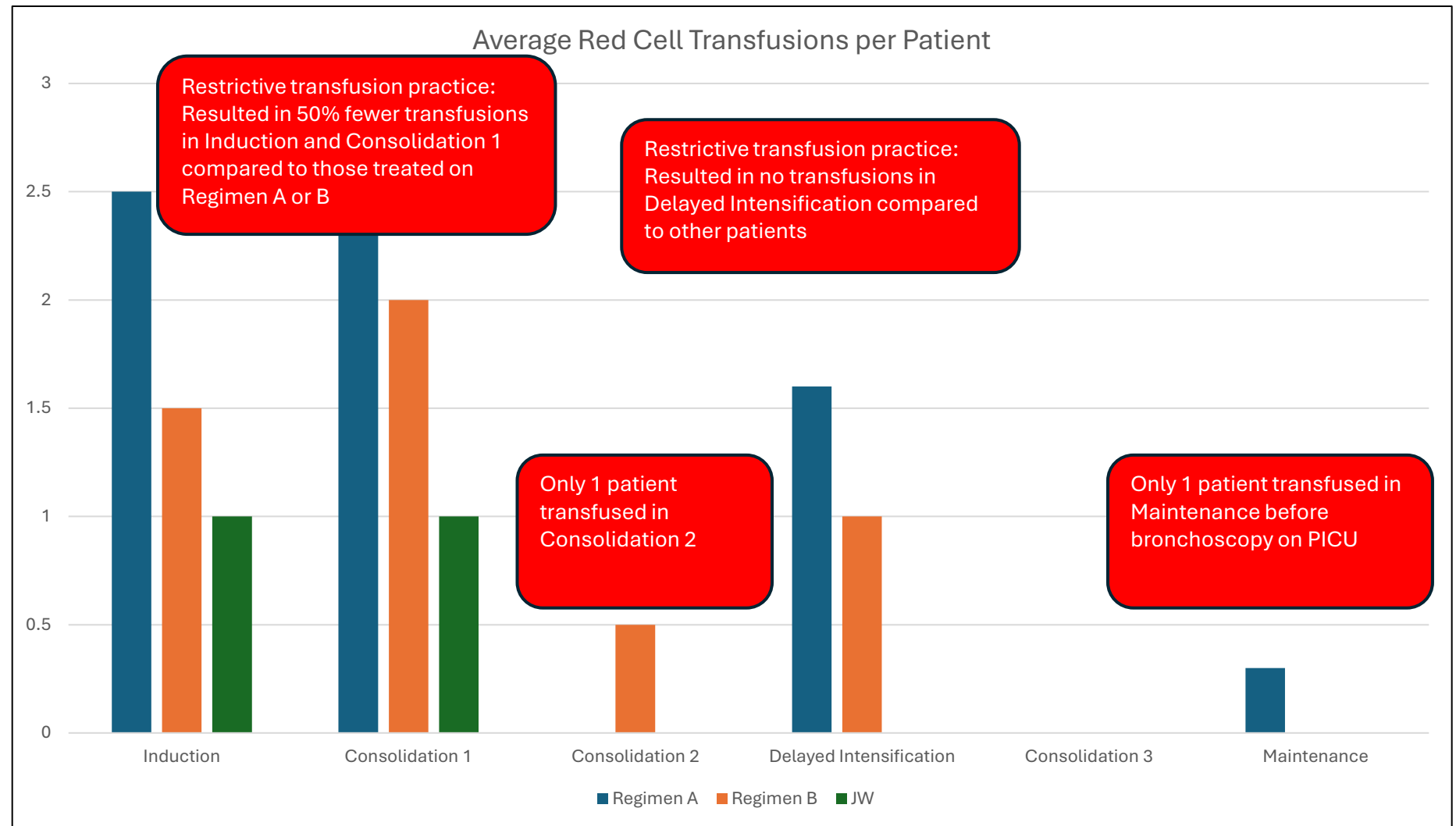
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Vincristine,
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Asparaginase,
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Cyclophosphamide

Consolidation 2
6-Mercaptopurine,
HD Methotrexate,
Asparaginase

Maintenance
Vincristine,
Dexamethasone,
6-Mercaptopurine,
Methotrexate



Indications for Transfusion

Haemoglobin leading to transfusion – Threshold <70 or symptomatic

	Regimen A	Regimen B	Jehovah's Witness	Comments
Induction	30-77	40-72	71	62% asymptomatic
Consolidation 1	52-76	62-73	47	60% asymptomatic
Consolidation 2	-	68-74	-	100% asymptomatic
Delayed Intensification	45-73	63-87	-	71% asymptomatic
Consolidation 3	-	-	-	-
Maintenance	57-75	-	-	Chest infection on PICU

1 Transfusion given to JW patient on a Friday 'in case she needed one over the weekend'

5 Transfusions – “Looked Pale” but patient asymptomatic, Hb range 52-87

Risk of silent stroke/cerebral infarct if Hb <55 – only 6/38 transfusions in asymptomatic patients

Cost of transfusion in 10 patients with ALL

- 1 transfusion reaction (<2%) – Urticaria and wheeze while on PICU with neutropenic sepsis
- 61 Red Cell Transfusions given = 63 units
- Total cost of red cells based on current NHSBT price: £11,578
- 28 Platelets Transfusions given
- Total cost of platelets based on current NHSBT price: £7706
- 31 transfusions give to those with Hb>60 and asymptomatic so could have saved 31 units of red cells totalling £5,697 in 10 patients over an 18-month period, just assessing the intermediate risk patients

Conclusions

- Outcome of ALL treatment without transfusion support reduces outcome significantly (96% OS vs 40% OS of paediatric cases in literature)
- Transfusions are most commonly given during induction, Consolidation 1 and Delayed Intensification – when anaemic due to disease at presentation or following cytoreductive chemo
- The patient who was a JW only needed a total of 2 transfusions, much less than those on the same or less intensive treatments
- Restrictive transfusion practice seems to work in children with ALL
- Transfusion thresholds could be lowered for red cells but must take into consideration risk of silent stroke/infarcts, coexisting problems and symptoms
- Reduction in transfusion will save money for Trusts and reduce pressure on NHSBT blood supply
- New therapeutic options, Blinatumomab, should be assessed in front line situations and may allow further reduction in transfusions

Recommendations

- Clinical assessment *and* haemoglobin quantification needed before each transfusion
- Better definition of symptomatic is needed and should not include “looks pale” or “tired”
- Red cell transfusion threshold could be reduced to 60
- Approach HaemStar program for help to collect national retrospective data
- Approach ALLtogether 02 Trials team to consider addition of transfusion management into bolt on trial

Any Questions?