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Can I go home now? The safety and efficacy of a new UK paediatric febrile neutropenia protocol for risk-stratified early discharge on oral antibiotics

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ABSTRACT

Objective To evaluate a new protocol of risk stratification and early discharge for children with febrile neutropenia (FN).

Design Prospective service evaluation from 17 April 2020 to 16 April 2021.

Setting 13 specialist centres in the UK.

Patients 405 children presenting with FN.

Intervention All children received intravenous antibiotics at presentation. Risk stratification was determined using the Australian-UK-Swiss (AUS) rule and eligibility for homecare assessed using criteria including disease, chemotherapy, presenting features and social factors. Those eligible for homecare could be discharged on oral antibiotics after a period of observation proportional to their risk group.

Main outcome measures Median duration of admission and of intravenous antibiotics, and percentage of patients with positive blood cultures, significant infection, readmission within 7 days of initial presentation, intensive care unit (ICU) admission, death from infection and death from other causes.

Results 13 centres contributed 729 initial presentations of 405 patients. AUS rule scores were positively correlated with positive blood cultures, significant infection, ICU admission and death. 20% of children were eligible for homecare with oral antibiotics, of which 55% were low risk (AUS 0–1). 46% low-risk homecare eligible patients were discharged by 24 hours vs 2% homecare ineligible. Homecare readmission rates were 14% overall and 16% for low-risk cases (similar to a meta-analysis of previous studies). No child eligible for homecare was admitted to ICU or died.

Conclusions Use of the AUS rule and homecare criteria allow for safe early outpatient management of children with FN.

INTRODUCTION

The management of febrile neutropenia (FN) is a vital part of paediatric oncology/haematology practice and constitutes a significant proportion of supportive care workload. Within the UK, care of a child with cancer is coordinated by one of 20 principal treatment centres (PTCs), with over 100 paediatric oncology shared care centres (POSCUs) providing defined aspects of care such as initial management of FN closer to the child's home. Historically, children with FN episodes have been

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Febrile neutropenia (FN) is a common emergency presentation for children with cancer, but significant morbidity and mortality is rare.
- ⇒ Reducing length of hospital admissions for those at low risk of complications is important to patients and their families.
- ⇒ Multiple risk stratification rules exist to identify those children at low risk of complications, but none are both sensitive and specific.

WHAT THIS STUDY ADDS

- ⇒ The Australian-UK-Swiss (AUS) rule and homecare criteria identify children that can be safely discharged on oral antibiotics and parental monitoring.
- ⇒ Selected children with low-risk FN episodes require <24 hours of inpatient care.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ The Children's Cancer and Leukaemia Group continues to recommend the AUS-based homecare protocol as a safe way to manage low-risk FN episodes beyond the COVID-19 pandemic.
- ⇒ Future research should focus on identifying barriers to implementing homecare protocols, involving both professionals, patients and parents.

managed with inpatient antibiotic treatment until 'negative' blood cultures results were available and the fever has defervesced. A 2017 audit of UK practice found that for patients who were outpatients at presentation of FN, the median duration of admission was 3 days.¹

Early in the COVID-19 pandemic, actual and anticipated demands for hospital bed use were higher than those available within some areas.² When the risks of SARS-CoV2 infection in children with cancer were unknown, many families and professionals were keen to reduce stays, reducing the risk of hospital-acquired infection.

In response, the UK's Children's Cancer and Leukaemia Group (CCLG) published new national guidance for the management of FN. They advised



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using the three-item Australia-UK-Swiss (AUS) rule to risk-stratify patients and identify those who could be safely discharged home after a shorter duration of intravenous antibiotics. The AUS rule was developed in a large multicentre, prospective study, and validated in the international PICNICC+ dataset.^{3,4} Combined with an associated management pathway including homecare criteria, it was piloted in Melbourne Australia using an ambulatory intravenous antibiotic regimen.⁵ The programme was safe, resulted in significant reduction in bed occupancy and up to \$A12 000 lower healthcare costs per patient.⁶ The CCLG guidance was based on this programme, but used an oral antibiotic regimen, in line with National Institute for Health and Care Excellence (NICE) guidelines.⁷ This approach is also supported by the evidence that the majority of clinically significant positive blood cultures in this population are identified within 24 hours of the sample being taken.⁸

The new CCLG guidance was a significant change in practice, and to provide quality assurance to centres choosing to adopt this approach, we performed a 1-year prospective service evaluation designed to assess safety and efficacy.

METHODS

Overview of the guidelines

FN was defined as per NICE guidelines⁹ (neutrophils $\leq 0.5 \times 10^9/L$ and either fever $\geq 38^\circ C$ or clinical evidence of sepsis).⁷ It was recommended that all patients (both inpatient and outpatient) with FN received first-line intravenous antibiotics, as per local policy within 1 hour of arrival to hospital or inpatient febrile episode. The patient's AUS rule score was used to determine the minimum recommended period of intravenous antibiotics and inpatient observation (table 1). After initial inpatient treatment, children who met all eligibility criteria in table 1 could be discharged to a homecare programme.

Homecare involved treatment with oral antibiotics, parents taking their child's temperature every 4–6 hours when awake and daily clinical reviews via telephone until antibiotics were stopped. Prior to discharge, patients and their families received education about the homecare programme and must have tolerated one dose of oral antibiotics.

The suggested oral antibiotic regimen was ciprofloxacin plus co-amoxiclav (or clarithromycin if allergic to penicillin). Antibiotics could be stopped if that patient was clinically well; had been afebrile (temperature $< 38^\circ C$) for at least 24 hours; had negative blood cultures and the absence of a need for rationalising and/or continuation of antibiotics. Reasons for further medical review and/or admission are given in online supplemental table 1.

The CCLG low-risk FN programme modified the implementation toolkit from Melbourne.¹⁰ The guidance provided centres and clinicians with the option to adapt the recommendations based on local practice and service pressures. Children with homecare eligible episodes were not mandated to be sent home after the recommended period of observation and treating team discretion was included in the eligibility criteria.

Service evaluation

A service evaluation plan was developed prior to the introduction of the guideline and publicised via the CCLG website.¹¹ Pseudo-anonymised episode data relating to predefined outcomes was contemporaneously collected via Qualtrics software (online supplemental file). Centres were encouraged to submit data at discharge or 7 days of presentation, whichever was sooner. A separate data collection form was submitted at representation.

Table 1 AUS rule variables and homecare eligibility criteria

AUS rule	Yes	No
Preceding chemotherapy more intensive than ALL maintenance	1	0
Total white cell count $< 0.3 \times 10^9/L$	1	0
Platelet $< 50 \times 10^9/L$	1	0
Minimum observation period (if clinically stable and fulfil homecare criteria)		
AUS=0	AUS=1	AUS=2
4–8 hours	4–24 hours	24 hours
		AUS=3
		48 hours
Eligibility criteria for homecare		
Disease status: leukaemia/lymphoma in remission (as per last bone marrow aspirate or solid tumour stable/responding (as per oncologist)		
Low-risk disease group: NOT ANY OF—ALL induction, or acute infant leukaemias, acute myeloid leukaemia, postallogeneic haematopoietic stem cell transplant within 3 months or still on immunosuppression, congenital immunodeficiency, aplastic anaemia, Down syndrome Centres may have particular local concerns about other specific diagnosis		
No confirmed focus of infection requiring inpatient care*		
No medical complication requiring inpatient care†		
No severe sepsis at FN presentation‡		
Availability of a 24-hour caregiver		
Good education of patient and carer on reportable symptoms		
Availability of a telephone		
Within 1 hour of treating hospital		
Treating team preference		
No previous history of non-compliance with medical care		
Variations may consider excluding ANY patient who has received a fluid bolus, or had a past unplanned admission to ICU. If well, presence of infiltrates on CXR may not be a contraindication to oral antibiotic therapy. At the time of writing, SARS-CoV2/COVID-19-positive swabs should NOT NECESSARILY be a contraindication to homecare. *Including, but not limited to, central venous access device site infection, cellulitis, perianal cellulitis or pain, significant pneumonia, infection with multidrug-resistant bacteria. †Including, but not limited to, pain requiring intravenous analgesia, poor oral intake or excessive loss requiring intravenous hydration; respiratory distress or oxygen requirement. ‡Severe sepsis includes any of (i) altered conscious state, (ii) inotrope requirement, (iii) fluid bolus requirement > 40 mL/kg or (iv) respiratory support requirement. ALL, acute lymphoblastic leukaemia; AUS, Australian-UK-Swiss; CXR, chest X-ray; FN, febrile neutropenia; ICU, intensive care unit.		

The Paediatric Oncology Trainees Group and individual clinical leads were used to identify local data collection leads. Centres were encouraged to submit data from the date they implemented the new guidance, but implementation of the guideline, and participation in the service evaluation, was at the discretion of individual centres.

Teams were asked to contact the protocol team urgently regarding any serious adverse events related to infection (ICU admission or death) during this period. Stopping criteria were identified prior to implementation of the protocol (online supplemental table 2).

Data were collected on initial episodes from 17 April 2020 to 16 April 2021. Data submission was closed on 7 May 2021.

Analysis

The following prespecified core outcomes were analysed monthly, stratified by AUS rule score: median duration from start of FN episode (attendance at hospital if outpatient, onset of signs/symptoms if inpatient) to discharge, percentages of patients with any positive blood cultures, significant infection requiring intravenous antibiotics, representation within 7 days of initial

episode, readmission within 7 days of initial episode, ICU admission, death from infection and death from other causes during that episode. The percentage of cases eligible for homecare as per table 1 and stratified by centre was calculated. Fisher's exact test was used to determine if the percentage of homecare eligible patients with an AUS rule 0–1 subsequently readmitted was significantly above 15% (expected percentage from systematic review of similar approaches).¹² Duration of intravenous antibiotics was added to the required dataset 6 weeks after the start of the project, and included in subsequent analyses. Hypothesis tests were considered statistically significant if $p < 0.05$.

Analyses were performed using a custom script in the R statistical environment using the 'dplyr', 'knitr', 'readxl', 'janitor', 'scales', 'reshape2', 'ggplot2', 'qwraps2' and 'ggalluvial' packages. The script was run 13 times over the year and all outputs shared with the study authors and contributors.

Prior to final analysis, data were assessed for inconsistencies and local centres contacted to provide clarification for selected episodes. If the inconsistency could not be resolved, the relevant outcome for the episode was omitted from analysis.

RESULTS

Thirteen centres (5 PTCs and 8 POSCUs) contributed 729 initial FN episodes in 405 patients (range 3–203 episodes/centre). Six hundred and six episodes (83%) were from PTCs. There were a further 79 episodes within 7 days of an initial episode, 64 of which were representations following discharge after the initial episode and 15 where the child remained an inpatient after an episode resolved and then developed further FN symptoms. Not all centres contributed cases throughout the whole study either because they did not initially implement the protocol and/or stopped submitting cases (online supplemental figure 1); 97% episodes had data submitted for all the initial prespecified core outcomes.

The most common underlying diagnosis was acute lymphoblastic leukaemia (ALL) (online supplemental table 3). The diagnostic label of some patients changed during the study due to treatment decisions (eg, ALL where the patient then went on to have haematopoietic stem cell transplant (HSCT)). There were significant differences in the cohorts from different centres with respect to diagnosis and AUS score distribution (online supplemental tables 4 and 5, Fisher's exact test $p < 1 \times 10^{-7}$ for both).

The core outcomes for all patients are summarised in table 2. AUS rule scores were positively correlated with percentages of

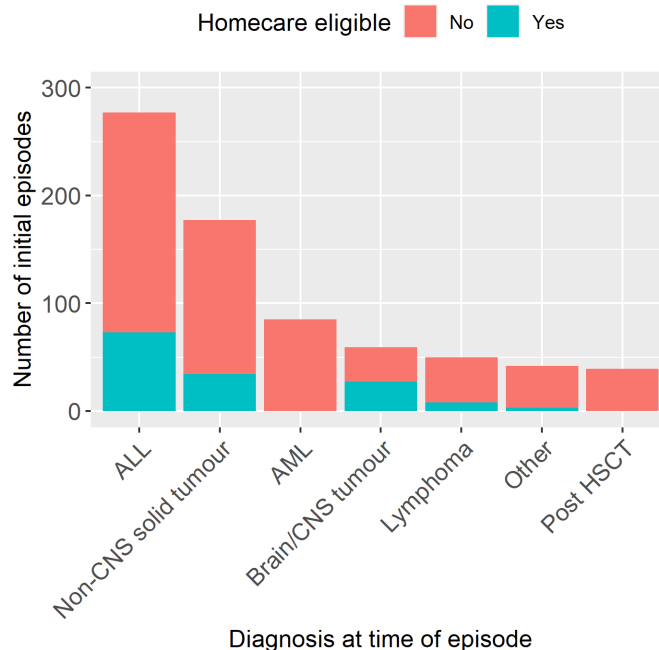


Figure 1 Diagnosis at time of febrile neutropenia episode. ALL, acute lymphoblastic leukaemia; AML, acute myeloid leukaemia; CNS central nervous system; HSCT, haematopoietic stem cell transplant. N=729.

positive blood cultures, significant infections and ICU admission and median duration of intravenous antibiotics.

A total of 145 initial episodes (20%) were eligible for homecare with oral antibiotics (range 0%–42%/centre) (online supplemental figure 2). As some disease groups were excluded from homecare (see table 1), the underlying diagnoses of children with a homecare-eligible episode were different to those ineligible (figure 1). Some episodes had multiple reasons recorded for ineligibility while others just one (figure 2). Importantly, there were cases where each of the five criteria were the only reason for ineligibility (ie, non-redundancy of eligibility criteria). Four centres specified additional diagnoses that were considered high risk. These included Philadelphia-positive ALL (two centres), high-risk neuroblastoma during COJEC induction (three centres), postautologous HSCT (one centre) and all sarcomas (two centres). Clinician preference was a reason for

Table 2 Core outcomes stratified by AUS score

	AUS: 0 (n=72)	AUS: 1 (n=230)	AUS: 2 (n=243)	AUS: 3 (n=186)
Duration of intravenous antibiotics (days) n; median (IQR)	69; 3 (1, 5)	209; 3 (2, 6)	216; 4 (3, 8)	169; 7 (3, 11)
Duration from episode to discharge (hours) n; median (IQR)	71; 72 (28, 228)	226; 96 (52, 192)	238; 120 (72, 240)	178; 192 (78, 336)
Outcomes				
Positive blood culture (excl contaminants)	12 (17%)	36/229 (16%)	49 (20%)	57 (31%)
Significant infection requiring intravenous antibiotics	13 (18%)	29/229 (13%)	56 (23%)	57 (31%)
Representation within 7 days	5 (7%)	25 (11%)	12 (5%)	17 (9%)
Readmission within 7 days	5 (7%)	22 (10%)	11 (5%)	16 (9%)
ICU admission	0 (0%)	2/229 (1%)	4 (2%)	8 (4%)
Death from infection	0 (0%)	0/229 (0%)	0 (0%)	2 (1%)
Death from other cause	0 (0%)	0/229 (0%)	3 (1%)	2 (1%)

All data are count (%), unless otherwise specified.
AUS, Australian-UK-Swiss; ICU, intensive care unit.

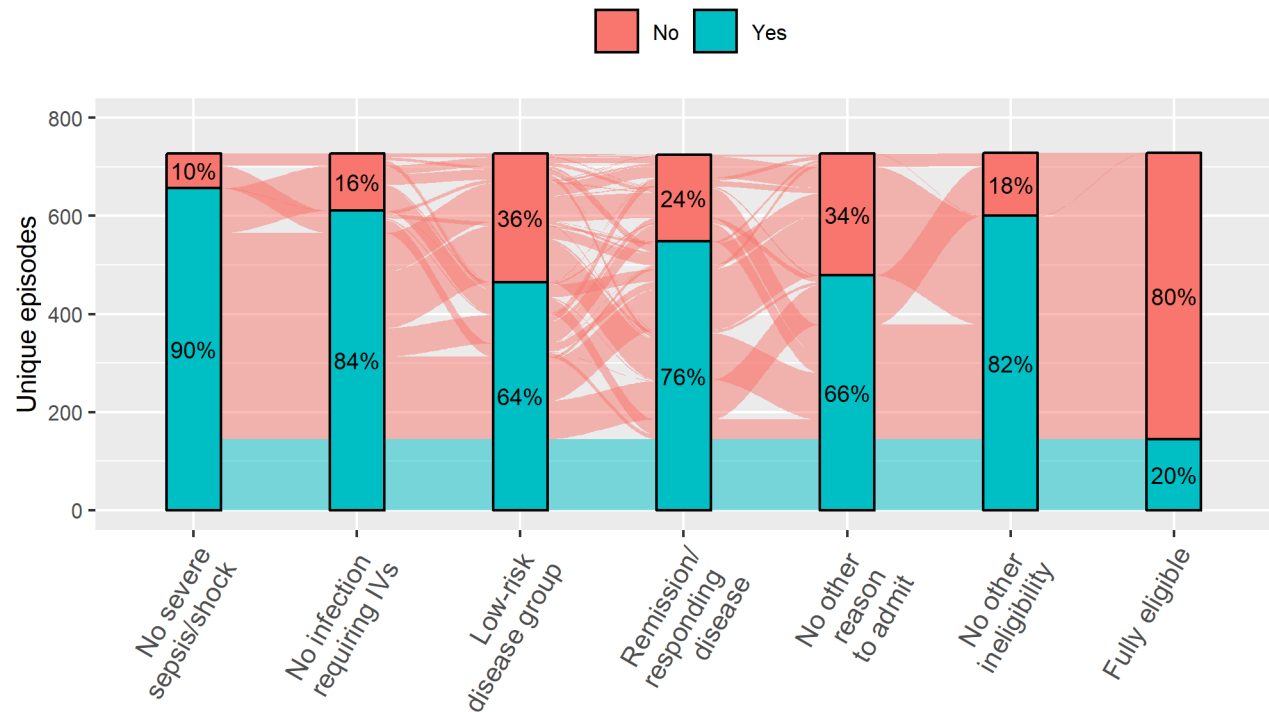


Figure 2 Reasons for non-eligibility. Bars summarise percentage meeting each eligibility criteria. Flows between bars represent individual episodes coloured by overall eligibility. Flow widths are proportional to the number of episodes. N=729.

ineligibility in 71 initial episodes; in 38 (5.2%) of these it was the only reason for ineligibility.

Duration from the start of FN episode to discharge was significantly lower in those eligible for homecare ($p < 0.001$ Mann-Whitney U test). Median duration of admission stratified by AUS rule score was 24, 32, 58 and 70 hours for AUS 0–3 respectively in those eligible compared with 72, 96, 120 and 192 hours median duration overall (figure 3). Forty-eight per cent low-risk (AUS 0–1) homecare eligible episodes were discharged within 24 hours, compared with 2% AUS 0–1 but homecare ineligible.

Those eligible for homecare were more likely to be low risk compared with those that were not (54% vs 37%, respectively, χ^2 test $p = 0.0003$).

Sixty-four patients represented within 7 days of the initial episode (23 homecare eligible, 41 ineligible and therefore received standard care prior to representation). A further 15 patients remained inpatients and had another FN episode within 7 days and were excluded from analysis. Reasons for representation are described in online supplemental table 6 and were not significantly different between those eligible for homecare and those that were not (Fisher's exact test $p = 0.111$); 23/145 (14%) homecare eligible episodes represented within 7 days, of which, 20 (90%) were readmitted. Readmission rates were 16% in the low-risk group (AUS 0–1), which was not different to the expected rate of 15% based on a meta-analysis of previous studies of ambulatory/oral regimens for low-risk patients (binomial exact test $p = 0.754$).⁷

Overall, 14 FN episodes resulted in admission to ICU and 7 children died during that inpatient episode (2 of infection, 5 of other causes). No child eligible for homecare with AUS score 0–1 went to ICU or died within 7 days of the episode. No representation within 7 days of discharge resulted in ICU admission or death.

There were 172 (21%) FN episodes with at least one documented positive blood culture (excluding contaminants as

defined by the treating team). One hundred ninety organisms were identified, of which 39% were Gram-negative organisms (58% enterobacteriales, 15% *Pseudomonas*, 23% others and 4% unspecified), and 61% were Gram-positive (25%

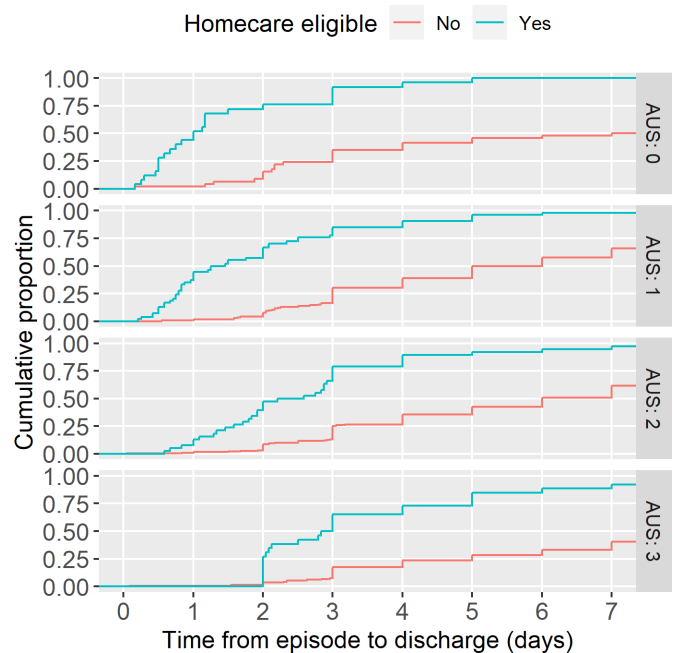


Figure 3 Duration of admission. Empirical cumulative distribution function for length of stay from time of febrile neutropenia episode to hospital discharge faceted by Australian-UK-Swiss (AUS) score. Data only for those alive at time of discharge and censored beyond 7 days as centres were asked to submit episodes after 7 days of inpatient stay. N=722

coagulase-negative staphylococci (CoNS) and 12% viridans streptococci) (online supplemental table 7). In children eligible for homecare, there were a total of 15 positive blood cultures (10 at initial presentation, 5 at representation); 5/15 (33%) were Gram-negative, but 8/15 (53%) were CoNS.

None of the criteria for stopping the project were met. A sensitivity analysis with one episode per patient, selected at random, did not show important differences in the core outcomes (online supplemental table 8).

DISCUSSION

This service evaluation assessed new national guidance developed responsively at the outbreak of the COVID-19 pandemic, to use the AUS rule as a means of safely determining which patients with FN can be managed with homecare. The direct impact of COVID-19 infection in children with cancer has been described elsewhere.^{13 14}

Twenty per cent of episodes were eligible for homecare, none of which resulted in ICU admission or death. This adds to the growing data suggesting that there is a group of patients with FN who can be safely managed at home.

The percentage of episodes identified as low risk (AUS 0–1) was 41.4% in this study, compared with 44% in the Australian and European PICNICC datasets. There was a greater chance of significant infection with higher AUS values, showing consistency of the rule's performance across time points and geographical locations.^{3 4} The rate of readmission following early discharge was consistent with that described within a meta-analysis of previously published data,¹² an Australian implementation study⁵ and with the rate of readmission reported in the CCLG's 2017 audit of FN within the UK (where patients were discharged after a longer period of hospital admission).¹

A previous study found parents desire shorter courses of intravenous antibiotics and are willing to accept a chance of readmission.^{15 16} It was shown parents view the use of risk stratification positively and would like the communication of their child's risk to then come to a shared decision about preferred place of care for the FN episode. Data from Australia collected during the COVID-19 pandemic (after the implementation of the new UK guidance) found that parents and professionals were even more supportive of home-based care of low-risk FN based on the AUS rule than before.¹⁷

We found variation in the percentage of children eligible for homecare in the different centres. This could be due to differences in the patient cohorts (impacting on the percentage meeting eligibility criteria) and clinician's anxiety about early discharge.^{15 16} The duration of inpatient stay for some AUS 0–1 homecare episodes was longer than recommended. This may represent logistical barriers to discharge or uncertainty/anxiety from the treating team about the new protocol. The latter is supported by our finding that 5% of episodes were ineligible for homecare due to treating team preference alone, despite an extensive list of other reasons for ineligibility.

Within this dataset, most representations after discharge with FN (in both homecare eligible and ineligible episodes) resulted in readmission to hospital, although this was not required by the guideline. This may reflect caution of healthcare professionals who are used to managing this population as inpatients. Only around a quarter of these episodes had a significant infection requiring antibiotics, and none resulted in ICU admission or death.

It is not possible to draw conclusions about total duration of stay for all episodes as duration was capped at 7 days. This was

a deliberate decision: at the time of the launch of the new guidance, the focus was on quick turnaround of safety data on early discharge to key stakeholders.

The rate of bacteraemia found in this study is higher than that seen in the AUS rule derivation study,⁴ with differences in the handling of contaminants a likely contributor. The criteria for submission of blood culture results was 'any positive blood cultures (excluding contaminants)'. No further definition of a contaminant was detailed. Contributors were not always directly involved in the care of the patient during the episode and so blood culture results submitted may not have been clinically significant. This 'overcalling' of infections further supports this approach as being safe.

Strengths and limitations

The main limitation is some relevant episodes may not have been submitted. The impact of this reporting bias was minimised by using a standardised entry form requiring information easily gained from medical notes, encouraging early data collection and circulating regular interim analyses to encourage submission. Consistent with this, most centres had a consistent number of cases over time.

We did not ask whether children were discharged to homecare, only whether they were eligible. It is therefore plausible that some notionally homecare eligible patients discharged after 36–48 hours were a standard discharge after confirmation of negative blood cultures.

Our study included only a minority of UK centres, perhaps reflecting differences in priorities and capacity to implement significant changes during a pandemic, or other barriers to implementation that we hope to identify in future studies.

Finally, we did not collect whether episodes had started as inpatients or outpatients so direct comparison to previous CCLG audits of purely outpatient episodes is not possible.

Conclusions

Using the AUS rule and homecare criteria identifies children who can be safely discharged on oral antibiotics. Further research in reducing therapy for children with FN should focus on whether this is safe for a greater proportion of children, the best timing for discharge and how to support centres in implementing homecare regimens. Our findings have been shared within the CCLG supportive care group; we anticipate more centres will implement the guidance and a follow-up evaluation is planned.

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Patient consent for publication Not applicable.

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Supplementary Materials

Supplementary Table 1 - reason for review

Reasons for medical review include:

- Ongoing fever (>72 hours from presentation) or new fever after being afebrile for 24 hours
- Feeling unwell/new symptoms and signs
- Parental concern
- Significant decrease in oral intake or significant increase in output (vomiting and diarrhoea)
- Positive blood culture or new infection identified after transfer home
- Severe or persistent pain
- Chills/rigor/shaking
- Not afebrile by day 5 of home-based care

Reasons for re-admission include:

- Fever > 38°C beyond 5 days from the start of the febrile neutropenic episode
- Clinically unwell / unstable
- Infection requiring in-patient care

Supplementary Table 2 - Criteria for stopping service evaluation

RED CRITERIA: IMMEDIATE DISCONTINUATION AND REVERTING TO ORIGINAL POLICY	AMBER CRITERIA: MODIFICATION OF MINIMUM ADMISSION DURATIONS
<ul style="list-style-type: none"> • Avoidable death or ICU admission from bacterial sepsis in a 0/1 score group discharged before 36h 	<ul style="list-style-type: none"> • High numbers of re-admissions (>90%ile expected) in the 0/1 score group discharged before 36h: expected value 15% • High numbers of re-presentations within the first 24h after presentation (>50%)

Supplementary Table 3 - Diagnosis at first recorded episode

Diagnosis at 1st recorded episode	n	% total
Acute lymphoblastic leukaemia	169	41.7%
Acute myeloid leukaemia	33	8.1%
Brain/Central Nervous System tumour	34	8.4%
Ewing's sarcoma	21	5.2%
Germ cell tumour	3	0.7%
Hepatoblastoma	5	1.3%
High risk neuroblastoma	15	3.7%
Low/intermediate risk neuroblastoma	1	0.2%
Lymphoma	25	6.2%
Osteosarcoma	17	4.2%
Other	24	5.9%
Other sarcoma	4	1.0%
Post haematopoietic stem cell transplant (allogeneic)	22	5.4%
Post haematopoietic stem cell transplant (autologous)	2	0.5%
Renal tumour	14	3.5%
Retinoblastoma	2	0.5%
Rhabdomyosarcoma	14	3.5%

Supplementary Table 4 Diagnoses for each episode by centre

	PTC 1 n=123	PTC 2 n=203	PTC 3 n=46	PTC 4 n=157	PTC 5 n=77	POSCU 1 n=7	POSCU 2 n=20	POSCU 3 n=3	POSCU 4 n=9	POSCU 5 n=25	POSCU 6 n=23	POSCU 7 n=17	POSCU 8 n=19
ALL	31%	38%	46%	44%	10%	43%	20%	0%	67%	24%	74%	71%	79%
AML	18%	6%	11%	6%	39%	14%	15%	0%	0%	8%	4%	0%	0%
Brain/CNS tumour	7%	12%	11%	6%	0%	29%	15%	0%	0%	16%	9%	0%	5%
Lymphoma	11%	7%	7%	6%	10%	0%	0%	67%	0%	0%	0%	0%	0%
Non-CNS solid tumour	28%	21%	20%	29%	22%	14%	45%	0%	11%	36%	0%	29%	11%
Other	5%	7%	7%	8%	1%	0%	5%	33%	11%	0%	0%	0%	5%
Post HSCT	0%	8%	0%	1%	17%	0%	0%	0%	11%	16%	13%	0%	0%

Supplementary Table 5 AUS score distribution by centre

	PTC 1 n=123	PTC 2 n=203	PTC 3 n=46	PTC 4 n=157	PTC 5 n=77	POSCU 1 n=7	POSCU 2 n=20	POSCU 3 n=3	POSCU 4 n=9	POSCU 5 n=25	POSCU 6 n=23	POSCU 7 n=17	POSCU 8 n=19
AUS score													
0	5%	8%	15%	13%	1%	71%	10%	33%	33%	0%	9%	18%	26%
1	31%	38%	26%	38%	14%	14%	10%	33%	44%	16%	57%	24%	16%
2	39%	31%	28%	29%	45%	0%	30%	0%	11%	64%	17%	24%	37%
3	25%	22%	30%	20%	39%	14%	50%	33%	11%	20%	17%	35%	21%

Supplementary Table 6 - Outcomes of representations

	Homecare eligible: No (N = 43)	Homecare eligible: Yes (N = 21)
Time to representation (hours)		
Median (IQR)	120 (72, 144)	96 (72, 120)
Reason for representation		
Positive blood culture	4 (9%)	5 (24%)

New symptoms	27 (63%)	8 (38%)
Persistent symptoms	11 (26%)	8 (38%)
Outcomes		
Significant infection requiring IV antibiotics	10 (23%)	6 (29%)
ICU admission	0 (0%)	0 (0%)
Death from infection	0 (0%)	0 (0%)
Death from other cause	0 (0%)	0 (0%)

Supplementary Table 7 - Organisms isolated in bloods cultures

Organism	n	% total
Abiotrophia defectiva	1	0.5%
Acinetobacter spp	3	1.6%
Bacillus spp	3	1.6%
Campylobacter	2	1.1%
Candida albicans	1	0.5%
Citrobacter spp	2	1.1%
CoNS	48	25.3%
Diphtheroids spp	1	0.5%
Enterobacter cloacae	7	3.7%
Enterococcus spp	9	4.7%
Escherichia coli	21	11.1%
Fusobacterium spp	4	2.1%
Klebsiella spp	10	5.3%
Kocuria spp	3	1.6%
Micrococcus spp	5	2.6%
Moraxella spp	3	1.6%
MRSA	1	0.5%
MSSA	11	5.8%
mycobacterium mucogenicum	2	1.1%
Neisseria Cinerea	1	0.5%
NOS	8	4.2%
other	1	0.5%
Pantoea septica	1	0.5%

Pseudomonas spp	11	5.8%
Rhizobium radiobacter	1	0.5%
Rothia Mucilaginosa	2	1.1%
Serratia spp	2	1.1%
Stenotrophomonas	1	0.5%
Strep pneumoniae	1	0.5%
Streptococcus spp	2	1.1%
VGS	22	11.6%

Supplementary table 8

Core outcomes for randomly selected unique episodes, one per patient

Number of episodes submitted: 405

Initial presentations where homecare criteria met 87 (21%)

Core outcome data

	AUS: 0 (N = 54)	AUS: 1 (N = 131)	AUS: 2 (N = 127)	AUS: 3 (N = 93)
Duration of IV antibiotics (Days)				
n;Median (IQR)	53; 3 (1, 4)	117; 3 (2, 6)	112; 5 (3, 9)	83; 6 (3, 10)
n;Duration of admission (hrs)	53; 72 (28, 216)	128; 96 (48, 192)	125; 144 (72, 240)	90; 168 (72, 330)
Outcomes				
Positive blood culture (excl contaminants)	10 (19%)	18/130 (14%)	26 (20%)	34 (37%)
Significant infection requiring IV antibiotics	12 (22%)	15/130 (12%)	33 (26%)	31 (33%)
Representation within 7 days	3 (6%)	10 (8%)	7 (6%)	10 (11%)
Readmission within 7 days	3 (6%)	8 (6%)	7 (6%)	9 (10%)
ICU admission	0 (0%)	2/130 (2%)	4 (3%)	3 (3%)
Death from infection	0 (0%)	0/130 (0%)	0 (0%)	1 (1%)
Death from other cause	0 (0%)	0/130 (0%)	1 (1%)	0 (0%)

Initial presentations meeting homecare criteria

	AUS: 0 (N = 21)	AUS: 1 (N = 34)	AUS: 2 (N = 18)	AUS: 3 (N = 14)
Duration of admission (hrs)				
n;Median (IQR)	20; 26 (16, 39)	34; 30 (18, 68)	18; 58 (37, 72)	13; 68 (48, 96)
Outcomes				
Positive blood culture (excl contaminants)	1 (5%)	2 (6%)	1 (6%)	0 (0%)
Representation within 7 days	1 (5%)	6 (18%)	2 (11%)	1 (7%)
Readmission within 7 days	1 (5%)	4 (12%)	2 (11%)	1 (7%)

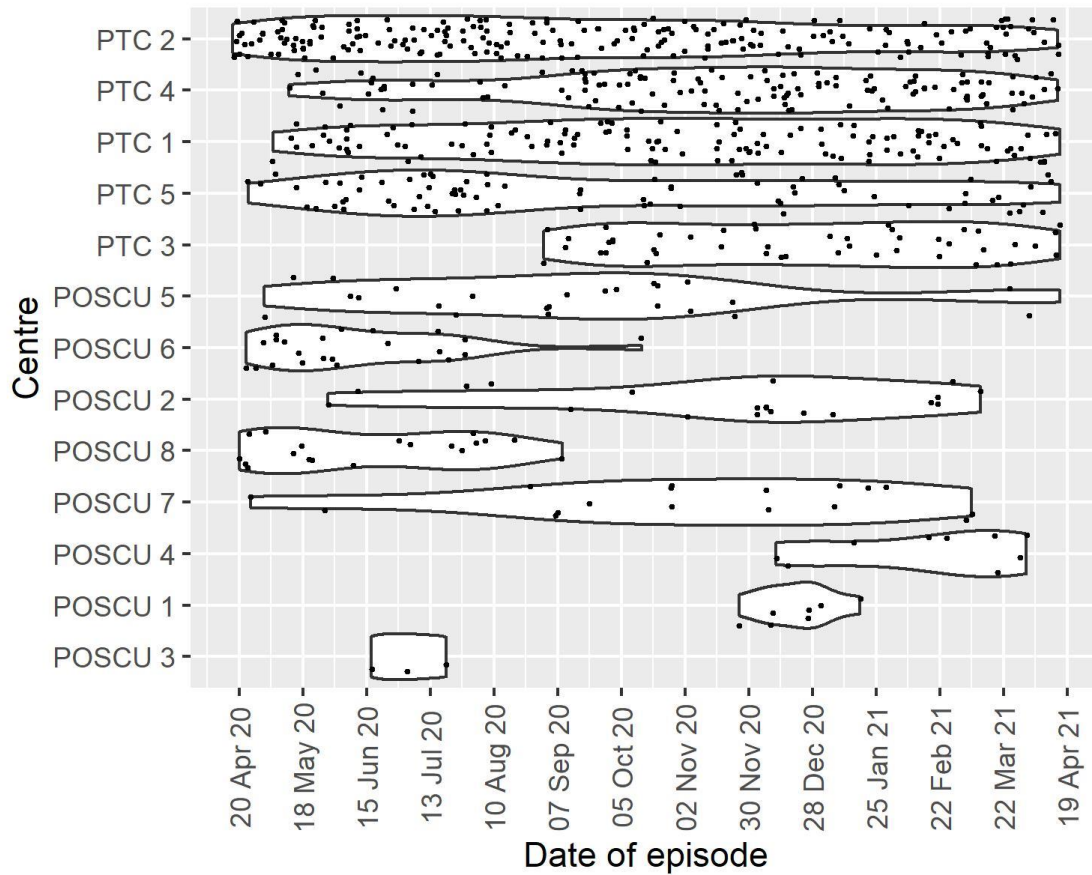
Percentage of AUS 0-1 readmitted

9%

Binomial test for significance of readmission in AUS 0-1 different to expected (15%)

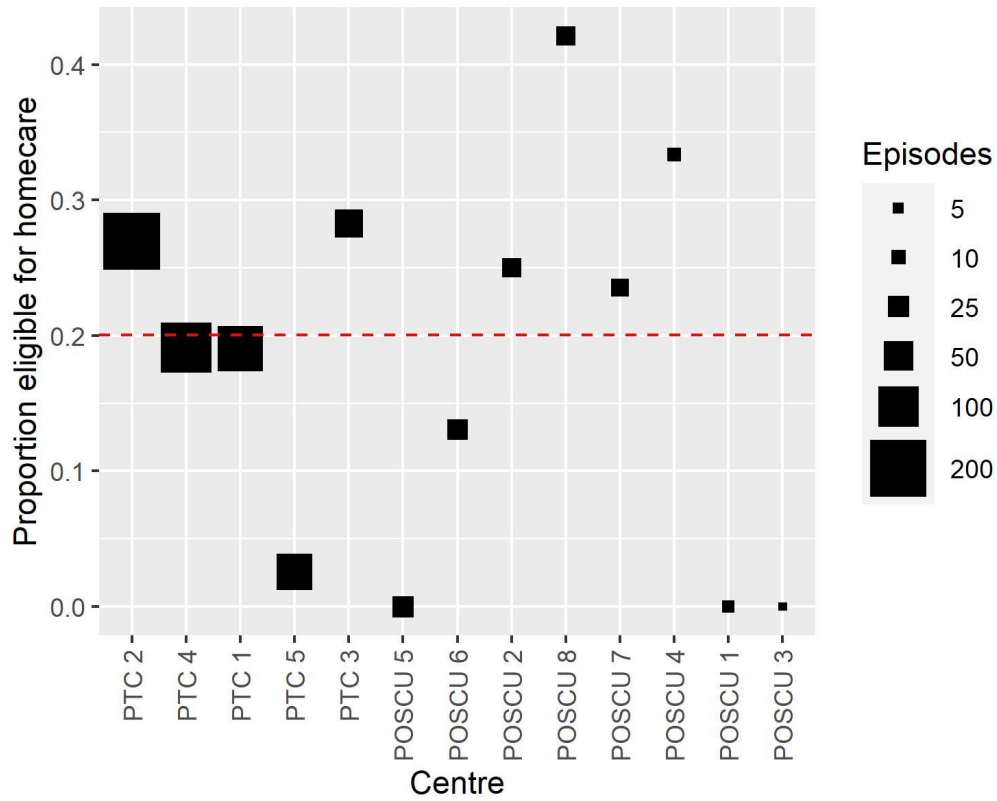
p= 0.261

Supplementary Figure 1 - Episodes per centre over time.



Each point represents an episode and violins are smoothed density estimates. PTC = principal treatment centre, POSCU = paediatric oncology shared care unit

Supplementary Figure 2 - Proportion of initial episodes eligible for homecare by centre.



Area of each square is proportional to the number of episodes submitted by the centre. Dotted red line represents proportion of all episodes

Supplementary File 1 – data collection tool**CCLG Febrile Neutropenia Survey 2020**

Start of Block: Default Question Block

Q2 In light of the current coronavirus pandemic and the resultant pressures put on our services the supportive care group has produced new guidance over management of one of our most common reasons for admission.

It is clearly important that there is a mechanism to evaluate such a major change to current practice and even more so to ensure this is carried out in order to ensure patient safety This form takes around 2 minutes to complete per patient.

Please include **every** patient with febrile neutropenia (regardless of management followed). Please input data at discharge or 7 days, whichever is sooner. If a patient re-presents within 7 days, please complete the form again, with the re-presentation questions only. (Don't worry ... the analysis will supersede original outcome data and won't double-count.)

The cumulative data will be analysed on a weekly basis and used to evaluate the protocol at a national level. Please ensure you input patients as soon as possible.

This protocol and evaluation have been adapted from the paediatric low-risk FN program developed by Gabrielle Haeusler, National Centre for Infections in Cancer, Australia and in collaboration with Bob Phillips and Jess Morgan, University of York, and the CCLG team including Sujith Samarasinghe, Barry Pizer, Richard Grundy and Jessica Bate.

End of Block: Default Question Block

Start of Block: General information

Q1 Centre name (If you are answering from a POSCU please click Other)

▼ PTC(1) ... Other (21)

Display This Question:

If Centre name (If you are answering from a POSCU please click Other) = Other

Q16 Centre name (Don't worry about the full name – e.g. North Staffs rather than “North Staffordshire Hospital NHS Trust” is fine)

Q3 Unique case identifier (You may have your own, or perhaps use two initials plus day of birth: I'm RP07 for example)

Q15 Is this a unique episode or a representation within 7 days (please log both incidents separately)?

- Unique episode (1)
- Representation with 7 days (2)

End of Block: General information

Start of Block: Underlying diagnosis

Display This Question:

If Is this a unique episode or a representation within 7 days (please log both incidents separately)? = Unique episode

Q4 Patients underlying diagnosis

▼ ALL (1) ... Other (16)

Display This Question:

If Patients underlying diagnosis = Other

Q5 Underlying diagnosis:

End of Block: Underlying diagnosis

Start of Block: Block 2

Display This Question:

If Is this a unique episode or a representation within 7 days (please log both incidents separately)? = Unique episode



Q6 Date of febrile neutropenia episode

Display This Question:

If Is this a unique episode or a representation within 7 days (please log both incidents separately)? = Unique episode

Q7 AUS risk stratification score:

	Yes (1)	No (2)
Preceding chemotherapy more intensive than ALL maintenance (1)	<input type="radio"/>	<input type="radio"/>
White cell count (2)	<input type="radio"/>	<input type="radio"/>
Platelets (3)	<input type="radio"/>	<input type="radio"/>

Display This Question:

If Is this a unique episode or a representation within 7 days (please log both incidents separately)? = Unique episode

Q8 Total score (sum of "yes" answers)

- 0 (1)
- 1 (2)
- 2 (3)
- 3 (4)

End of Block: Block 2

Start of Block: Block 7

Display This Question:

If Is this a unique episode or a representation within 7 days (please log both incidents separately)? = Unique episode

Q17 Did the patient meet the following criteria for early hospital discharge?

	Yes (1)	No (2)
Leukaemia/lymphoma in remission or solid tumour stable/responding (1)	<input type="radio"/>	<input type="radio"/>
Low risk disease group: NOT ANY OF acute lymphoblastic leukaemia (ALL) induction, or acute infant leukaemias, acute myeloid leukaemia (AML), post allogeneic haematopoietic stem cell transplant (HSCT) within 3 months or still on immunosuppression, congenital immunodeficiency, aplastic anaemia, Down Syndrome. (2)	<input type="radio"/>	<input type="radio"/>
No confirmed focus of infection requiring hospital care (including but not limited to central line infection, perianal cellulitis, pneumonia) (3)	<input type="radio"/>	<input type="radio"/>
No medical complication requiring inpatient care (including, but not limited to, pain requiring intravenous analgesia, poor oral intake or excessive loss requiring intravenous hydration; respiratory distress or oxygen requirement) (4)	<input type="radio"/>	<input type="radio"/>
No severe sepsis or septic shock at presentation (5)	<input type="radio"/>	<input type="radio"/>

Display This Question:

If Is this a unique episode or a representation within 7 days (please log both incidents separately)? = Unique episode

Q18 Was there any other reason not to discharge the patient as per the protocol (eg parental concern, professional choice, previous non-compliance, social concerns, lack of adequate transport)?

End of Block: Block 7

Start of Block: Time to initial discharge

Display This Question:

If Is this a unique episode or a representation within 7 days (please log both incidents separately)? = Unique episode

Q9 Time from presentation to initial discharge (Please provide in hours if <72 hours, or days if >72hours)

_____ Hours (1)

_____ Days (2)

Q25 Duration of IV antibiotics (in days, 0=single dose, if longer than 14 please use "14")

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14

Days ()	
----------	--

End of Block: Time to initial discharge

Start of Block: Representation

Display This Question:

If Is this a unique episode or a representation within 7 days (please log both incidents separately)? = Representation with 7 days

Q19 How long after the initial assessment (not initial discharge), did re-presentation occur?

_____ hours (1)

_____ days (2)

Display This Question:

If Is this a unique episode or a representation within 7 days (please log both incidents separately)? = Representation with 7 days

Q23 What was the date of their re-presentation?

Display This Question:

If Is this a unique episode or a representation within 7 days (please log both incidents separately)? = Representation with 7 days

Q22 Was the patient admitted to hospital following their re-presentation?

Yes (1)

No (2)

Display This Question:

If Is this a unique episode or a representation within 7 days (please log both incidents separately)? = Representation with 7 days

Q20 What was the main reason for re-presentation?

Persistence of original symptoms (1)

Development of new symptoms (2)

Requested by hospital due to positive blood culture (3)

Requested by hospital for other reason (4)

Display This Question:

If What was the main reason for re-presentation? = Requested by hospital for other reason

Q21 Why was the re-presentation requested by the hospital?

End of Block: Representation

Start of Block: Positive blood cultures

Q10 Did the patient have any positive blood cultures during this episode (excluding contaminants)?

- Yes (1)
- No (2)

Display This Question:

If Did the patient have any positive blood cultures during this episode (excluding contaminants)? = Yes

Q11 What organisms were found?

End of Block: Positive blood cultures

Start of Block: Significant outcomes

Q12 Did the patient experience any of the following outcomes (tick all that apply)?

	Yes (1)	No (2)
Significant clinical infection requiring IV antibiotics (eg periorbital cellulitis, joint infection, CLABSI) (1)	<input type="radio"/>	<input type="radio"/>
ICU admission (2)	<input type="radio"/>	<input type="radio"/>
Death from infection (3)	<input type="radio"/>	<input type="radio"/>
Death from other reason (4)	<input type="radio"/>	<input type="radio"/>

End of Block: Significant outcomes

Start of Block: Block 4

Q13 Any further comments about this patient's febrile neutropenia episode?

End of Block: Block 4

Start of Block: Block 5

Q14 Please provide your email address so that if we have any further questions about this febrile neutropenia episode, we can contact you. (We will not use your email address for any other purpose.)

End of Block: Block 5
