Critical Review Form
Cohort Study

PGY-2

Impact of individualized pain plain on the emergency management of children with sickle cell disease, Pediatr Blood Cancer 2014; 61: 1747-1753.

Objective: **To evaluate whether a "detailed individualized pain management plans developed as a result of successful implementation of a standard protocol jointly by the emergency physician and primary hematologist, improve patient satisfaction with pain management, and reduce hospital admission as well as readmission rates." (p. 1747)**

Methods: **Observational study at Children's Hospital Pittsburgh (CHP) from 2002 thru 2009 (?). In 2002, CHP created an algorithm (Figure 1 below) for emergency department (ED) pain management in acute vasocclusive crises (VOC) based on (unreferenced) American Pain Society Guidelines and emphasizing early initiation of intravenous morphine or hydromorphone to obtain significant pain relief within 1-2 hours of ED arrival. This algorithm was implemented via "extensive education of the ED staff, physicians, and pediatric residents" after "sickle cell staff determined the optimal medication regiments, after discussions with patients and families, and created an 'individualized pain plain'". (p. 1748) Each plan included a list of current home pain medications, other medications, ED analgesic dose and frequency of administration, and inpatient pain management recommendations (Figure 2, page 1749). During weekday daylight hours a sickle cell nurse coordinator visited each patient and was available to support the ED staff. If drug or dose or toxicity issues occurred, the plans were updated by the hematologist.**

The authors obtained data from four Pediatric Health Information System hospitals with similar patient populations to compare admission and 1-week readmission rates, as well as average hospital length of stay. In 2009, the authors administered patient and parent satisfaction surveys to children and parents to evaluate "quality of care" and patient/parent satisfaction. In the 5-11 age group, pain was assessed using the 0 to 5 scale of the Baker-Wong Faces scale and (undescribed) modifications to this scale were used for older patients. These surveys also evaluated both patient and parent perceived quality of care (example: "niceness of ED staff" to the patient), pain control achieved, and overall satisfaction (example: likelihood to return to that ED).

Statistically, the Methods section reports performing "logistic binomial regression with chi-square test to determine whether there has been a significant change in admission rates since the inception in 2002", as well as "descriptive statistics and calculated p-values for each survey question". (p. 1749) However, the authors report no logistic regression or p-values in the results. The authors also do not report primary or secondary outcomes or any sample size assumptions.

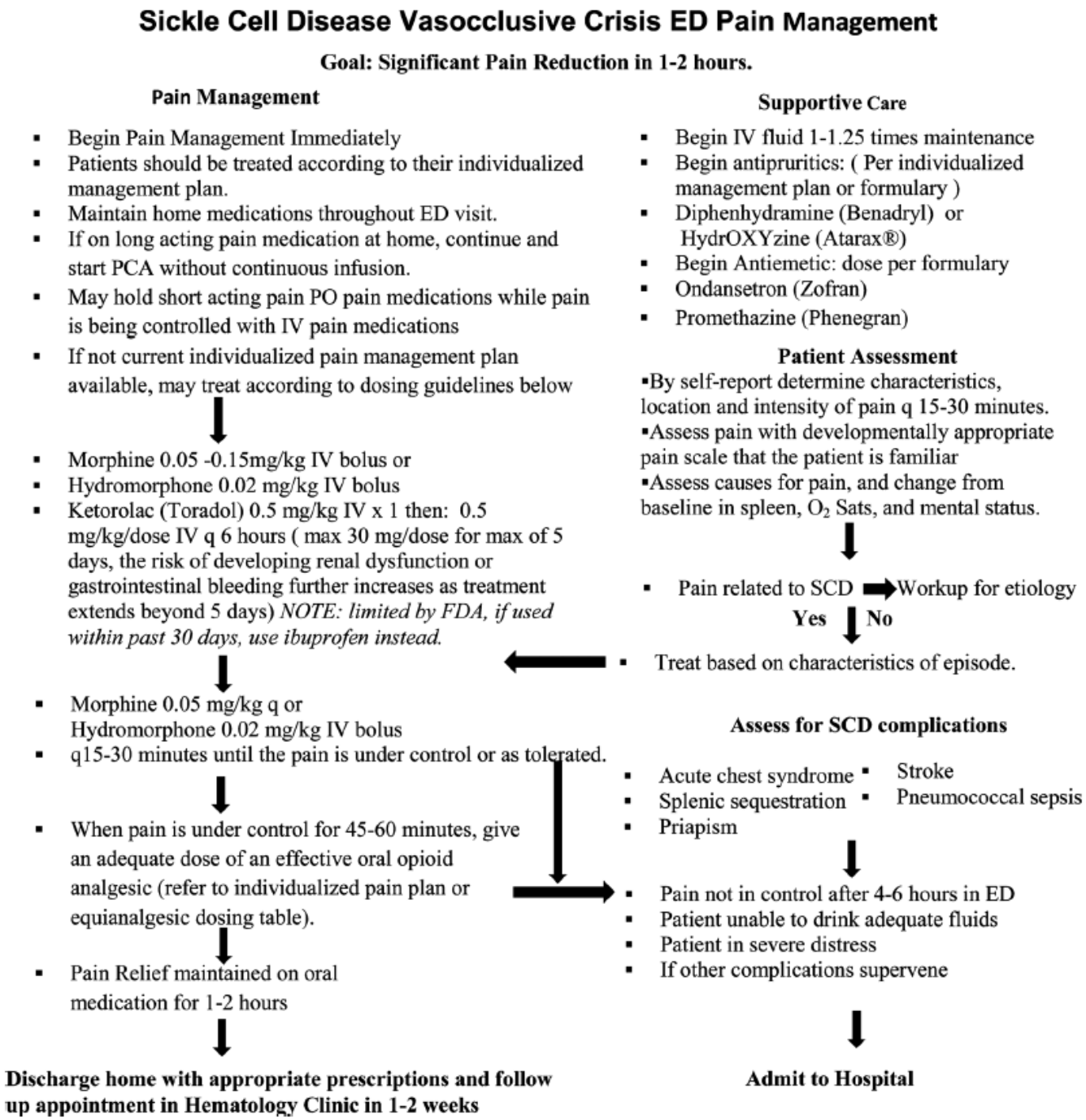

Fig. 1. Algorithm for the management of sickle cell associated vaso-occlusive pain.

Critical Review Form: Cohort Study

Guide	Comments
Are the results valid?	
Did experimental and control groups being the study with a similar prognosis?	
Did the study address a clearly focused issue?	Yes – is the introduction of an individualized care plan for acute painful vasocclusive crisis in pediatric sickle cell patient associated with improvements in patient-centric analgesia or process measures of admission rates or ED return rates.

Did the authors use an appropriate method to answer their question? - Is a cohort study a good way of answering the question under the circumstances?	No – the authors report an observational study with a comparator from 4 hospitals within the Pediatric Health Information System for some outcomes. However, multiple issues limit this study's ability to provide compelling results – or even hypothesis generating results. For example, they fail to: • cite or adhere to STROBE reporting standards for observational research; • describe how (and by whom) ED staff were educated and how CHP ED teams had access to the individual care plan; • evaluate the fidelity with which the protocol was implemented into ED care (via medication doses ordered or time to medications); • clarify primary and secondary outcomes; • cite a *clinically* significant threshold for Baker-Wong Faces scale in either age group; • quantify univariate statistical significance of findings; • quantify regression analysis results to differentiate whether any factor is independently associated with any observed "improvements"'; • report 95% Confidence Intervals as measures of precision; • describe how longitudinal outcomes were obtained and whether those outcome assessors were blinded to the study's hypothesis.
Was the cohort recruited in an acceptable way? - Was the cohort representative of a defined population? - Was there something special about the cohort? - Was everybody included who should have been included?	Uncertain because the authors provide no description of when, how, or by whom sickle cell patients and their parents were "recruited". Presumably, recruitment occurred during episodes of Sickle Cell Clinic care and not during an episode of acute pain crisis in the ED, but this is not explicitly detailed. Table 1 (p. 1751) does not provide sufficient demographic details to permit comparison of populations, but is under-representative of male sickle cell patients. Details that would help readers compare populations would include ethnicity, prior ED visits for sickle pain in last 12-months, insurance status, and parental health literacy.
Was the exposure accurately measured to minimize bias? - Did they use subjective or objective measurements? - Do the measures truly reflect what you want them to (have they been validated)? - Were all the subjects classified into exposure groups using the same procedure?	No – the authors do not directly measure adherence to the individual pain plan such as initial opioid dose or time to first dose. Observational studies cannot prove a cause-effect relationship. The best-case scenario for an observational study is that an association between an exposure (individual patient pain plan) and outcome (subjective improvement in pain relief) is demonstrated. In this study, multiple other factors could have been associated (or causative) of the observed outcomes, including mere publication/dissemination of the American Pain Society guidelines prior to 2002, education of the CHP staff, empowering of the patients/parents by the process of creating the individualized care plans, or alignment of patient-hematologist-ED provider pain objectives.
Was the outcome accurately measured to minimize bias? - Did they use subjective or objective measurements? - Do the measures truly reflect what you want them to (have they been validated)? - Has a reliable system been established for detecting all the cases (for measuring disease occurrence)? - Were the measurement methods similar in the different groups? - Were the subjects and/or the outcome assessor blinded to exposure (does this matter)?	Uncertain for *all* outcomes because the authors do not provide sufficient detail: • Healthcare utilization – was this determined by hospital record review or telephone follow-up? Either way, when did this evaluation of utilization occur? • Pain management – when (and how often) was the Baker-Wong Faces assessed? Were any adverse effects assessed? • Quality of care – when were patients and parents queried for perceptions of waiting room length of stay, ED length of stay, and delay to first dose of analgesia? Obviously, the longer the delay between these events and the query, the less accurate the responses will be. In addition to the how and the when, the authors do not cite any validation of the instruments used to quantify utilization, pain control, or quality of care. Nor do they provide details about who obtained those results, how they were trained, or whether they were blinded to the study hypothesis.
Have the authors identified all important confounding factors and have they taken account of the confounding factors in the design (i.e. modelling, regression, propensity analysis, or sensitivity analysis to correct, control or adjust for confounding factors)?	No. In addition to incomplete reporting of patient demographics, methods/timing used to evaluate outcomes, and statistical relevance, the authors neglect to provide the results for the regression analysis noted in the Methods section. They identify neither univariate significance nor multivariate evaluation of independent association between the individualized care plan intervention and the various outcomes.

Was the follow up of subjects complete and was the follow up of subjects long enough?	Uncertain how long patients were "followed" for the outcomes. The 1-week ED returns or hospital admission outcome is probably sufficient for most ED providers.
What are the results?	
What are the results of this study?	• The study reports on only 36 pediatric patients (9 boys, 27 girls) and 31 parents (all female), limiting internal validity. Only 7 of the children were in the 5-11 year age range. • On average parents rated pain management as better than their children in the post-ED period (2.12 vs. 2.59 with 5 = "extraordinary") • Although statistical analyses are not reported in the manuscript, Figure 3A (p 1750) appears to demonstrate a consistent decline in the proportion of CHP sickle cell patients admitted (from 65% in 2003 to 46% in 2008) compared static PHIS admission rates (66% admitted in 2003, 70% admitted in 2008). • Although statistical analyses are not reported, Figure 3B demonstrates nearly identical 1-week readmission rates between 2003-2008 (CHF range 3.2% to 8%; PHIS range 4.8% to 7.7%) with no grossly observable temporal trends. • Patients reported longer delays than parents for median time to pain medications (25 minutes vs. 20 minutes), but agreed on time until placed into room (median 10 minutes for both). • Patients and parents in both age groups noted reduction in pain from pre- to post-ED period (Table 1) as well as satisfaction with pain management and overall care (Table 2) though whether these differences are either statistically or clinically significant is unknown. • 52% of patients and 73% of parents rated overall pain management as "very good" or better and over 93% of both age groups would return to the CHP ED.
How precise are the results? (i.e. what 95% CIs were associated with the results?)	Unknown – 95% CI's are not reported.
Do you believe the results?	No – the methods and analyses leave too many biases possible to confidently ascribe individual pain plans as associated (let alone causative) of the observed results.
Will the Results Help Me Locally?	
Were the study patients similar to my patient?	Unknown because demographics presented are inadequate to judge.
Do the results of this study fit with other available evidence?	Yes – Based on Tanabe et al (published 4-years after this study), there is biological plausibility for a cause-effect relationship whereby benefits outweigh risks for individual pain plan guided VOE management in the ED.

Limitations

1) **Failure to cite or adhere to STROBE reporting standards for observational research.**
2) **Inadequate details regarding patient demographics, validity of the outcome instruments used, or fidelity of uptake of the pain protocol into ED analgesia prescribing. Additional details required to reproduce the authors' methods would include training and blinding of the outcome assessors, as well as timing of when those outcomes were evaluated.**

3) **No univariate or logistic regression results presented, so unable to define statistically significant".**
4) **No confidence intervals reported.**
5) **Consistent confusion throughout the Results and Discussion regarding cause-effect relationship of observational data. At best, observational studies yield associations not causation. The level of confidence that an observed association is likely to be causative raises with reporting of Hill criteria, but the Hill criteria are not reported in this manuscript.**
6) **The small sample size limits internal validity (i.e. that the results reflect "truth" with the study institution).**
7) **The single-center design limits external validity to similar pediatric EDs. More importantly, the pediatric population and median 10-minute delay from waiting room to ED bed significantly limit external validity for adult sickle cell populations receiving care in adult EDs with much longer waiting room delays.**

Bottom Line

As detailed above, multiple design and reporting flaws limit our ability to confidently extract knowledge from this observational data. However, (largely consensus driven) NHLBI guidelines published in 2014 provide an ethical mandate to explore interventions like individualized care plans that theoretically safely improve time to analgesia for sickle cell patients with VOE pain crises. This study demonstrates one institutions' innovation in creating individual care plans prior to the NHLBI guidelines. Quality improvement teams and future researchers can learn from the methodological and reporting flaws that limit readers ability to reproduce this innovation or to confidently ascribe care plan to improved patient outcomes.