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Post-Trial Sustainability and Scalability of the Benefits of a Medical Home for High-Risk Children with Medical Complexity

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Abstract

Objective.—To assess the sustainability of the benefits relative to usual care of a medical home providing comprehensive care for high-risk children with medical complexity (≥ 2 hospitalizations or ≥ 1 pediatric intensive care unit [PICU] admission in the year before enrollment) after we made comprehensive care our standard practice and expanded the program.

Study design.—We conducted pre-post comparisons of the rate of children with serious illness (death, PICU admission, or >7-day hospitalizations) and health-system costs observed after program expansion (March 2014–June 2015) to those during the clinical trial (March 2011–August 2013) for each of the trial's treatment groups (usual care [n=96]; and comprehensive care [n=105]) (primary analyses), and among all children given comprehensive care (n_{Post Trial}=233 [including trial usual care children who transitioned to comprehensive care post trial and newly enrolled medically complex children]; and n_{Trial}=105) (secondary analyses). We also analyzed the findings for the trial patients as a 2-phased stepped wedge study.

Results.—In intent-to-treat analyses, rates of children with serious illness and costs were reduced or unchanged post trial vs. trial for the trial's usual care group (rate ratio [RR], 0.36 [95% Confidence Interval, 0.20–0.64]; cost ratio [CR], 0.68 [0.28–1.68]), the trial's comprehensive care group (RR, 0.74 [0.39–1.41]; CR, 0.67 [0.51–0.89]), and among all children given comprehensive care (RR, 0.97 [0.61–1.52]; CR, 0.75 [0.61–0.93]). Conservative stepped wedge analyses identified overall benefits with comprehensive care across both study periods (RR, 0.46 [0.30–0.72]; CR, 0.64 [0.43–0.99]).

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Conclusions: Major benefits of comprehensive care did not diminish with post-trial program expansion.

Keywords

Comprehensive-Care; Serious Illnesses; Health System Costs

Children with medical complexity (CMC) have significant chronic conditions that require care from a multitude of providers in different settings, placing them at increased risk for fragmentation, duplication, and high expenditures.(1-4) To address these challenges, the medical home model of care has emerged as a promising approach to strengthen primary care delivery by emphasizing care coordination around the patient's needs. (5-11) However, despite broad recommendation and diffusion of the medical homes, few randomized trials have assessed their effectiveness,(4, 6-8, 11, 12) and the greatest benefits were reported in our small single center trial that was stopped early for benefit and cost effectiveness.(4) Our trial (n=201) assessed a medical home in Houston, Texas providing comprehensive care carefully designed to promote prompt effective care at all hours for high-risk chronically ill CMC (predefined as having 2 hospitalizations, or 1 pediatric intensive care unit [PICU] admission during the year before enrollment and >50% estimated risk of hospitalization). (4) The results of the trial indicated that when compared with usual care, our comprehensive care model of primary care reduced the rate of children with serious illness (death, PICU admission, or prolonged hospitalization >7 days) by over 50% (rate ratio (RR) 0.45 [95% Confidence Interval (CI), 0.28-0.73]) and lowered health system costs by more than 40% (cost ratio [CR] = 0.58; [0.38-0.88]).(4)

Whether such a resource-intense intervention can be scaled up and achieve comparable benefits in clinical practice is of great importance for CMC, given that they account for approximately 40% of all pediatric deaths and hospital spending in the U.S, but make up fewer than 1% of all children. (13) For this reason, we undertook a detailed assessment of the effects of comprehensive care following our trial when we made comprehensive care our standard practice for high-risk CMC and substantially increased the number of children and personnel in our program. With the ongoing commitment to optimize the outcomes of CMC in our program, our primary hypotheses were that the post-trial rates of children with serious illness and the inflation-adjusted health system costs would markedly decrease relative to those during the trial for usual care trial patients who were given the choice to transition to comprehensive care post trial and would not increase relative to those during the trial for the trial comprehensive care patients. Our secondary hypothesis was that the rate of children with serious illnesses and health system costs among all eligible patients given comprehensive care after the trial (including newly enrolled CMC, the comprehensive care trial patients, and the usual care trial patients who accepted to transition to comprehensive care post trial) would be similar to those of the comprehensive care patients during the trial.

Methods

Our institutional review board approved this study as a quality improvement (QI) project involving no experimental procedures or foreseeable increased risk in assessing whether outcomes changed after the trial.(14, 15)

Setting.

The High-Risk Children's Clinic of the University of Texas at Houston (UTH) McGovern Medical School is a patient-centered medical home for CMC. Children who require hospital care in our center are usually treated in the Children's Memorial Hermann Hospital (CMHH), a private institution adjacent to our medical school that serves as the UTH tertiary teaching hospital.

Population.

The eligibility criteria was the same during and after our trial and included high-risk chronically ill CMC with 2 hospitalizations, or 1 PICU admission in the year prior to enrollment, and an estimated 50% or higher risk of hospitalization with usual care during the coming year. After the trial, comprehensive care was offered to all newly identified CMC meeting the trial's eligibility criteria, as well as CMC who had refused consent for the trial or had been originally randomized to usual care. With this expansion, our panel nearly tripled from 105 patients during the trial to a total of 280 patients being treated in the High-Risk Children's Clinic during the post trial period (Figure). At enrollment, the children were prospectively classified by the High-Risk Children's Clinic medical director as either high risk (51-75% estimated risk) or very high risk (>75% estimated risk) of hospitalization with usual care based on their diagnoses, current medical status, past medical history, and socioeconomic risk factors. Those classified as very high risk were found to be more likely to be hospitalized than were those classified as high risk among not only those given usual care during the trial (85% vs 67%) but also all those given comprehensive care during and after the trial (85% vs. 43% and 72% vs 30%, respectively).(4)

Comprehensive care was provided in our High-Risk Children's Clinic with a low patient-to-primary-care provider ratio of ≤ 50 during the trial and ≤ 75 after clinic expansion. Clinic visits typically lasted 45-60 minutes. Providers and parents frequently communicated by telephone and email. Parents had direct access 40 hours/week to their child's assigned primary care provider in the clinic and 24/7 cell phone access to the provider on call (either the general pediatrician or one of the 3 Pediatric Nurse Practitioners). The medical director, a Spanish-speaking pediatric pulmonologist, provided continuous backup, and a pediatric gastroenterologist, neurologist, allergist/immunologist, infectious disease specialist, and an adolescent pediatrician attended the clinic once monthly and were also available for consultation by telephone at all hours. The clinic was also staffed by a nutritionist and a social worker. To promote prompt effective care at any hour, same week-day care is provided for acute illnesses or complications, and our providers communicate directly with the responsible attending physician in the Emergency Department (ED), pediatric floor, or PICU whenever the children are referred to CMHH. Our staff reviewed hospital records each weekday to identify all children who had been seen in the ED or admitted to CMHH. The

patient's assigned primary care provider then helped in coordinating care and assuring prompt follow-up clinic visits. Moreover, during weekly staff meetings, the staff scrutinized the prior care given by our team to any patient seen in the ED or admitted to the hospital to identify potential opportunities for preventing future hospital encounters.

CMC who received usual care during the trial or elected to receive usual care after the trial were treated by pediatricians in private offices or by faculty-supervised residents in the UTH general pediatrics clinic. At UTH, chronic problems were treated at subspecialty clinics by referral and at a twice-weekly clinic for children with special health care needs staffed by a pediatrician, social worker, and nutritionist who provided consultation and referrals but not primary care. As in other centers, calls from parents at night and on weekends to our general pediatrics service were taken by on-call faculty or faculty-supervised pediatric residents.

Our primary outcomes were the rate of children with a serious illness (causing death, pediatric ICU admission, or hospital stay > 7days) and total health system costs. Secondary outcomes included the individual components of serious illness, clinic costs, hospital costs, ED visits, hospitalizations, PICU admissions, and hospital and PICU days. To identify ED visits and hospitalizations, we reviewed the hospital logs each weekday for CMHH and assessed claims data from the 16 Memorial Hermann Health System area hospitals and billing data from Texas Medicaid. As during the trial, the parents were asked during each visit to the clinic about any ED visit or hospitalization. Parents of children who received usual care were called every 3 months to identify any ED or hospital services and were compensated with a \$20 gift card for each call. Cost data were assessed as described below using similar methods to the original trial.(4)

Comparisons of Different Treatment Groups.

We conducted pre-post analyses by comparing the rates of children with serious illness and health-system costs after program expansion (March 2014-June 2015) to those observed during the trial (March 2011-August 2013) within each of the trial's treatment groups (usual care [n=96]; and comprehensive care [n=105]) (primary analyses, Figure) and among all children given comprehensive care post trial (n=233 [including usual care children who transitioned to comprehensive care post trial and newly identified children with medical complexity]) and during the trial (n=105) (secondary analyses, Figure). We prospectively planned to exclude the 6 months between September 2013 and February 2014 as a transition period needed to expand and equip clinic space and recruit and train additional staff to more than double the total patients given comprehensive care.

Our primary analysis was an intent-to treat analysis that included all trial patients except those who died during the trial or who moved out of state (and whose outcomes and costs could not be accurately determined). The secondary analyses assessed all post-trial patients, including new enrollees who met the trial eligibility criteria and were enrolled in the comprehensive care program through December 2014 (Figure) to allow each patient to be assessed for at least 6 months as during the trial.

To minimize confounding due to potential differences in baseline risk despite our efforts to use the same eligibility criteria across both study periods, our primary analyses included

only patients randomized during the trial. Nonrandomized patients who enrolled in comprehensive care post trial were only included in secondary analyses. We also compared findings after the trial with those during the trial for the predefined secondary outcomes.

As detailed in the Appendix (available at www.jpeds.com) we also performed supplementary analyses of the findings for trial patients across both study periods as a stepped wedge study which allows adjustment for changes in health over time and is considered particularly useful in evaluating the effects of implementing into routine practice interventions previously shown to be effective in parallel group randomized trials.(16)

Economic Evaluation and Statistical Analyses.

Hospital costs were estimated by multiplying charges by department-specific cost-to-charge ratios specified in the hospital's annual Medicare cost report. Clinic costs for outpatient services and physician fees for patients originally randomized to usual care before transitioning to comprehensive care were estimated using relative value units (RVUs) from the 2017 Medicare Fee Schedule.(17) Clinic costs for physician services for comprehensive care were estimated using the High-Risk Children's Clinic total expenditures to account for the low patient-to-staff ratio and the provision of multiple nonbillable services not included in estimates derived from conventional claims-based methods. Costs for outpatient services provided in our center but outside the High-Risk Children's Clinic (such as diagnostic imaging tests, labs, etc) were calculated using the standard RVU-based method. The costs for hospitalizations and ED visits utilized outside our system were estimated based on the mean cost per bed-day and ED visit observed at CMHH. The costs for outpatient care occurring outside our center were estimated based on RVUs.

Because pharmacy claims data were not available, outpatient pharmaceutical costs were not assessed. All costs were inflated to 2017 US dollars based on the consumer price index for medical services.(18)

All statistical and economic analyses were conducted under the intent-to-treat analyses principle using multilevel mixed models or generalized estimating equation (GEE) models accounting for within-subject correlation across the two time periods. Treatment group differences between the trial and the post-trial period in the proportion of children with an outcome were evaluated using a Poisson GEE model with robust standard errors. Total numbers of secondary outcomes were analyzed with negative binomial mixed regressions. Differences in costs were analyzed with gamma GEE regressions with log-link and robust standard errors. To evaluate differences between the trial period and the post-trial period within each original treatment group (comprehensive care or usual care), terms for original treatment group, period, and for treatment-period interaction were included in the models in both primary and secondary analyses. The supplementary stepped wedge analysis used similar Poisson GEE and gamma GEE regression models including main effects for treatment and study period.(19) All models were adjusted for the stratifying variables used in the original trial (receipt of maternal high school diploma [yes, no], estimated baseline hospitalization risk [51-75%; >75%]), and length of follow-up.

All analyses were performed using Stata software version 15.1 (StataCorp) and R software version 3.3.3 (R Foundation for Statistical Computing). The 95% CI for the RR and CR were displayed (CIs that do not include a value of 1.0 are generally indicative of a $P < .05$).

Results

Of the 91 usual care survivors at the end of the trial, the parents of 45 patients (49%) agreed for them to transition to comprehensive care (Figure). All 91 patients were included in the post-trial analyses under the intention-to-treat principle. Excluding 2 children who moved out of state, 100 of the 102 surviving trial comprehensive care patients were included. The post-trial period involved 121 child-years for the trial usual care group and 133 child-years for the trial comprehensive care group. For the secondary analyses, a total of 233 patients (273 child-years) given comprehensive care post trial were included (100 trial comprehensive care survivors, 45 usual care children who transitioned to comprehensive care, and 88 newly identified CMC through December 2014) vs. 105 (184 child-years) during the trial.

For the primary analyses, the patients within each of the trial groups were similar during and after the trial except of course for age which increased in the comprehensive care group from a mean age of 4.6 ± 4.1 years at trial enrollment to 6.9 ± 4.3 years post trial and from 4.6 ± 3.9 years to 7.0 ± 4.0 years in the usual care group (Table I). For the secondary analyses, the increased referral of patients classified as very high risk prompted by the trial results, as well as the transition to comprehensive care of all but 2 of the 10 very high-risk usual care survivors, resulted in a higher proportion of children given comprehensive care who were very high risk post trial than during the trial (23% vs. 12%, $p = 0.02$) (Table 2; available at www.jpeds.com).

Outcome and Cost Analyses Addressing the Primary Hypotheses.

Primary Hypothesis A: Findings for the Usual Care Trial Group (Table 3).—As hypothesized, the trial's usual care group experienced a marked decrease in the rate of children with serious illness after the trial (7.4 vs. 22 per 100 child-years; rate ratio [RR], 0.36 [0.20-0.64]). Secondary medical outcomes were also decreased (RR = 0.21-0.5). However, the change in hospital and clinic costs were offsetting, and the reduction in mean total health system costs was not statistically significant (\$20,774 post trial vs. \$29,203 per child-year during the trial; CR, 0.68 [0.28-1.68]).

Primary Hypothesis B: Findings for the Comprehensive Care Trial Group (Table 4).—Despite the major program expansion, the rate of children with serious illness post trial did not increase (7 vs. 10 per 100 child-years; RR, 0.74 [0.39-1.41]). For secondary outcomes, the rate of ED visits and PICU days were significantly reduced post trial. Mean total health system costs per child-year were lower post trial than during the trial (\$12,425 vs. \$18,019; CR, 0.67 [0.51-0.89]), mainly due to reduced hospital costs (\$5,438 vs. \$10,693; CR, 0.51 [0.30-0.88]).

Secondary Hypothesis: Findings for All Patients Receiving Comprehensive Care During and After the Trial (Table 5; available at www.jpeds.com).—As

hypothesized, after adjusting for the greater proportion of comprehensive care patients who were very high risk after the trial than during the trial, the RR of children with serious illness among all patients given comprehensive care post-trial (including new enrollees) was similar to that for all children given comprehensive care during the trial (0.97 [0.61-1.52]). The adjusted RR for each secondary outcome was <1.0 , but the 95% CI included 1.0 for all but ED visits and PICU days. The adjusted costs were lower post trial than during the trial (CR, 0.75 [0.61-0.93]).

Supplemental Stepped Wedge Analyses of Trial Patients Across Both Study Periods

After adjusting for study time period, this analysis showed a significant overall effect of comprehensive care across the two periods in reducing children with serious illness (RR, 0.46 [0.30-0.72]) that was similar to the effect of comprehensive care that was observed in the trial (RR, 0.45 [0.28-0.73]). (4) The overall treatment effect was conservatively estimated as under the intent-to-treat principle the children who continued to receive usual care in the second study period were analyzed as having received comprehensive care. The stepped wedge analysis of costs after adjusting for study time period also showed a significant overall cost reduction with comprehensive care during the two periods (CR, 0.64 [0.42-0.99]) that was comparable with the cost reduction observed in the trial (CR, 0.58 [0.38-0.88]). (4)

Discussion

Our prior randomized trial of comprehensive care was relatively small and stopped early due to substantial reductions in both serious illness and health system costs relative to those with usual care that prompted the expansion of the comprehensive care program. Yet, each of the analyses for our primary and secondary hypotheses, as well as the findings from the supplementary post hoc analyses are consistent with comparable if not greater benefits in clinical practice following program expansion than during the trial. Few post-trial follow-up studies of successful medical interventions have been conducted (20-22) and to the best of our knowledge none has assessed the post-trial effectiveness of medical homes in any age or condition. We believe the continued success of our medical home model of primary care likely results from the sustained effort to promote prompt and effective care at all hours and to identify and reduce unnecessary ED visits and hospitalizations through a combination of features such as: 1) a low patient-to-provider ratio to allow for frequent, proactive communication with the parents by phone and e-mail; 2) cell phone access to primary care providers 24/7; 3) acute same day care, chronic care, and specialty care all provided in the same clinic; 4) extensive provider-to-provider consultation; 5) weekly scrutiny of the care provided in the clinic before any ED visit or hospitalization; and 6) prompt clinic visits after ED visits or hospitalization. As indicated in prior systematic reviews (6-8, 11), similar features were used in the only other randomized trial of a medical home that identified major clinical benefits or cost reductions (12). Given the complexity and amount of resources needed to replicate our medical home model of complex care, the benefits we identified both during and after the trial seem only likely to be achievable in academic centers with the adequate staffing, infrastructure, and commitment to provide such care.

Strengths of our study include prospective data collection during and after the trial, predefined hypotheses for different patient groups, use of intent-to-treat analyses, and assessment of health-system costs using state-of-the-art methods. The use of the stepped wedge analysis is an innovative approach that might be used for evaluating post-trial effectiveness of other interventions in clinical practice. All findings considered, we infer that the post-trial clinical benefits and cost savings after we made comprehensive care our standard practice and substantially expanded the program was at least comparable with that during the trial, suggesting successful scalability of comprehensive care.

Although our prior randomized trial and this study indicate that effective care management and care coordination through comprehensive care can substantially improve outcomes and lower total costs for CMC, inadequate outpatient reimbursements are a predictable barrier for implementing and disseminating this or similar models of care. As documented during our clinical trial, the costs to our medical school for providing comprehensive care were considerably greater than the revenues.⁽⁴⁾ Sustainable reimbursement mechanisms for providers of such care will be required before the large potential reductions in Medicaid expenditures and total health system costs for CMC can be realized in centers across the U.S.

Despite our efforts to use the same eligibility criteria across both study periods, changes in outcomes over time may be influenced by factors unrelated to treatment, including unadjusted changes in patient population and hospital admission and discharge practices. In addition, a tendency for the health of CMC to improve over time irrespective of their care, would reduce the rate of serious illness and costs post trial as could be expected for children in this study (4.6 years mean age at enrollment in the trial). However, the observed reduction in the rate of children with serious illness in the usual care group was substantially decreased ($RR = 0.36 [0.20-0.64]$ (Table 3), and the rate in the comprehensive care group was unchanged ($0.74[0.39-1.41]$) (Table 4). If reductions in serious illness were due only to temporal improvements in health and not to comprehensive care being more effective than usual care, we would expect similar reductions in both groups. Moreover, the analyses of the 2 study periods as a stepped wedge study provided no evidence that the overall benefits of comprehensive care controlling for study period were less than during the trial (see Appendix for further information). The benefits of providing comprehensive care to usual care patients following the trial might have actually been underestimated rather than overestimated in these intent-to-treat analyses, because children who were offered comprehensive care but received usual care after trial were analyzed as if they had received comprehensive care.

A limitation of our study is the unavailability of outpatient pharmacy costs. It is unclear whether inclusion of such costs would affect the estimated overall cost savings with comprehensive care relative to usual care. Costs for homecare were not included because they are primarily influenced by baseline status, were expected to change during the study with the shift in Texas to Managed Care Medicaid, and difficult to estimate, particularly with this shift. . Lastly, the generalizability of our findings and model of care to different centers and other CMC, especially those who may be older and not predominantly affected by respiratory disorders, is uncertain.

Our findings supply evidence of similar if not improved value of comprehensive care as provided in our center after program expansion. These findings in conjunction with those in the previous trial strongly support the scalability, clinical benefits, and cost savings of our comprehensive model of pediatric complex care. Unfortunately, such resource-intensive models of care are not adequately reimbursed. New alternative reimbursement mechanisms will be needed to implement comprehensive care or other similar programs for high-risk medically complex children in other centers.

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APPENDIX

Analysis of Observations During and After the Parallel Group Randomized Trial as a Stepped Wedge Trial

Rationale.

The stepped wedge randomized trial is a relatively new and increasingly popular type of trial. (1-4) Stepped wedge trials involve sequential roll-out of an intervention to groups over a number of time periods. All groups receive the intervention by the end of the trial. An example is shown in Appendix Figure 1 below. Each group serves as its own control in a before-after comparison and also as control for other groups in comparisons across time. Thus, this design allows both between-group and within-group analyses adjusting for temporal changes in outcomes.

Partly because the analyses can be adjusted for temporal changes, stepped wedge trials in which the intervention is initiated in different groups in a random order are generally considered to be a stronger design than nonrandomized studies, including the frequently used before and after comparison of interventions introduced into clinical practice. The stepped wedge design is usually recommended when it is not ethical, desirable, or feasible to conduct a conventional parallel group randomized trial or to evaluate the effects of implementing into routine practice interventions previously shown to be effective in parallel group randomized trials.(2)

The number of groups and the number of study phases vary in different stepped wedge trials. Our assessments of patients originally enrolled in the trial can be viewed as a two-phased stepped wedge trial in which comprehensive care was made available to half of the patients (randomly selected) in the first phase (the parallel randomized trial) and all the patients in the second phase (the post-trial period) after the benefits of comprehensive care has been clearly demonstrated (Appendix Figure 2). The exclusion of the transition period was preplanned to allow assessment of the scalability, as well the sustainability of the benefits of comprehensive care after major expansion of the clinic had occurred.

Stepped wedge designs are ordinarily used in cluster trials with a limited number of centers and potential differences between groups receiving the intervention in different periods. The fact that we have randomized patients rather than centers reduces the likelihood of significant differences between groups that may well occur in conventional cluster stepped wedge trials.

Analyses.

In estimating the effect of comprehensive care over both periods, intent-to-treat analyses were performed using Poisson GEE and gamma GEE with log link regression models including main effects for treatment and study period, and accounting for within-subject correlation, length of follow-up, and the stratifying variables used in the original trial (receipt of maternal high school diploma [yes, no], estimated baseline hospitalization risk [51-75%; >75%]).

Results.

After adjusting for study time period, this analysis showed a significant overall effect of comprehensive care across the two periods in reducing children with serious illness (RR, 0.46 [0.30-0.72]) that was similar to the effect of comprehensive care that was observed in the trial (RR, 0.45 [0.28-0.73]). (5) The stepped wedge analysis of costs adjusting for study time period also showed a significant overall cost reduction with comprehensive care during the two periods (CR, 0.64 [0.42-0.99]) that was comparable to the cost reduction observed in the trial (CR, 0.58 [0.38-0.88]). (5)

Interpretation.

Comprehensive care was shown to be superior to usual care in the trial.(5) In these intent-to-treat stepped wedge analyses, patients who received usual care in the second period were analyzed as if they had received comprehensive care. With half of the parents in the usual care trial group opting to continue usual care when offered comprehensive care after the trial, intent-to-treat analyses provided a conservative estimate of the benefits of comprehensive care in the post-trial period and, thus, the overall treatment effect of comprehensive care across both periods. Even so, the findings noted above with similar results over both study periods to those during the trial provide no evidence that the benefits of comprehensive care diminished after program expansion.

	Period 1	Period 2	Period 3	Period 4	Period 5
Group 1					
Group 2					
Group 3					
Group 4					

Appendix Figure 1.

Illustration of a general stepped wedge study.

Light grey cells represent control periods; dark grey cells represent intervention periods.

	Period 1: Trial Period (March 2011-August 2013)	Transition Period (Sept. 2013- Feb. 2014)	Period 2: Post-Trial Period (March 2014-June 2015)
Group 1 (Trial Comprehensive Care Group)			

Group 2 (Trial Usual Care Group)			
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Appendix 2.

The current study as a stepped wedge design to assess the effect of comprehensive care across both study periods for patients enrolled in the parallel group randomized trial.

Light grey cells represent control periods; dark grey cells represent intervention periods; shaded dark grey cells represent a transition period in which Group 2 was allowed to transition to comprehensive care.

Appendix References

1. Copas AJ, Lewis JJ, Thompson JA, Davey C, Baio G, Hargreaves JR. Designing a stepped wedge trial: three main designs, carry-over effects and randomisation approaches. *Trials*. 2015 8 17;16:352. [PubMed: 26279154]
2. Mdege ND, Man MS, Taylor Nee Brown CA, Torgerson DJ. Systematic review of stepped wedge cluster randomized trials shows that design is particularly used to evaluate interventions during routine implementation. *J Clin Epidemiol*. 2011 9;64(9):936–48. [PubMed: 21411284]
3. Hemming K, Haines TP, Chilton PJ, Girling AJ, Lilford RJ. The stepped wedge cluster randomised trial: rationale, design, analysis, and reporting. *BMJ*. 2015 2 6;350:h391. [PubMed: 25662947]

4. Hussey MA, Hughes JP. Design and analysis of stepped wedge cluster randomized trials. *Contemp Clin Trials*. 2007 2;28(2):182–91. [PubMed: 16829207]
5. Mosquera RA, Avritscher EB, Samuels CL, Harris TS, Pedroza C, Evans P, et al. Effect of an enhanced medical home on serious illness and cost of care among high-risk children with chronic illness: a randomized clinical trial. *JAMA*. 2014 12 24–31;312(24):2640–8. [PubMed: 25536255]

Abbreviations:

CMC	children with medical complexity
ED	emergency department
PICU	pediatric intensive care unit
RR	rate ratio
CR	cost ratio
CI	confidence interval
QI	quality improvement
UTH	University of Texas at Houston
CMHH	Children's Memorial Hermann Hospital
RVUs	relative value units
GEE	generalized estimating equation

References

1. Burke R, Liptak GS. Providing a primary care medical home for children and youth with spina bifida. *Pediatrics*. 2011 12;128(6):e1645–57. [PubMed: 22123894]
2. Agrawal R, Shah P, Zebracki K, Sanabria K, Kohrman C, Kohrman AF. Barriers to care for children and youth with special health care needs: perceptions of Illinois pediatricians. *Clin Pediatr (Phila)*. 2012 1;51(1):39–45. [PubMed: 21856963]
3. Greenberg JO, Barnett ML, Spinks MA, Dudley JC, Frolkis JP. The "medical neighborhood": integrating primary and specialty care for ambulatory patients. *JAMA Intern Med*. 2014 3;174(3):454–7. [PubMed: 24474526]
4. Mosquera RA, Avritscher EB, Samuels CL, Harris TS, Pedroza C, Evans P, et al. Effect of an enhanced medical home on serious illness and cost of care among high-risk children with chronic illness: a randomized clinical trial. *JAMA*. 2014 12 24–31;312(24):2640–8. [PubMed: 25536255]
5. Cohen E, Jovcevska V, Kuo DZ, Mahant S. Hospital-based comprehensive care programs for children with special health care needs: a systematic review. *Arch Pediatr Adolesc Med*. 2011 6;165(6):554–61. [PubMed: 21646589]
6. Kuhlthau KA, Bloom S, Van Cleave J, Knapp AA, Romm D, Klatka K, et al. Evidence for family-centered care for children with special health care needs: a systematic review. *Acad Pediatr*. 2011 Mar-Apr;11(2):136–43. [PubMed: 21396616]
7. Homer CJ, Klatka K, Romm D, Kuhlthau K, Bloom S, Newacheck P, et al. A review of the evidence for the medical home for children with special health care needs. *Pediatrics*. 2008 10;122(4):e922–37. [PubMed: 18829788]
8. Jackson GL, Powers BJ, Chatterjee R, Bettger JP, Kemper AR, Hasselblad V, et al. Improving patient care. The patient centered medical home. A Systematic Review. *Ann Intern Med*. 2013 2 05;158(3):169–78. [PubMed: 24779044]

9. Liptak GS, Murphy NA. Providing a primary care medical home for children and youth with cerebral palsy. *Pediatrics*. 2011 11;128(5):e1321–9. [PubMed: 22042817]
10. Jessop DJ, Stein RE. Providing comprehensive health care to children with chronic illness. *Pediatrics*. 1994 4;93(4):602–7. [PubMed: 8134215]
11. van den Berk-Clark C, Doucette E, Rottnek F, Manard W, Prada MA, Hughes R, et al. Do Patient-Centered Medical Homes Improve Health Behaviors, Outcomes, and Experiences of Low-Income Patients? A Systematic Review and Meta-Analysis. *Health Serv Res*. 2018 6;53(3):1777–98. [PubMed: 28670708]
12. Broyles RS, Tyson JE, Heyne ET, Heyne RJ, Hickman JF, Swint M, et al. Comprehensive follow-up care and life-threatening illnesses among high-risk infants: A randomized controlled trial. *JAMA*. 2000 10 25;284(16):2070–6. [PubMed: 11042755]
13. Simon TD, Berry J, Feudtner C, Stone BL, Sheng X, Bratton SL, et al. Children with complex chronic conditions in inpatient hospital settings in the United States. *Pediatrics*. 2010 10;126(4):647–55. [PubMed: 20855394]
14. Fan E, Laupacis A, Pronovost PJ, Guyatt GH, Needham DM. How to use an article about quality improvement. *JAMA*. 2010 11 24;304(20):2279–87. [PubMed: 21098772]
15. Portela MC, Pronovost PJ, Woodcock T, Carter P, Dixon-Woods M. How to study improvement interventions: a brief overview of possible study types. *BMJ Qual Saf*. 2015 5;24(5):325–36.
16. Mdege ND, Man MS, Taylor Nee Brown CA, Torgerson DJ. Systematic review of stepped wedge cluster randomized trials shows that design is particularly used to evaluate interventions during routine implementation. *J Clin Epidemiol*. 2011 9;64(9):936–48. [PubMed: 21411284]
17. Centers for Medicare and Medicaid Services (2017) physician fee schedule search. <https://www.cms.gov/apps/physician-fee-schedule/search/search-criteria.aspx>. Accessed February 2017.
18. US Department of Labor; Bureau of Labor Statistics. Consumer price indexes. <https://www.bls.gov/data/#prices>. Accessed March, 2017.
19. Hussey MA, Hughes JP. Design and analysis of stepped wedge cluster randomized trials. *Contemp Clin Trials*. 2007 2;28(2):182–91. [PubMed: 16829207]
20. Zoungas S, Chalmers J, Neal B, Billot L, Li Q, Hirakawa Y, et al. Follow-up of blood-pressure lowering and glucose control in type 2 diabetes. *N Engl J Med*. 2014 10 09;371(15):1392–406. [PubMed: 25234206]
21. Heart Protection Study Collaborative G. Effects on 11-year mortality and morbidity of lowering LDL cholesterol with simvastatin for about 5 years in 20,536 high-risk individuals: a randomised controlled trial. *Lancet*. 2011 12 10;378(9808):2013–20. [PubMed: 22115874]
22. Wiles NJ, Thomas L, Turner N, Garfield K, Kounali D, Campbell J, et al. Long-term effectiveness and cost-effectiveness of cognitive behavioural therapy as an adjunct to pharmacotherapy for treatment-resistant depression in primary care: follow-up of the CoBaT randomised controlled trial. *Lancet Psychiatry*. 2016 2;3(2):137–44. [PubMed: 26777773]

Figure 1.

Flowchart of study patients

* Enrolled by December 2014 to allow for at least 6 months of follow-up to assess effect of comprehensive care as in the trial.

Table 1

Baseline characteristics of trial patients included in the primary analyses.

Baseline Characteristic, No. (%)	Trial Comprehensive Care Group			Trial Usual Care Group		
	Post-Trial Period ^a (n=100)	Trial Period ^b (n=105)	P Value ^c	Post-Trial Period ^d (n=91)	Trial Period ^e (n=96)	P Value ^c
Age category^f			<0.01			<0.01
0-12 mo.	0 (0)	22(21)		0 (0)	20(21)	
13 mm-2 y	17 (17)	29 (28)		12 (13)	27 (28)	
3-5 y	38 (38)	22 (21)		36 (40)	22 (23)	
6-11 y	32 (32)	26 (25)		31 (34)	18 (19)	
12-18	13 (13)	6 (6)		12 (13)	9 (9)	
Gender			0.89			0.99
Male	61 (61)	65 (62)		53 (58)	56 (58)	
Female	39 (39)	40 (38)		38 (42)	40 (42)	
Race or ethnicity			0.99			0.94
African-American	43 (43)	45 (43)		32 (35)	33 (34)	
Non-Hispanic white	10 (10)	10 (10)		9 (10)	11 (11)	
Hispanic	47 (47)	50 (48)		50 (55)	52 (54)	
Insurance Status			0.91			0.90
Medicaid insurance	91 (91)	97 (92)		82 (90)	87 (91)	
Other insurance	9 (9)	8 (8)		9 (10)	9 (9)	
Risk Stratum^g			0.59			0.60
High risk	90 (90)	92 (88)		81 (89)	83 (86)	
Very high risk	10 (10)	13 (11)		10 (11)	13 (14)	
Maternal Education			0.78			0.87
High-school diploma	76 (76)	78 (74)		72 (79)	75 (78)	
No high-school diploma	24 (24)	27 (26)		19 (21)	21 (22)	
Diseases						
Congenital	36 (36)	38 (36)	0.98	27 (30)	31 (32)	0.70
Respiratory	80 (80)	85 (81)	0.86	71 (78)	75 (78)	0.99
Neurological	36 (36)	40 (38)	0.76	32 (35)	36 (38)	0.74
Gastrointestinal Disorders	33 (33)	36 (34)	0.85	22 (24)	26 (27)	0.65
of other organs	22 (22)	26 (25)	0.64	19 (21)	22 (23)	0.74
Treatments						
Mechanical ventilation	9 (9)	12 (11)	0.57	8 (9)	10 (10)	0.71
Gastrostomy tube	30 (30)	33 (31)	0.83	20 (22)	24 (25)	0.63

Values in bold type show statistically significant differences ($P \leq 0.05$) between groups.

^a133 child-years.

^b184 child-years.

^cDifferences between treatment groups were compared using chi square test.

^d121 child-years.

^e172 child-years.

^fThe mean age at trial enrollment in the CC group was 4.6 years and 6.9 years in the post-trial period. In the UC group, the mean age at trial enrollment was 4.6 years and 7.0 years post trial.

^gBaseline risk of hospitalization in the year following enrollment estimated based on the clinical judgment of the medical director (R.A.M.): high risk = 51-75% estimated risk; very high risk >75% estimated risk.

Table 2

Baseline characteristics of patients included in the secondary analyses.

Baseline Characteristic	All Patients Given Comprehensive Care, No. (%)		<i>P</i> Value ^d
	Post-Trial Period ^{a,b} (n=233)	Trial Period ^c (n=105)	
Age Ranges			0.004
0-12 mo.	19 (8)	22 (21)	
13 mm-2 y	56 (24)	29 (28)	
3-5 y	68 (29)	22 (21)	
6-11 y	61 (26)	26 (25)	
12-18	29 (12)	6 (6)	
Gender			0.93
Male	143 (61)	65 (62)	
Female	90 (39)	40 (38)	
Race or ethnicity			0.41
African-American	90 (39)	45 (43)	
Non-Hispanic White	22 (9)	10 (10)	
Hispanic	113 (49)	50 (48)	
Other	6 (3)	0 (0)	
Insurance Status			0.80
Medicaid insurance	211 (91)	97 (92)	
Other insurance	22 (9)	8 (8)	
Risk Stratum^e			0.02
High Risk	179 (76)	92 (88)	
Very High Risk	54 (23)	13 (12)	
Maternal Education			0.48
High-School Diploma	179 (78)	78 (74)	
No High-School Diploma	51 (22)	27 (26)	
Non Reported	3 (1)	0 (0)	
Diseases			
Congenital disorders	87 (37)	38 (36)	0.84
Respiratory disorders	184 (79)	85 (81)	0.68
Neurological disorders	93 (40)	40 (38)	0.75
Gastrointestinal disorders	92 (39)	36 (34)	0.36
Disorders of other organs	73 (31)	26 (25)	0.22
Treatments			
Mechanical ventilation	34 (14)	12 (11)	0.43

Baseline Characteristic	All Patients Given Comprehensive Care, No. (%)		<i>P</i> Value ^d
	Post-Trial Period ^{a,b} (n=233)	Trial Period ^c (n=105)	
Gastrostomy tube	81 (35)	33 (31)	0.55

Values in bold type show statistically significant differences ($P \leq 0.05$) between groups.

^aIncluding all 100 children in the post-trial comprehensive care group, 45 children in the post-trial usual care group who transitioned to comprehensive care post trial, and 88 new eligible children enrolled in comprehensive care post trial for at least 6-months.

^b273 child-years.

^c184 child-years.

^dDifferences between treatment groups were compared using chi square test.

^eBaseline risk of hospitalization in the year following enrollment estimated based on the clinical judgment of the medical director (R.A.M.): high risk = 51-75% estimated risk; very high risk >75% estimated risk.

Table 3

Analyses addressing primary hypothesis that the post-trial rates of serious illness and the inflation-adjusted health system costs would be markedly decreased from those during the trial for the trial usual care group.

	Trial Usual Care Group				
Outcome Measure	Post-Trial Period (n=91) ^a		Trial Period (n=96) ^b		
Medical Outcome	No.	Unadjusted Rate/100 Child-Years	No.	Unadjusted Rate/100 Child-Years	Adjusted Rate Ratio (95% CI) ^c
Children with a serious illness ^d (Primary Medical Outcome)	9	7	38	22	0.36 (0.20-0.64)
Deaths	0	0	5	3	--
Children with a PICU admission	9	7	26	15	0.52 (0.29-0.94)
Children with a hospital stay > 7 d	5	4	28	16	0.28 (0.13-0.62)
Episodes of serious illnesses	24	20	76	44	0.38 (0.20-0.73)
Emergency department visits	113	93	328	190	0.46 (0.34-0.62)
Admissions	70	58	226	131	0.43 (0.30-0.62)
Days in a hospital	544	449	1094	634	0.26 (0.13-0.50)
PICU admissions	13	11	44	25	0.48 (0.24-0.94)
PICU days	48	40	178	103	0.21 (0.07-0.58)

Cost Outcome, 2017 us\$	Unadjusted Mean Cost/Child-Year Post Trial	Mean Cost/Child-Year During the Trial	Adjusted Cost Ratio (95% CI) ^c
Total health system costs (Primary Cost Outcome)	\$20,774	\$29,203	0.68 (0.28-1.68)
Clinic Costs	\$4,570	\$1,877	2.40 (1.86-3.09)
Hospital Costs	\$16,204	\$27,326	0.57 (0.18-1.78)

Abbreviation: PICU, pediatric intensive care unit; CI, confidence interval.

Values in bold type show statistically significant differences ($P < 0.05$) between periods.

^a 121 child-years.

^b 172 child-years.

^c Adjusted for maternal education, risk stratum, and length of follow-up.

^d Death, PICU admission, or hospitalization >7d.

Table 4

Analyses addressing primary hypothesis that the post-trial rates of serious illness and the inflation-adjusted health system costs would be similar to those during the trial for the trial comprehensive care group.

	Trial Comprehensive Care Group				
Outcome Measure	Post-Trial Period (n=100) ^a		Trial Period (n=105) ^b		
Medical Outcome	No.	Unadjusted Rate/100 Child-Years	No.	Unadjusted Rate/100 Child-Years	Adjusted Rate Ratio (95% CI) ^c
Children with a serious illness ^d (<i>primary medical outcome</i>)	9	7	18	10	0.74 (0.39-1.41)
Deaths	0	0	3	2	--
Children with a PICU admission	6	5	14	8	0.60 (0.27-1.30)
Children with a hospital stay > 7 d	6	5	13	7	0.68 (0.28-1.61)
Episodes of serious illnesses	13	10	29	16	0.61 (0.28-1.33)
Emergency department visits	72	54	165	90	0.52 (0.29-0.95)
Admissions	55	41	127	69	0.59 (0.30-1.17)
Days in a hospital	201	151	506	276	0.46 (0.14-1.46)
PICU admissions	7	5	17	9	0.57 (0.23-1.40)
PICU days	11	8	52	28	0.26 (0.08-0.90)

Cost Outcome, 2017 us\$	Unadjusted Mean Cost/Child-Year Post Trial	Unadjusted Mean Cost/Child-Year During the Trial	Adjusted Cost Ratio (95% CI) ^c
Total health system costs (<i>primary cost outcome</i>)	\$12,425	\$18,019	0.67 (0.51-0.89)
Clinic Costs	\$6,987	\$7,317	0.91 (0.81-1.04)
Hospital Costs	\$5,438	\$10,693	0.51 (0.30-0.88)

Abbreviation: PICU, pediatric intensive care unit; CI, confidence interval.

Values in bold type show statistically significant differences ($P < 0.05$) between periods.

^a 133 child-years.

^b 184 child-years.

^c Adjusted for maternal education, risk stratum, and length of follow-up.

^d Death, PICU admission, or hospitalization >7d.

Table 5

Analysis of the secondary hypothesis that serious illness rates and inflation-adjusted health system costs among all eligible children given comprehensive care after the trial would be similar to those among the comprehensive care group during the trial.

	Patients Given Comprehensive Care		
Outcome Measure	Post-Trial Period (n=233) ^a Adjusted Rate/100 Child- years	Trial Period (n=105) ^b Adjusted Rate/100 Child-years	Adjusted Rate Ratio (95% CI) ^c
Medical Outcome			
Children with a serious illness ^d (<i>primary medical outcome</i>)	15.5	15.9	0.97 (0.61-1.52)
Deaths	0.4	2.8	0.16 (0.02-1.70)
Children with a PICU admission	10.3	12.8	0.80 (0.48-1.35)
Children with a hospital stay > 7 d	9.1	11.4	0.79 (0.44-1.45)
Episodes of serious illnesses	23.6	32.0	0.74 (0.42-1.32)
Emergency department visits	112.2	170.8	0.66 (0.48-0.90)
Admissions	86.7	118.4	0.73 (0.53-1.00)
Days in a hospital	490.4	830.7	0.61 (0.35-1.05)
PICU admission	13.7	18.0	0.72 (0.35-1.49)
PICU days	114.3	316.0	0.36 (0.14-0.92)
Cost Outcome, 2017 US\$	Adjusted Mean Cost/Child-Year	Adjusted Mean Cost/Child-Year	Adjusted Cost Ratio (95% CI) ^c
Total health system costs (<i>primary cost outcome</i>)	\$24,675	\$32,547	0.75 (0.61 –0.93)
Clinic Costs	\$7,027	\$10,554	0.67 (0.64-0.70)
Hospital Costs	\$17,817	\$20,968	0.84 (0.60-1.17)

Abbreviation: PICU, pediatric intensive care unit; CI, confidence interval.

Values in bold type show statistically significant differences ($P < 0.05$) between periods.

^a273 child-years.

^b184 child-years.

^cAdjusted for maternal education, risk stratum, and length of follow-up.

^dDeath, PICU admission, or hospitalization >7d.