# Evolution of treatment options and outcomes for hypoplastic left heart syndrome over an 18-year period

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**Objectives:** We aimed to describe management strategies for neonates with hypoplastic left heart syndrome over the past 18 years in the United States and to identify determinants of institutional management decisions.

**Methods:** Neonates with hypoplastic left heart syndrome were retrospectively identified by use of the Nationwide Inpatient Sample 1988–2005. Treatment was categorized as (1) transplantation, (2) Norwood operation (as defined by Risk Adjustment in Congenital Heart Surgery), (3) transfer to another facility, or (4) no surgical intervention (comfort care).

**Results:** A total of 3286 neonates were identified, yielding a national estimate of 16,781 ± 586 cases. Of these, 2% (348 ± 47) underwent transplantation, 16% (2767 ± 286) had Norwood operations, 25% (4143 ± 156) were transferred to another facility, and 57% (9523 ± 436) had comfort care. Changes in practice patterns occurred over time, with an increasing number of neonates undergoing Norwood, concomitant with decreasing numbers undergoing transplantation ($P < .001$). Bias toward the Norwood operation over time paralleled a significant, nearly linear decrease in the in-hospital mortality rate for the Norwood operation, from 86% in the earliest sextile to 24% in the most recent sextile ($P < .001$). Prevalence of transfer to definitive care hospitals remained constant over time, as did the number of infants (approximately half) who received no surgery (comfort care).

**Conclusions:** Despite improved surgical outcomes, the majority of infants continue to receive no surgical care. There has been an increase in the number of infants offered the Norwood operation for hypoplastic left heart syndrome over the past 2 decades, which seems to have come mostly owing to a decrease of transplants. The advent of prenatal diagnosis has not decreased the proportion of neonates born at institutions unequipped to provide definitive care. (J Thorac Cardiovasc Surg 2010;139:119-27)



Hypoplastic left heart syndrome (HLHS) remains one of the most challenging diagnoses in the field of congenital heart disease. Despite recent innovative techniques in surgical treatment, including the hybrid strategy (pulmonary arterial banding with ductal stenting) and ABO-incompatible transplantation, long-term survival remains suboptimal and quality of life incompletely assessed.[1-3] It is unclear what factors motivate an institutional choice toward surgical treatment versus no intervention, especially considering the lack of consensus among physicians, 40% of whom recommended a disparate treatment strategy than they would themselves choose.[1,4-9] Additionally, given the comparatively poor long-term prognosis of HLHS, especially among certain subsets of patients with concomitant syndromes (Turner syndrome, 22q deletion), the option for compassionate care without intervention (comfort care) may be underused in the United States,[10,11] although data elucidating the incidence of comfort care are lacking.

There have been three major reports[1,4,5] chronicling the national practice patterns for infants with HLHS. However, none of these included the most recent era with the introduction of newer management strategies, fetal intervention, and widespread prenatal diagnosis, which may have major impact on treatment selection. Additionally, prior reports have not included the entire spectrum of United States hospitals treating infants with HLHS, nor used a validated and widely accepted algorithm to define the Norwood operation.[12]

We therefore undertook this study to determine current practice national patterns for HLHS and identify determinants associated with a decision toward a particular management strategy. We also focused on national in-hospital mortality and morbidity trends over the course of an 18-year period.

## METHODS

### Data Set: The Nationwide Inpatient Sample (NIS)

The NIS is the largest all-payer inpatient care database in the United States. The NIS is managed under the Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality.[13] The database is a stratified, cross-sectional sample that includes approximately 20% of all non-federal hospital discharges in the United States. The sampling protocol is such that when a hospital is chosen, all discharges from that hospital for

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**Abbreviations and Acronyms**

CI = confidence interval
HLHS = hypoplastic left heart syndrome
ICD-9-CM = International Classification of Diseases, ninth revision, clinical modification
NIS = Nationwide Inpatient Sample
OHTx = transplantation
RACHS-1 = Risk Adjustment in Congenital Heart Surgery



the selected time period are included. To ensure the representative nature of the database, the NIS is stratified by geographic region, urban versus rural location, teaching status, hospital ownership, and hospital bed size. This study's data were derived from the combination of the NIS databases from 1988 to 2005, and our analysis uses sampling weights provided within the NIS to derive national estimates. The sampling frame of the NIS has been nearly constant over time except for a modification in 1998, which excluded short-term rehabilitation hospitals from the sampling frame. To account for this small change, we have used the revised NIS trend weights, published by the Agency for Healthcare Research and Quality,[13] which allows one to compare across years with the same effective sampling scheme. The NIS is not a self-selecting, and potentially growing, set of hospitals reporting their data. Rather, it is a national sample of hospitals representing 20% of all discharges. Additionally, it is designed to provide national estimates, not a total of participating hospitals. NIS data are available from 1988 to 2005 over which time the number of states participating in the NIS has grown from 8 to 37. In 2005, the database contained discharge data on approximately 8 million hospital stays at 1054 hospitals in 37 states.

### Patients and Hospitals

We sought to identify the most homogeneous population of infants with HLHS, whose morphologic features would be amenable to either Norwood operation or transplantation (OHTx), and therefore excluded those infants with other complex cardiac anomalies (eg, total anomalous pulmonary veins, heterotaxy syndrome). The NIS database was searched for the individual years 1988 to 2005, selecting out hospital discharges that met the following criteria: (1) infants 30 days of age or younger; (2) possessed a primary International Classification of Diseases, ninth revision, clinical modification (ICD-9-CM) diagnosis code of 746.7 (HLHS) without concomitant cardiac diagnoses; (3) underwent a surgical procedure (Norwood operation or OHTx), were transferred to another facility, or were discharged from the hospital or died in-hospital without any intervention (comfort care). Discharges with additional cardiac procedure codes were excluded. Because there is no ICD-9-CM code for the Norwood operation, we used the Risk Adjustment in Congenital Heart Surgery (RACHS-1) definition with slight modification to identify these patients as described in Appendix 1. The ICD-9-CM procedure code 37.5 was used to identify patients undergoing OHTx.

To minimize an important source of error, we also determined, to the extent possible, the final disposition of transferred neonates. The NIS contains admission codes identifying neonates who were received in-transfer from another hospital. We therefore were able to determine the disposition of neonates who were transferred from a hospital included in the NIS sample that year to a hospital that was also included within the NIS sample that year. We incorporated this admission code and then reanalyzed our data set to investigate trends in final treatment for neonates who were transferred over time. We then compared the disposition of the transferred neonates at the receiving hospital to the disposition of neonates who were not transferred.

### Statistical Analysis

Overall descriptive statistics were computed. Treatment groups were compared by the Rao–Scott $\chi^2$ for categorical variables or $t$ test for continuous variables. Years were grouped into sextiles and annual RACHS-1 volume for each unique hospital was calculated. The probability for each management option was investigated by multivariable ordinal regression models (PROC SURVEYLOGISTIC), adjusted for patient and hospital level characteristics. Risk-adjusted in-hospital mortality was also compared among surgical treatment strategies (OHTx or Norwood) with multivariable ordinal regression using PROC SURVEYLOGISTIC. C-indices were generated for all logistic regression models to provide insight into model discrimination. SAS software, version 9.1 (SAS Institute, Inc, Cary, NC) was used to fit the models to account for the survey design of the NIS, the potential clustering of outcomes within a hospital, and the decrease in clustering occurring over increasing time intervals. Institutional review board approval was obtained, but given the de-identified nature of the NIS, patient consent was waived for this study.

## RESULTS

### Case Mix

We identified 3286 cases from 586 NIS hospitals during the study period, yielding a national estimate of 16,781 ± 586 cases. Of these, 2% (348 ± 47) were OHTx, 16% (2767 ± 286) were Norwood operations, 25% (4143 ± 156) were transfers to other facilities, and 57% (9523 ± 436) involved comfort care. Demographics and clinical characteristics of the study patients are shown in Table 1. Age was not included because our inclusion criteria limited the study population to neonates (≤30 days of age). Overall, there was a significant increase in the proportion of neonates undergoing the Norwood operation over time (weighted frequency 39.9 ± 14.6 [2% of total cases] in the first sextile [1988–1990] versus 923.8 ± 164.2 [24% of cases] in the most recent sextile [2003–2005]; $P < .001$). In contradistinction, OHTx prevalence declined steadily from a peak of 120 ± 13 (5% of cases) in the third sextile (1994–1996) to 14 ± 6 (<1% of cases) in the most recent sextile ($P < .001$). Despite the increased national popularity of the Norwood operation, however, the proportion of neonates having nonoperative therapy, either comfort care or transfer ($P = .03$), also rose modestly over time (Figure 1).

Hospital length of stay was longest for patients undergoing OHTx (65 ± 4 days), with Norwood patients having an average length of stay of 30 ± 1 days. Importantly, those neonates undergoing no intervention still had an average length of stay of 11 ± 1 days.

### Mortality

There were 975 total deaths out of 3286 neonates (national estimate of 5002 ± 215) during the study period, yielding an overall mortality rate of 30%. Overall mortality was higher for the Norwood operation (n = 178/975; 18%) than for OHTx (n = 21/975; 2%). However,

**TABLE 1. Demographic and clinical characteristics of study patients among treatment types**

| Variable | Norwood | OHTx | Comfort care | Transfer |
|---|---|---|---|---|
| Female | 1047 ± 135 (38%) | 151 ± 27 (43%) | 3586 ± 186 (38%) | 1475 ± 83 (36%) |
| Race | | | | |
| White | 1106 ± 137 (54%) | 187 ± 28 (76%) | 3578 ± 214 (60%) | 1737 ± 80 (65%) |
| Black | 235 ± 47 (11%) | 0 (0%) | 687 ± 81 (11%) | 359 ± 47 (14%) |
| Hispanic | 354 ± 67 (17%) | 37 ± 13 (15%) | 1342 ± 163 (22%) | 391 ± 38 (15%) |
| Asian/PI | 44 ± 14 (2%) | 9 ± 4 (4%) | 76 ± 16 (1%) | 38 ± 11 (1%) |
| Native Am | 28 ± 6 (1%) | 0 (0%) | 32 ± 14 (1%) | 15 ± 9 (1%) |
| Other | 285 ± 59 (14%) | 13 ± 5 (5%) | 287 ± 47 (5%) | 117 ± 23 (4%) |
| Charges (USD) | 249,161 ± 11,066 | 406,245 ± 25,856 | 60,422 ± 4,230 | 10,928 ± 957 |
| LOS (d) | 30 ± 1 | 65 ± 4 | 11 ± 1 | 2 ± 0.2 |
| Hospital type | | | | |
| Rural | 0 (0%) | 0 (0%) | 250 ± 9 (2%) | 285 ± 11 (7%) |
| Urban NT | 249 ± 80 (9%) | 84 ± 30 (24%) | 2521 ± 187 (27%) | 1303 ± 62 (31%) |
| Urban T | 2518 ± 274 (91%) | 264 ± 36 (76%) | 6738 ± 394 (71%) | 2555 ± 142 (62%) |
| Annual RACHS-1 volume | 246 (17–723) | 237 (82–298) | 112 (0–723) | 0 (0–723) |

*OHTx,* Transplant; *PI,* Pacific Islander; *Am,* American; *USD,* United States dollars; *LOS,* length of hospital stay; *NT,* nonteaching; *T,* teaching.

Norwood-specific mortality decreased nearly linearly over time, from 86% (6/7) in the earliest sextile to 24% (47/191) in the most recent sextile, whereas in-hospital mortality for OHTx remained constant (Figure 2).

Multivariable factors increasing the probability of in-hospital death included earlier year sextile ($P < .001$) for earliest year sextile compared with most recent sextile, lower annual RACHS-1 case volume ($P=.002$), and female gender. Norwood operation was not associated with an increased risk of death ($P=.40$), but OHTx was protective ($P=.002$; Table 2).

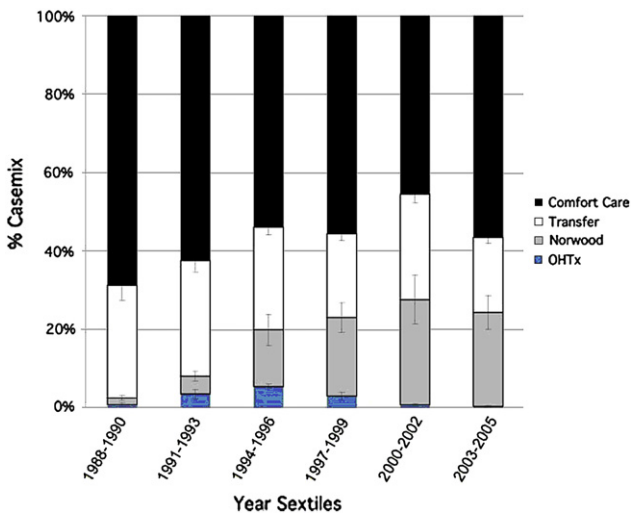


**FIGURE 1.** Distribution of case-mix in year sextiles. An increase in the Norwood operation is seen over time concomitant with a small decrease in the number of OHTx. Despite increasing application of the Norwood operation, comfort care remains the most common treatment choice. Raw numbers (estimates) of the total number of neonates with HLHS within each sextile are as follows: sextile 1: 406 total (national estimate, 2393); sextile 2: 458 total (national estimate, 2469); sextile 3: 437 total (national estimate, 2202); sextile 4: 583 total (national estimate, 2921); sextile 5: 606 total (national estimate, 2935); sextile 6: 796 total (national estimate, 3862).

## Evolution of Treatment Patterns for Transferred Patients

Because an important number of patients within our study were transferred to another hospital, we investigated the disposition of these neonates over time. The proportion of patients transferred in over time has remained relatively constant over time, from 43% (248/572) in 1988 to 40% (738/938) in 2005 (Figure 3). Regarding disposition of the transferred-in patients, we found, as expected, an increase

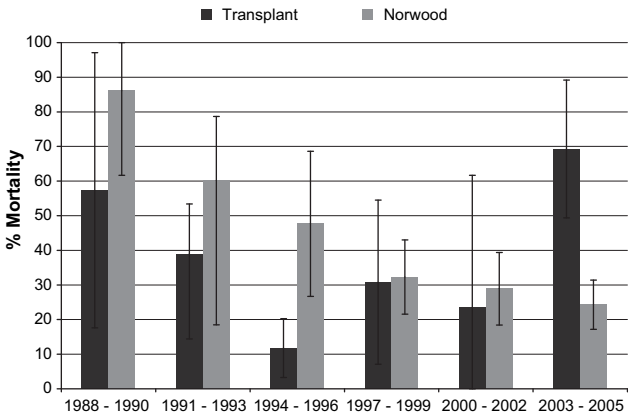


**FIGURE 2.** Mortality for the Norwood operation and OHTx is displayed over time, divided into year sextiles. Norwood mortality decreased in a nearly linear manner over time. Note the widening confidence intervals for OHTx mortality within all but 1 of the year sextiles, indicating that increased mortality may be confounded the small number of OHTx cases in these periods.

**TABLE 2. Multivariable factors associated with in-hospital mortality**

| Variable | Odds ratio | 95% CI | *P* value |
|---|---|---|---|
| Treatment type | | | |
| Comfort care* | (reference category) | | |
| Norwood | 1.13 | 0.85–1.49 | .40 |
| OHTx | 0.47 | 0.29–0.76 | .002 |
| Year sextile | | | |
| 1988–1990 | 6.00 | 4.14–8.70 | <.001 |
| 1991–1993 | 4.31 | 3.05–6.10 | <.001 |
| 1994–1996 | 3.91 | 2.74–0 5.61 | <.001 |
| 1997–1999 | 2.19 | 1.52–3.17 | <.001 |
| 2000–2002 | 1.58 | 1.09–2.29 | <.001 |
| 2003–2005* | (reference category) | | |
| Annual RACHS volume | 0.98 | 0.98–1.0 | 002 |
| Male | 0.83 | 0.70–0.99 | .04 |
| Hospital type | | | |
| Rural | 0.91 | 0.66–1.27 | .58 |
| Urban nonteaching | 1.01 | 0.76–1.35 | .93 |
| Urban teaching | (reference category) | | |

*CI,* Confidence interval. *Reference category.

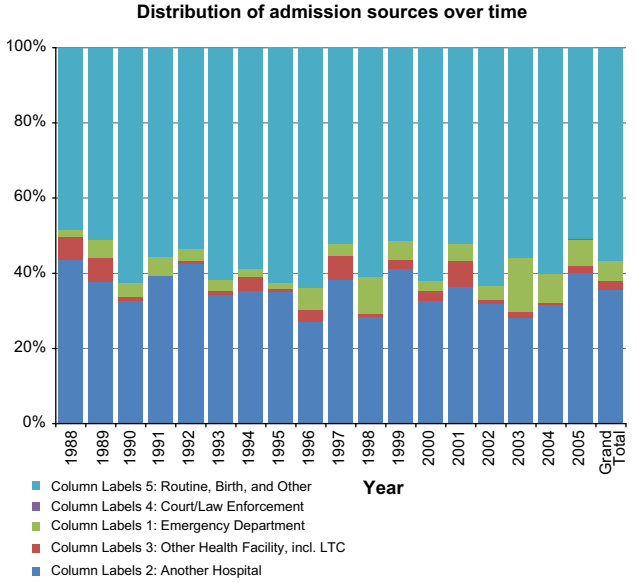


**FIGURE 3.** Graphic display of the admission sources for neonates with HLHS over time. The years are shown on the *horizontal axis* and the proportion of neonates with each admission code is on the *vertical axis*. The legend at the figure right shows the different codes within the NIS. Neonates who were transferred in bear an admission code ''admitted from another hospital,'' shown in *dark blue*. The number of transferred neonates has decreased only slightly during the 18-year period. *LTC,* Long-term care.

in the number of neonates who underwent subsequent surgical intervention at the receiving hospital over time, from 4% (11/248) in 1988 to 47% (348/738) in 2005. There was a corresponding decrease in the proportion of patients having comfort care at the receiving hospital, although this group still comprised nearly 50% of the total (Figure 4).

## Determinants of Treatment Selection

Institutions could be broadly classified into those that predominantly chose surgical treatment, either Norwood or OHTx (eg, interventional hospitals), and those that predominantly chose nonoperative management or transferred patients admitted with a diagnosis of HLHS to other institutions (eg, noninterventional hospitals) (Figure 5). There were clear treatment biases, with the majority of hospitals choosing to transfer neonates with HLHS or provide comfort care. A minority of hospitals uniformly provided the Norwood operation and a small number provided OHTx as the only interventional option, with the other neonates admitted to that hospital either receiving comfort care or being transferred to another facility. Importantly, hospitals providing both Norwood operation and OHTx have the highest percentage of intervention in neonates with HLHS and used transfer with decreasing frequency. Excepting the patients that are transferred, these data also demonstrate that the type of care primarily performed at the initial admitting institution is a primary determinant in the treatment that a neonate with HLHS receives. Neonates admitted to noninterventional hospitals generally do not undergo operation whereas neonates admitted to interventional hospitals generally undergo either Norwood or OHTx.

There was a significant increase in the percent of neonates initially admitted to a hospital capable of providing surgical intervention over time from 2.5% (95% confidence interval [CI], 1.1–3.9) in the earliest sextile (1988–1990) to 23.0% (95% CI, 17.3–28.6) in the fourth sextile (1997–1999) ($P < .001$). However, after this initial increase, the prevalence of initial admission to an interventional hospital has remained nearly constant with only 24.3% (95% CI, 17.8–30.8) of neonates in the recent era (2003–2005) admitted to definitive care institutions (Figure 6).

Multivariate modeling uncovered several factors associated with a patient undergoing operative treatment for HLHS. Significantly fewer patients underwent the Norwood procedure or OHTx in the earliest year sextile (1988–1990) than in the most recent year sextile (2003–2005) (regression coefficient –2.0; $P < .001$). Patients at rural hospitals were less likely to undergo operative intervention for HLHS than those at urban teaching hospitals (regression coefficient, –14.5; $P < .001$) as were those neonates admitted to hospitals with lower annual RACHS-1 categorized pediatric surgical case volume (regression coefficient, –0.004; $P < .001$).

## Influence of Hospital Volume on Management Strategy

The median annual number of RACHS-1 coded cases performed among included hospitals was 107 (range, 0–723). Higher annual RACHS-1 volume was significantly associated with a decision toward Norwood operation (odds ratio, 1.004; 95% CI, 1.004–1.005; $P < .001$). Figure 5 is

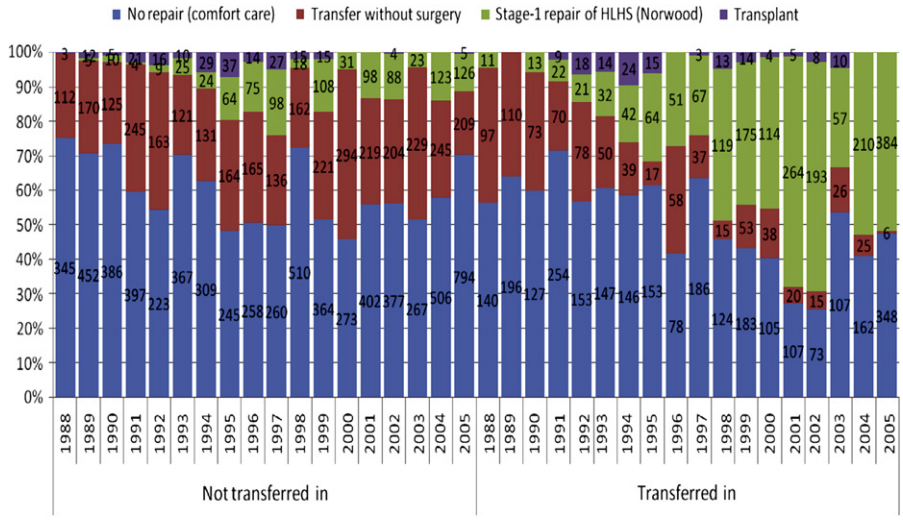


**FIGURE 4.** Number of neonates having each treatment type over time segregated by whether they were transferred from another hospital *(transferred in)* or whether they were admitted directly *(not transferred in)*. The legend at top describes the color-coded 4 treatment types, the years are shown at the *horizontal axis*, and the proportion of neonates having each treatment type is on the *vertical axis*. Regarding the subset of patients who were transferred, there has been an increase in the number of neonates who underwent subsequent surgical intervention at the receiving hospital over time, from 4% (11/248) in 1988 to 47% (348/738) in 2005. There was a corresponding decrease in the proportion of patients having comfort care at the receiving hospital, although this group still comprised nearly 50% of the total in 2005.

a graphic description of the proportion of neonates managed with a particular treatment strategy within each hospital as a function of increasing percent intervention, excluding those hospitals whose annual RACHS-1 volume was less than 3 cases, and segregating OHTx and non-OHTx hospitals. There are clear treatment biases, with the majority of hospitals choosing to transfer neonates with HLHS or provide comfort care. A minority of hospitals uniformly performed the Norwood operation as the only surgical therapy and a small number provide only OHTx. Importantly, hospitals providing both the Norwood operation and OHTx had the highest percentage of intervention in neonates with HLHS and used transfer with decreasing frequency.

## DISCUSSION

We have documented the national changes in management strategy for HLHS over an 18-year period. National use of the Norwood procedure has increased commensurate with declining in-hospital mortality. A portion of this increase in use has come at the expense of OHTx, which has declined substantially. Despite the increased popularity of the Norwood operation in the recent era, the majority of neonates with HLHS still receive no intervention or require transfer to a definitive care hospital. Importantly, we found that institutional biases exist, whereupon infants with HLHS seem to receive the type of care primarily offered at the admitting institution, whether this be surgical intervention or comfort care.

Three earlier reports by Gutsegell and Massaro,[5] Gutsegell and Gibson,[4] and Chang, Chen, and Klitzner[1] have elucidated similar trends albeit in an earlier time period before the widespread use of prenatal diagnosis and fetal intervention. These earlier reports, though, showed a more

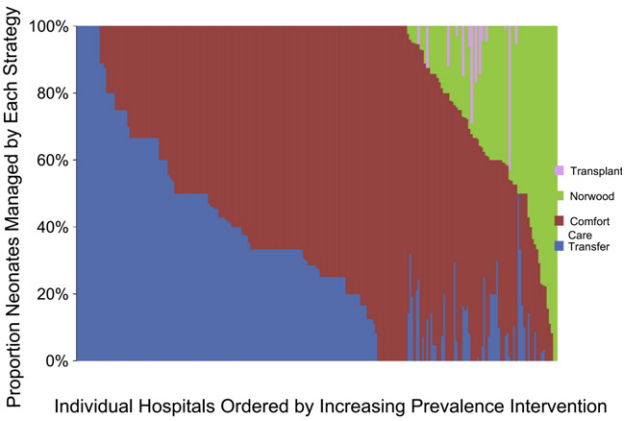


**FIGURE 5.** Graphic description of the proportion of neonates managed with a particular treatment strategy within each hospital *(vertical axis)*, as a function of increasing percent intervention, excluding those hospitals whose annual HLHS volume was less than 3 cases. The different colored shaded areas are confluent histograms from each institution and represent the 4 possible treatment options. There are clear treatment biases, with the majority of hospitals choosing to transfer neonates with HLHS or provide comfort care *(blue and red shaded areas at left)*. A minority of hospitals uniformly choose Norwood operation *(green areas)*, and a small number provide only OHTx *(pink areas)*. Importantly, hospitals providing both the Norwood operation and OHTx have the highest percentage of intervention (and are therefore located at the far right on the plot) in neonates with HLHS and used transfer with decreasing frequency.

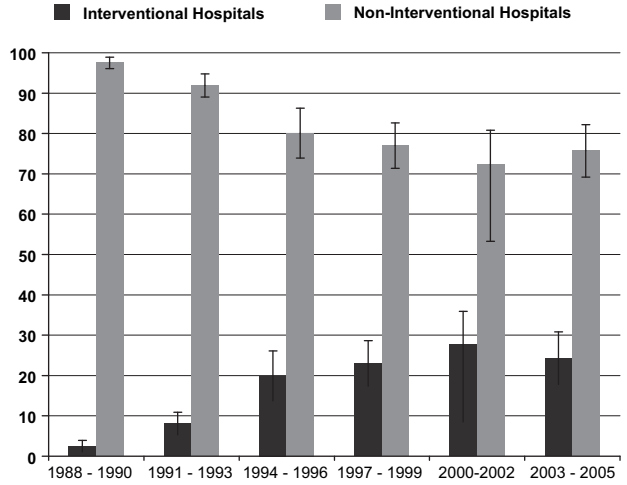


**FIGURE 6.** Percent of neonates with HLHS admitted to either an interventional or noninterventional hospital *(vertical axis)* segregated by year sextiles. An interventional hospital was defined as a hospital that provided either Norwood operation or OHTx at least once during an annual period. A significant increase in the proportion of neonates admitted to interventional hospitals is noted up to 1999, after which point there is no significant increase.



precipitous increase in Norwood prevalence, up to 60% in one study,[4] coupled with a lower prevalence of nonoperative management. On the basis of their data, Chang, Chen, and Klitzner[1] predicted that the Norwood operation would be undertaken in 50% of neonates by 2004. Our study, in contradistinction, suggests that although the Norwood operation has increased nationwide, it is still performed in the minority (25%) of infants in the recent sextile). Moreover, we found that the average percentage of neonates undergoing no intervention over the entire 18-year period was higher than that reported by Chang, Chen, and Klitzner[1] at nearly 58% and declined only slightly over time. Discrepant findings may be due in part to differences in the sampling population. We used the NIS, which may be more representative of the overall treatment patterns within all US hospitals (including community and nonteaching institutions) as opposed to a consortium of university hospitals as was used in the studies by Gutsegell and Gibson[4] and Gutsegell and Massaro,[5] which may have biased their data toward more aggressive treatment protocols.

We also found that an important number of neonates were transferred to other hospitals after initial admission, presumably because they required a higher level of care than available at the admitting institution. The proportion on neonates transferred after initial admission to rural or urban nonteaching hospitals (38%) underscores this contention. The cost of care for these infants, over 10,000 USD, was not inconsequential, and it is likely that definitive care was delayed in these infants. Infants with certain morphologic features requiring urgent intervention, including an intact or highly restrictive atrial septum, are particularly fragile and thereby prenatal triage to a facility equipped to provide definitive care would be advantageous to improve outcome.[14-16] Studies by Vlahos,[14] Rychik,[17] and their colleagues have reported nearly 50% 30-day mortality for this subset compared with 9% for age-matched control patients with HLHS. We attempted to identify infants within this category by selecting those in whom a preoperative balloon atrial septostomy was performed, but the number (n = 10) identified was insufficient to determine whether an important proportion required transfer or received comfort care. However, this limitation notwithstanding, our study highlights an enduring shortcoming of care for infants with HLHS. Our data suggest that even with widespread availability of prenatal diagnosis, an important number of neonates, especially in the rural setting, are still admitted to hospitals not able to provide definitive care. Elucidation of antenatal surveillance and treatment paradigms focused on families residing in rural areas may lead to an overall survival benefit.

Over the 18-year study period, use of the Norwood operation increased nearly linearly concomitant with steadily decreasing national rates of OHTx from a peak in 1996 of nearly 5% of total HLHS cases to less than 1% of total cases in 2005. Although we cannot determine the precise causes of this decline from our retrospective analysis, we agree with Chrisant and colleagues[8] that decreasing national OHTx rates reflect a trend toward Norwood palliation. The bias toward the Norwood operation is compounded by improved short-term outcomes coupled with the fact that infants with HLHS have particularly high pretransplant attrition, with nearly 25% dying before receiving an organ despite relatively short wait-list times of less than 18 months.[6]

A traditional perception has been that the United States is considerably more aggressive in treating infants with HLHS surgically than other developed countries,[10] a dichotomy articulated by Elliott as ''life at any cost'' in the United States compared with a European approach of ''quality is more important than quantity.'' It is unlikely that incidence rates of HLHS have important global variation, but it certainly is true that termination rates in the United States are lower (near 17%), thus increasing the potential number of neonates born with HLHS.[18] Brackley and colleagues[19] reported a 44% termination rate in an active center in the treatment of HLHS in Birmingham, and another unit in London reported a 63% elective rate of termination in prenatally diagnosed HLHS.[20] Surprisingly, though, despite the emerging popularity of the Norwood operation in US hospitals, we also found that ''no treatment'' (comfort care) still represents the most common treatment option for infants with HLHS nationwide. Furthermore, our study found that comfort care was used in over 50% of neonates in the most recent sextile, suggesting that physicians may be adopting a more balanced approach to infants with HLHS.

Motivation for selection of a treatment strategy is complex, involving the desires and belief systems of both physician and parents. Vandvik and Forde[21] reviewed the characteristics of 20 mothers of neonates with HLHS, 10 of whom had children who survived surgery and 10 of whom had children who died after the mothers opted for comfort care. Mothers choosing comfort care (a choice motivated by a desire to ''prevent suffering'') were more educated, more likely to be employed in health care, and reported a better childhood environment than those mothers choosing surgery (a choice perceived as the only acceptable option). Physician influences were examined in a recent provocative article by Kon, Ackerson, and Lo.[7] These authors examined how 454 physicians in the United States made treatment recommendations to parents of infants with HLHS and what factors motivated these recommendations. These investigators found that 26% of physicians did not discuss comfort care, and 25% of those at nontransplant centers do not discuss OHTx with parents, indicating that physicians recommend the treatment preferred at their own institution even when they predict better outcomes with another approach.[7]

## LIMITATIONS

Using an administrative discharge database such as the NIS predisposes our study to coding errors and limits our outcomes to investigation of in-hospital mortality. We have tried to limit the influence of coding errors by requiring that study patients both possessed a diagnosis code for HLHS and fulfilled the RACHS algorithm for a Norwood operation. Furthermore, although we have included an analysis of the final disposition of patients who were transferred to other facilities, the lack of patient identifiers precludes us from knowing the final disposition (ie, Norwood, OHTx, death) of all patients transferred from the initial hospital and introduces the possibility that we have counted some patients twice.

## CONCLUSION

Clinical management of neonates with HLHS has evolved over time, with an increased proportion of neonates undergoing the Norwood operation. However, there are strong institutional biases toward a particular management strategy, and nonoperative treatment is still used in the majority of US hospitals. Hospitals performing a higher number of RACHS cases most likely treat neonates surgically, and those hospitals providing both OHTx and the Norwood operation intervene in the highest proportion of neonates. Despite the more widespread application of prenatal diagnosis, a substantial number of neonates are initially admitted to hospitals not equipped to provide definitive care.

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**APPENDIX 1. RACHS-1 DEFINITIONS AND ALGORITHM USED TO IDENTIFY NORWOOD**

**Operation**

**Require:**

Dx 746.7 Hypoplastic left heart syndrome
Proc 35.41 Enlargement of existing atrial septal defect
or 35.42 Creation of septal defect in heart
Proc 39.0 Systemic–pulmonary artery shunt
or 35.92 Creation of conduit between right ventricle and pulmonary artery
Proc 38.35 or 38.45 Resection of thoracic vessel
or 38.34 or 38.44 Resection of abdominal aorta
or 38.64 or 38.65 Other excision of vessel/aorta
or 38.84 or 38.85 Other surgical occlusion of vessel/aorta
or 39.56, 39.57, 39.58 Repair of blood vessel
or 39.59 or 36.99 Other operation on vessel of heart

**Cannot have:**

Proc 35.94 Creation of conduit between atrium and pulmonary artery
Proc 35.95 Revision corrective procedure on heart
Proc 39.21 Cavo–pulmonary artery anastomosis

**Allow:**

Dx 745.5 Ostium secundum atrial septal defect
Dx 746.3 Congenital stenosis of aortic valve
Dx 746.5 Congenital mitral stenosis
Dx 747.0 Patent ductus arteriosus
Dx 747.10 Coarctation of aorta
Dx 747.22 Atresia and stenosis of aorta
Dx 747.89 Other anomalies of great veins
Proc 37.33 Excision of other lesion/tissue of heart

**Cannot have:**

Any other cardiac diagnosis (Dx)

## Discussion

**Dr David Clarke** *(Denver, Colo).* The data examined from the NIS include presumably administrative data from about 20% of hospitals stratified by location, size, teaching, and so forth. Even if we assume the sample is representative of the entire country, intrinsic errors known to exist in administrative data, especially in the specialty of surgery for congenital heart disease, multiplied by five does not instill confidence in findings even of this well-done analysis.

Can you confirm that the source of the information is indeed administrative hospital data and ideally say something to boost my trust in its veracity?

**Dr Karamlou.** Yes, this is administrative data and although miscoding is a potential important confounder, this confounder is not solely isolated to just administrative data. As you know, other clinical databases are somewhat confounded by differing percentages of miscoding. We have tried to reduce the influence of miscoding by using both a diagnosis for HLHS as well as an accepted algorithm for coding the Norwood operation, which does not have a distinct procedure code in administrative data.

Second, I think if you look outside of the cardiac surgery and thoracic surgery literature. the NIS is actually very widely used in other surgical specialties.

Third, this is an administrative database and thus is based on billing and things like the final disposition of these neonates and patients. These are among the factors that are likely to be coded with greater accuracy than a diagnosis, for instance. However, your point is well taken.

**Dr Clarke.** Second, although it is not really clear in your manuscript, I learned by talking with you yesterday that your cases were selected on the basis of criteria including an age of less than or equal to 30 days at the time of admission. Is it possible that patients could be admitted more than once and therefore be double counted in your sampling?

**Dr Karamlou.** Double counting—you have obviously read the paper—is another of the potential limitations of this study. One of the things that it is possible to do in the NIS, and which we hope to do, is to code patients. You can figure out which infants were transferred in as their initial diagnosis and so potentially there are two ways to at least reduce this possible confounding. One is to look at transfers and admitting diagnosis. The second is to calculate on a mean prevalence of the incidence of surgical intervention and apply that constant to the neonates, the 20% that were transferred; then those patients would fall into the bucket of surgical intervention, and it may reduce some of that confounding. As yet, we have not done either of those two things.

**Dr Clarke.** Third, the overall mortality in this study is reported as 30%. Although some of the survivors had surgical therapy, a large group was either transferred to another facility or discharged alive. We therefore do not really know what happened to many of these babies. It is likely that most of the transfers received some form of therapy, and it is very plausible to me over the years that an increasing number of those who were discharged probably were eventually treated. Do you believe this study actually represents the evolution of the global management of HLHS or are we really here just peeking at this horse race through a keyhole?

**Dr Karamlou.** I think it certainly does represent the evolution of treatment strategies. What we are stating is that this is the treatment that is initially provided when a neonate is admitted to a particular institution. I think the findings of this paper are very important if you look at certain morphologic subsets of infants with HLHS, those patients who have an intact atrial septum, for example. Even if they receive subsequent surgical therapy, it may come at a great cost to those neonates who probably need to be triaged to an institution that can provide surgical therapy right then.

The other important thing that you mentioned is that we do not know the final disposition of the neonates who were transferred. However, using one of the two methods that I just spoke to you about, I think it is possible to at least learn a bit more about the percentage that were transferred.

**Dr David Ross** *(Edmonton, Alberta, Canada).* I am astounded that you showed such a high rate of nonintervention. In Edmonton, since 2004, our first-stage mortality is 6% for HLHS, and I know there are many other centers achieving these results. Yet, when you talk to neonatologists, it is the only condition for which nontreatment is offered. There are neonatal and infant cancers that have far worse survival with far more toxic treatment. If you offer

nontreatment for them, you are told, no, that would be immoral. But nontreatment is offered to half of the neonates with HLHS. Even *Streptococcal* infection in the neonate has a far worse survival, far worse neurologic survival, and yet no one would ever dream of not treating it. That is my comment.

My question is this: Do you have any idea why this is continuing and why these children are singled out for discrimination? Second, do you have any ideas how to fix this?

**Dr Karamlou.** I guess I take a little bit of issue with what you said. I am not making a value judgment that every infant with HLHS should have surgical therapy. This is actually a dichotomy that was articulated very well by Martin Elliott in an editorial that he wrote. That is, in the United States we seem to really favor surgical intervention and it is sort of ''life at any cost,'' regardless of the quality of life of those children. This is in contradiction to in the United Kingdom, for example, or Europe, where nonoperative therapy is selected by a higher proportion of well-educated persons and even physicians with infants with HLHS. Having said that, I think one of the primary determinants of nonoperative therapy is that the infant goes to an institution that does not provide surgical management. I think that is one of the important findings in this study.

**Dr Thomas Spray** *(Philadelphia, Pa).* Despite the fact that we may not want to believe your results, I think they are probably valid. If you go to a national meeting with a group of pediatric cardiologists and you ask them whether they offer nonintervention, the majority say yes. In fact, if you ask them what they would do with their own child, the majority would say nonintervention. So your study may actually reflect the true situation.

I would like to make a comment again about these administrative data sets. If you believe that only 20% of the data is represented, you would believe that there were 45,000 or more children with HLHS born in the time frame of the study, which is probably a vast overestimate of the number in the United States, at least. That probably is not correct. If you look at an individual institution and you look at the coding, when we tried to do that in our institution there was at least a 30% discrepancy in terms of coding accuracy, and this is not validated data. That is one of the real problems with your study, and we are seeing more and more studies using these national data sets. I would only suggest that maybe something worth considering is a control population. Take a group in which you would assume that there is pretty consistent intervention, say transposition, and in the same data set look at what happens when you look at transposition rather than HLHS. Do they get transferred? Do they get operated on? Are they offered nonintervention? If you see that there is a relatively high incidence of nonintervention, then it would lead me to believe that these data sets are not really accurate. Then there is the whole problem, as was already brought up by Dr Clarke, that you do not track what happens to the individual patient; if the patient is transferred, that patient may get nonintervention or the patient may get intervention. For the patients who are classified as nonintervention in your group, you do not know whether every one of those patients died while they were in the hospital (which theoretically they should have if they were given comfort care and nonintervention). It is important to track what happens to these patients or really you are just getting a snapshot. Now this is the best data set there is, and I concede that, but I just would suggest that you might want to try to use control populations to see whether you can sort out whether this is really accurate.

**Dr Karamlou.** I think that is an excellent idea, Dr Spray. I think I would just mention that even though we do not know the final disposition of the transferred neonates, that is still only 20% of our sample. Good idea.

**Dr Lawrence Cohn** *(Boston, Mass).* I have one question. This is outstanding that in the United States of America 57% of patients with a potentially treatable disease are not treated. I want to ask a question concerning the coding. Is this premortem or postmortem? Is this, in part, due to a big diagnostic problem? In other words, are all of these patients diagnosed with this syndrome as they come in and then given comfort care, or is this a postmortem diagnosis, with the patients being signed out on the administrative log and we say that they were given comfort care because the diagnosis was unknown?

**Dr Karamlou.** If that is true, then a large proportion of infants had the Norwood operation or transplant not for HLHS, which I find difficult to believe. Most of these diagnoses are administratively coded. I would assume that the majority of them are done preoperatively or before intervention, but there is no way to be sure whether or not necropsy findings were used in a proportion of them.

**Dr Cohn.** I just meant in the comfort care group where nothing was done, were these premortem or postmortem diagnoses?

**Dr Karamlou.** No, because a lot of the infants who had comfort care actually did not die in the hospital. In a large percentage of cases, the parents chose to take the neonates home so that they could die at home, so it would be a premortem diagnosis.

**Dr William Brenner** *(Los Angeles, Calif).* In 1977, the late great Helen Taussig shocked an audience at the Los Angeles Heart Association when somebody asked her about the future of congenital heart disease. She responded amniocentesis and abortion. That is not what the audience was expecting.

**Dr Karamlou.** I am not advocating that either, by the way.