Hospital Costs and Quality of Life During 4 Years After Very Preterm Birth

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Objective: To evaluate the effect of gestational age and prematurity-related morbidities on hospital costs and cost per quality-adjusted life-year (QALY) during the first 4 years of life.

Design: Population-based study using national register data and parental questionnaires.

Setting: Finland.

Participants: All 2064 very preterm children (gestational age <32 weeks or birth weight <1501 g) and all 200 609 full-term control individuals (mean [SD] gestational age, 37 [0] to 41 [6] weeks) born from January 1, 2000, through December 31, 2003.

Main Exposure: Prematurity.

Main Outcome Measures: Costs of hospital care and cost per QALY at 4 years of age according to gestational age and prematurity-related morbidities.

Results: By 4 years of age, the cost per QALY for full-term controls (in 2008 currency) was €11 824 ($17 381) and increasing with decreasing gestational age. The cost per QALY was €14 368 ($21 121) for those without any of the studied morbidities and €36 110 ($53 082) for those with 2 or more morbidities. The costs of the initial hospital stay comprised 79.5% of the total 4-year hospital costs in very preterm children.

Conclusions: We conclude that the cost per QALY in this patient group is at an acceptable level by 4 years of age. Because the initial hospital care episode accounted for most of the costs, the cost per QALY will decrease with each additional follow-up year.

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Table 1. Characteristics of Individuals With and Without Original Cost Data for the Initial Hospitalization

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>With Cost Data</th>
<th>Without Cost Data</th>
<th>P Value</th>
<th>With Cost Data</th>
<th>Without Cost Data</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Survivors</strong></td>
<td>(n=906)</td>
<td>(n=846)</td>
<td></td>
<td>(n=91)</td>
<td>(n=187)</td>
<td></td>
</tr>
<tr>
<td>Male sex, No. (%)</td>
<td>501 (55.3)</td>
<td>472 (55.8)</td>
<td>.85</td>
<td>57 (62.6)</td>
<td>110 (58.8)</td>
<td>.60</td>
</tr>
<tr>
<td>Gestational age, mean, d</td>
<td>208</td>
<td>211 &lt;.001</td>
<td></td>
<td>180</td>
<td>190 .003</td>
<td></td>
</tr>
<tr>
<td>Birth weight, mean, g</td>
<td>1243</td>
<td>1317 &lt;.001</td>
<td></td>
<td>767</td>
<td>905 .01</td>
<td></td>
</tr>
<tr>
<td>Length of stay, mean, d</td>
<td>67</td>
<td>61 .01</td>
<td></td>
<td>18</td>
<td>11 .21</td>
<td></td>
</tr>
<tr>
<td>Later morbidities, No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seizures</td>
<td>23 (2.5)</td>
<td>30 (3.5)</td>
<td>.26</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Cerebral palsy</td>
<td>52 (5.7)</td>
<td>57 (6.7)</td>
<td>.43</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Other ophthalmologic problems</td>
<td>123 (13.8)</td>
<td>117 (13.8)</td>
<td>.89</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Visual disorder</td>
<td>36 (4.0)</td>
<td>32 (3.8)</td>
<td>.81</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Hearing loss</td>
<td>17 (1.9)</td>
<td>28 (3.3)</td>
<td>.07</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Obstructive airway diseases</td>
<td>183 (20.2)</td>
<td>175 (20.7)</td>
<td>.72</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td><strong>Nonsurvivors</strong></td>
<td>(n=91)</td>
<td>(n=187)</td>
<td></td>
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</tr>
</tbody>
</table>

Abbreviation: NA, not applicable.

of the later costs are associated with prematurity-related morbidities.

**METHODS**

**POPULATION**

Ours was a national register study covering all live-born very preterm infants (gestational age <32 weeks or a birth weight of <1501 g) born in Finland from January 1, 2000, through December 31, 2003. The study was approved by the ethics committee of the National Institute for Health and Welfare. Very preterm infants were delivered in 5 hospitals that have a level III neonatal intensive care unit (NICU) and 19 hospitals that have a level I or II NICU, as defined by the American Academy of Pediatrics Committee on Fetus and Newborn. The number of very preterm infants born during the study period was 2495, of whom 395 were stillborn. Of the very preterm infants born alive, 1659 (79.0%) were born in the 5 level III NICUs. Twenty infants with incomplete medical birth register data, 47 infants with missing information on the length of their first care episode, and 3 infants with major disparity between birth weight and gestational age were excluded from the study, leaving a study sample of 2030 very preterm infants. There were 278 nonsurvivor infants, of whom 269 died before discharge home and 9 died after the initial discharge. All 200609 full-term infants, defined as gestational age from 37 weeks, 0 days to 41 weeks, 6 days born in Finland from January 1, 2000, through December 31, 2003 were used as a control group.

**DATA COLLECTION**

Register data used in this study were collected from the National Medical Birth Register and the Hospital Discharge Register, maintained by the National Institute for Health and Welfare. The cost data were collected from the hospital databases. The patient-level data were linked by means of unique encrypted identification codes. All very preterm births occur in the outpatient clinics of the same hospitals. There are no private children’s hospitals in Finland. The follow-up of healthy children in Finland is organized through well-child clinics; therefore, healthy children do not routinely visit the hospitals after the initial discharge. Preterm infants have their additional developmental follow-up visits in the outpatient clinics of the hospitals included in these data. In addition, all health problems requiring specialized care beyond primary care occur in the outpatient clinics of the same hospitals.

Five hospitals, 4 with level III NICUs and 1 with a level II NICU, provided us with cost data on the initial hospitalization of the very low-birth-weight infants. Two of the level III NICUs provided us with cost data for 4 years, one for 3 years (2001-2003) and one for 2 years (2002-2003). The level II NICU provided us with data for 4 years. Thus, cost data on the initial hospital stay were available for 997 infants (ie, 91 of the 278 nonsurvivors [32.7%] and 906 of the 1752 survivors [51.7%]).

Table 1 presents characteristics for those with and without original costs during the initial hospital stay. Most extremely preterm infants were born in hospitals with level III NICUs. Therefore, the gestational age and body weight were slightly higher for those with original costs because only 1 level II NICU provided us with the costs. However, the frequencies of later morbidities were similar in those with and without costs.

Costs of the initial length of stay (LOS) were imputed for those with missing cost data by assigning the mean cost per day of similar individuals (eg, sex, gestational age, multiple birth, and intrauterine growth) and multiplying it by the LOS. For full-term infants, the cost of the initial hospital stay was calculated according to diagnosis related groups based on patient-level cost accounting. The diagnosis related group costing sample covers approximately 30% of all acute hospital care in Finland. Cost items include diagnostic tests, procedures, medical services, support services, and overhead costs.

Cost data were available for 10 053 (20.2%) of the very preterm infants’ nonemergency outpatient visits and 144 847 (28.8%) of the controls’ nonemergency outpatient visits; 1305 (30.0%) and 46 220 (26.5%) for the very preterm infants’ and controls’ emergency visits, respectively; and 1534 (22.2%) and 39 678 (24.4%) for inpatient visits for the same groups, respectively. The costs for later hospital stays were entered into the database for those with costs missing pertaining to the type of visit (emergency outpatient, nonemergency outpatient, and inpatient) and the diagnosis. In 439 (8.7%) of the emergency outpatient visits and 11 661 (25.6%) of the nonemergency outpatient visits, the diagnosis was missing. In those cases we used the average costs of the emergency and nonemergency outpatient visits. Those costs, using the currency rate of €1=US$1.47, were €286 ($429) and €231 ($349), respectively.

Individuals were defined as having a morbidity related to prematurity if 1 or more of the following diagnoses, which have previously been shown to be overrepresented in our preterm population,22 were reported at least once to the Hospital Discharge Register by the end of 2006: cerebral palsy (International Statistical
17D27 contains 1 closed-ended question addressing each of the
HRQoL scores increased linearly from “all worst” to “home
grading loss (H90-91); visual disturbances or blindness (H53-54); and
Obstructive airway diseases 241 73.9 (63.0) 27.7 (22.0) 5.1 (4.0) 12.5 (7.0)
Hearing loss 20 83.3 (65.5) 55.8 (45.5) 2.7 (1.0) 5.7 (2.5)
Visual disorder 8 70.9 (70.5) 34.5 (18.0) 2.5 (1.5) 10.8 (5.0)
Other ophthalmologic problems 104 72.5 (64.0) 27.4 (21.5) 2.3 (1.0) 5.6 (2.0)
Cerebral palsy 31 68.4 (63.0) 47.1 (38.0) 1.8 (1.0) 8.9 (5.0)
Other diagnoses 1157 56.1 (49.0) 15.5 (13.0) 1.6 (1.0) 3.9 (1.0)
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Abbreviation: NA, not applicable.

**Table 2. Hospital Inpatient and Outpatient Visits During the First 4 Years of Life According to Gestational Age and Morbidities in the Very Preterm and Full-term Control Populations**

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of Patients</th>
<th>Length of Initial Hospitalization, d</th>
<th>Nonemergency Outpatient Visits, No.</th>
<th>Emergency Outpatient Visits, No.</th>
<th>Length of Other Hospital Stays, d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age, wk</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>17</td>
<td>136.7 (126.0)</td>
<td>44.0 (38.0)</td>
<td>3.1 (2.0)</td>
<td>14.6 (6.0)</td>
</tr>
<tr>
<td>24-25</td>
<td>135</td>
<td>122.1 (108.0)</td>
<td>39.4 (30.0)</td>
<td>3.8 (3.0)</td>
<td>12.1 (6.0)</td>
</tr>
<tr>
<td>26-27</td>
<td>231</td>
<td>94.4 (85.0)</td>
<td>30.0 (22.0)</td>
<td>4.0 (3.0)</td>
<td>8.6 (3.0)</td>
</tr>
<tr>
<td>28-29</td>
<td>385</td>
<td>67.5 (64.0)</td>
<td>25.7 (19.0)</td>
<td>2.6 (2.0)</td>
<td>8.2 (2.0)</td>
</tr>
<tr>
<td>30-31</td>
<td>756</td>
<td>48.0 (44.0)</td>
<td>16.7 (12.0)</td>
<td>2.0 (1.0)</td>
<td>5.7 (1.0)</td>
</tr>
<tr>
<td>≥32</td>
<td>228</td>
<td>43.8 (38.0)</td>
<td>17.2 (12.0)</td>
<td>2.0 (1.0)</td>
<td>5.5 (1.0)</td>
</tr>
<tr>
<td>All preterm survivors</td>
<td>1752</td>
<td>64.4 (55.0)</td>
<td>22.5 (16.0)</td>
<td>2.5 (1.0)</td>
<td>7.2 (2.0)</td>
</tr>
<tr>
<td>Live-born preterm nonsurvivors</td>
<td>278</td>
<td>13.9 (1.0)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Full-term control group</td>
<td>200 809</td>
<td>3.5 (3.0)</td>
<td>2.5 (0)</td>
<td>0.9 (0)</td>
<td>2.0 (0)</td>
</tr>
</tbody>
</table>

Classification of Diseases, 10th Revision [ICD-10] codes G80-83; seizure disorder (G40-47); later obstructive airway disease, including asthma and other obstructive airway diseases (J44-J45); hearing loss (H90-91); visual disturbances or blindness (H53-54); and other ophthalmologic problems, including disorders of ocular muscles, binocular movement, accommodation, and refraction (H90-92). Diagnoses for inpatient and outpatient visits were recorded. On the basis of the health care system in Finland, it can be expected that diagnoses of the studied disease groups can be reliably derived from hospital registers because these diseases are diagnosed and treated in specialized care in public hospitals.

The QALYs were based on health-related quality of life (HRQoL) according to a 17-dimension parental questionnaire (17D), as described in detail in an article by Rautava et al. The 17D contains 1 closed-ended question addressing each of the following health dimensions: mobility, vision, hearing, breathing, sleeping, eating, speech, elimination, school and hobbies, learning and memory, discomfort and symptoms, depression, distress, vitality, appearance, friends, and concentration. The questionnaire provides a single HRQoL score on a scale from 0 to 1, with 0 corresponding to being dead, 0.0162 to being unconscious or comatose, and 1 to having no problems in any dimension or full HRQoL. The QALYs by the age of 4 years were calculated by defining a HRQoL score for each day of life and then multiplying this by the number of days alive up to the age of 4 years. The HRQoL was assumed to be constant for all days after discharge from the initial hospitalization period. This home score was acquired from the parental 17D questionnaire at the age of 5 years. Separate HRQoL scores were estimated for the days of the initial hospitalization period in the very low-birthweight infants. Immediately after birth, the very low-birthweight infants were assumed to have an “all worst” HRQoL score, meaning that they were given the worst score for each 17D dimension; thus, the total 17D score was 0.13 after appropriate weighting of each dimension score. Before discharge to home, the HRQoL scores increased linearly from “all worst” to “home score,” which was reached on the day of discharge. If the infant died during the initial hospitalization period, the “all worst” score linearly decreased to 0 until the day of death. The QALY was estimated for those with missing QALY according to morbidities and gestational age.

**STATISTICAL ANALYSIS**

The number of hospital visits and LOS were presented as means and medians; the costs were presented as means and standard deviations. All analyses were made separately according to gestational age and morbidities. We performed $x^2$ tests on dichotomized variables; analyses of variance were used to compare means. $P<.05$ was considered statistically significant. All costs were presented in 2008 prices, and the discount rate was 3.0% per year. The average yearly rates were used in the currency conversions (for 2000, €1=$0.92; for 2003, €1=$1.13; for 2006, €1=$1.26; and for 2008, €1=$1.47). In the cost-per-QALY analysis, the total costs of care for survivors and nonsurvivors were divided by the total QALYs of survivors and nonsurvivors when calculating the cost per QALY according to gestational age. The nonsurvivors were removed from the analysis when determining the cost per QALY according to morbidities. The 95% confidence intervals were calculated by bootstrapping simulation. The analyses were performed with SAS statistical software, version 9.1 (SAS Institute Inc, Cary, North Carolina).

**RESULTS**

The need for and costs of all types of hospital care were clearly lower among full-term controls than among children born very preterm (Table 2 and Table 3; also, eTable 1 [available at http://www.archpediatrics.com]). The greatest difference was observed in the initial LOS. The mean LOS was 3.5 days in the controls and 64 days in the very preterm infants. The number of nonemergency outpatient visits of the children born very preterm was almost 10-fold compared with that of the controls (23 vs 2.5 visits; Table 3).
The need for hospital care and total costs of hospitalizations increased with decreasing gestational age in survivors. The initial hospital stay comprised 73.2% to 84.0% and the total first-year costs comprised 89.2% to 93.2% of the total 4-year costs in the very preterm population.

The QALYs and cost per QALY according to gestational age and morbidities are presented in Table 3. The median LOS for nonemergency outpatient visits (P < .001 for each). Obstructive airway diseases and having 2 or more diagnoses were associated with the highest costs for later inpatient stays (P = .001 and P < .001, respectively) and for emergency outpatient visits (P < .001).

The need for hospital care and total costs of hospitalizations increased with decreasing gestational age in survivors. The initial hospital stay comprised 73.2% to 84.0% and the total first-year costs comprised 89.2% to 93.2% of the total 4-year costs in the very preterm population. Figure 1 shows that hospital costs accumulated during the first year of life in all gestational age groups. The hospitalization costs decreased with age in all gestational age groups and in all morbidity groups (Figure 2). Gestational age was not significantly related to the costs of nonsurvivors; therefore, they are presented as 1 group in Tables 1 and 2. The median LOS in the nonsurvivors was 1 day.

The QALYs and cost per QALY according to gestational age and morbidities are presented in Table 4; see also eTable 2. No significant differences were found in the costs per QALY between male and female infants. The total hospital cost per QALY (in 2008 currency) was €1181 ($1736) for full-term controls at 4 years of age. In the preterm and cerebral palsy were associated with higher costs for nonemergency outpatient visits (P < .001 for each). Obstetric airway diseases and having 2 or more diagnoses were associated with the highest costs for later inpatient stays (P = .001 and P < .001, respectively) and for emergency outpatient visits (P < .001).

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The mean cost per QALY was €19,245 ($28,290), ranging from €11,824 ($17,381) for those born at 32 weeks of gestation or later to €54,324 ($79,856) for those born at 23 weeks. The cost per QALY was €14,368 ($21,121) for those without any of the studied morbidities and €36,110 ($53,082) for those with 2 or more morbidities.

**COMMENT**

Our study shows that the average cost per QALY (in 2008 currency) in very preterm children at 4 years of age was €19,245, ranging from €11,824 to €54,324 ($28,290; from $17,381 to $79,856). Hospitalizations occurring during the first year of life, particularly the initial hospitalization, accounted for most of the total 4-year cost of hospital care. The later costs were low even in the lowest gestational age groups. Therefore, the cost per QALY will decrease with each additional follow-up year.

In relation to previous US studies,15,17,20 our costs (in 2008 currency) of the initial hospital stay (€54,104; $79,533) were at the lower end; costs in those studies for very preterm survivors have been between €70,74015 and €116,18017 ($80,020 [2003 currency] and $145,880 [2006 currency]) when the reported prices were converted to 2008 prices. A Swedish study18 presented even lower costs than ours: the cost of initial hospitalization for those born at a gestational age less than 32 weeks, including both survivors and nonsurvivors, was €38,660 (US $56,830) in 2008.
prices. Likely explanations for the difference between the Swedish and US costs include real-wage differences and structural differences in the ways health care is organized in each country. In addition, the costs in the US studies are mostly based on costs to charges ratios.\textsuperscript{15,17,18,20} Charges are not accurate measures of hospital costs because they reflect different markups for different services. For example, a study\textsuperscript{16} of very low-birth-weight infants in California demonstrated that the average charge for the initial hospitalization overestimated treatment costs by 53%. Using the costs to charges method is especially problematic when comparing the costs among different institutes because of different pricing policies. In addition, because of inflation, it is necessary to reflect differences in the year in which the costs were incurred. International cost comparisons are also affected by the currency rates used because the rates can vary greatly across different periods.

Compared with earlier studies in which the data have been collected from smaller geographic regions or limited populations or the costs of hospital care have been derived from indirect estimations,\textsuperscript{14,15} our study included the hospitalization data of actual visits for a 4-year national population cohort. We could analyze all hospital visits during the first 4 years of life because all hospital care for premature infants is given in public hospitals and comprehensively registered in the national registers in Finland.\textsuperscript{28} Furthermore, we could distinguish inpatient care from outpatient care and emergency visits from nonemergency visits. Our limitation was that hospitalization costs were calculated from data from 5 hospitals but estimated for the rest. However, we could show that the patient characteristics were similar for those with and without original costs for the initial hospitalization. In addition, pediatric hospital care occurs in public hospitals in the entire country because there are no private pediatric hospitals in Finland. This factor supports our assertion of the homogeneity of costs.

We chose to study the actual hospitalization costs of the first 4 years of life and not to try to estimate future costs. Several factors support our approach. The cost per QALY was already relatively low at 4 years of life, and hospitalization costs decreased significantly with age in all gestational age groups and in all morbidity groups. Results from other studies also indicate a decreasing use of health care resources with age. Saigal et al\textsuperscript{29} showed an age-related decrease in the use of health care resources in extremely low-birth-weight infants in young adulthood in terms of hospitalizations, surgical procedures, visits to specialists, and use of rehabilitative services. Using a decision analytic model, Mangham et al\textsuperscript{21} estimated the costs to the public sector during the first 18 years after birth in England and Wales. They estimated that 97.4% of the incremental costs occurring during the first 18 years of life consist of the costs from the first 5 years of life, 1.6% from the primary-school years (ages 5-11), and only 1.1% from the secondary-school years (ages 11-18). Our study showed that two-thirds of the very preterm population without prematurity-related morbidities had few hospital stays and outpatient visits after the first year of life. Therefore, it is unlikely that adding an estimation of future visits would increase the cost per QALY ratio. Although we do not know the costs for future education and use of other health care services, we can assume that the cost per QALY will decrease because the cost of the initial hospitalization will be divided by an increasing number of life-years.

Our study focused on the costs of hospitalizations. Previous studies\textsuperscript{10,30} have shown that preterm children have more academic, motor, psychosocial, and behavioral difficulties at school age. These problems are likely to affect the need for special care, therapies, and social services, resulting in additional costs. In addition, the families of the preterm infants may carry an economic burden because of, for example, lost income and the increased costs of traveling and accommodation. Mangham et al\textsuperscript{21} estimated that of the costs during the first 18 years of life, 96.7% are incurred because of hospital inpatient and outpatient care, 0.9% because of community health care and social care, and 2.4% because of education. More studies are needed to assess the costs of school-aged prematurely born children with morbidities.

When evaluating the effectiveness of medical treatments, a standard method is incremental cost-effectiveness analysis. In our study, this approach was not applicable because incremental cost-effectiveness analysis compares 2 or more treatment strategies or technologies. In this context, withholding active treatment would result in death or severe morbidities. Theoretically, if the “not to treat” option would lead to the deaths of all infants, the added QALY would be 0 and the cost would be the cost of hospitalization of the mother, which on average would not exceed the cost for a healthy newborn (€1260 [US$1852; 2008 currency] in our study). The resulting incremental cost per QALY would be very close to the actual cost per QALY presented in our study, supporting cost-effectiveness of the care. However, in real life, the “not to treat” strategy would lead to severe morbidities with increasing costs. This supports even further the cost-effectiveness of active treatment.

We conclude from this national study with actual hospital costs of very preterm infants that the cost per QALY is at an acceptable level by 4 years of age. Prematurity-related later morbidities and decreasing gestational age increased the costs per QALY. The initial hospital stay accounted for most of the costs; thus, the cost per QALY will decrease with age. Most costs arising after the initial hospitalization were associated with morbidities related to prematurity. Therefore, offering high-quality neonatal care to prevent later morbidities in very preterm survivors has a long-term effect on the cost per QALY.
take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Korvenranta, Rautava, Gissler, Hallman, Häkkinen, Leipälä, Tammela, and Lehtonen. Acquisition of data: Korvenranta, Linna, Gissler, Hallman, and Peltola. Analysis and interpretation of data: Korvenranta, Linna, Rautava, Andersson, Hallman, Häkkinen, Leipälä, Tammela, and Lehtonen. Drafting of the manuscript: Korvenranta, Linna, Tammela, and Lehtonen. Critical revision of the manuscript for important intellectual content: Korvenranta, Rautava, Andersson, Gissler, Hallman, Häkkinen, Leipälä, Peltola, Tammela, and Lehtonen. Statistical analysis: Korvenranta, Linna, Gissler, and Häkkinen. Obtained funding: Häkkinen and Lehtonen. Administrative, technical, and material support: Korvenranta, Gissler, Hallman, and Peltola. Study supervision: Korvenranta, Andersson, Tammela, and Lehtonen.

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Online-Only Material: eTable 1 and eTable 2 are available at http://www.archpediatrics.com.

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The power of love to change bodies is legendary, built into folklore, common sense, and everyday experience. Love moves the flesh, it pushes matter around. . . . Throughout history, “tender loving care” has uniformly been recognized as a valuable element in healing.

—Larry Dossey