An expert panel reviewed a cluster of childhood leukemias in Fallon, Nevada, and suggested population mixing as an explanation. This hypothesis proposes that nonimmune children exposed to some unknown infection(s), through population mixing, are at increased risk of developing acute lymphoblastic leukemia and non-Hodgkin’s lymphoma. The United Kingdom Childhood Cancer Study registered 3,838 children with cancer and 7,669 matched controls aged 0–14 years during 1991–1996 in England, Scotland, and Wales. Local area characteristics for each child’s residential address at diagnosis were assigned from census data: volume and diversity of population mixing, material deprivation, and rural status. The best-fitting models were chosen for three diagnostic groups: acute lymphoblastic leukemia, non-Hodgkin’s lymphoma, and all other tumors. Elevated risks of acute lymphoblastic leukemia were found in areas with a low diversity of origins of migrants and for non-Hodgkin’s lymphoma in areas with a low diversity of origins of child migrants; for other tumors, no covariates were associated. This study, and a survey of 17 published reports on population mixing, suggests that a low diversity of migrant backgrounds may be associated with acute lymphoblastic leukemia. These findings do not support the population mixing hypothesis. Although they support the Greaves delayed infection hypothesis, other aspects of this hypothesis were not addressed.

Abbreviations: ALL, acute lymphoblastic leukemia; CI, confidence interval; NHL, non-Hodgkin’s lymphoma; OR, odds ratio.
communities in which the prevalence and range of infections are high (6). Population mixing has been defined in different ways by different studies, depending on the available data and the historical context. In this study, census data were used to assess the volume of people who moved and the diversity of their origins as markers of population mixing. The association between these three groups of tumors and population mixing in their residential neighborhoods was examined.

MATERIALS AND METHODS

A case-control approach was used. The base population was defined as all children aged 0–14 years born and resident in England, Wales, and Scotland (Great Britain); registered with a general practitioner; without a prior malignancy; and not in residential local authority care. Data collection was coordinated by 10 regional centers using a common protocol and data collection instruments. The study method has been described in detail elsewhere (5).

Cases were compared with controls on the basis of census information derived from the area in which each child was residing at the time of diagnosis. An index of deprivation was used as a measure of socioeconomic status, and children were classified as living in a rural region or not on the basis of the region’s population density. Population mixing was measured by using the information about the proportion of immigrants moving to the census area in the previous year and the diversity of their regions of origin.

Study subjects

Potentially eligible cases were children diagnosed with a confirmed malignancy at any site or a benign tumor of the central nervous system. Included were all diagnostic groups in Scotland between 1991 and 1994 and those in England and Wales between 1992 and 1994. Case accrual continued in England and Wales for NHL and for leukemias during 1995 and for leukemias alone in 1996. Diagnostic confirmation was obtained from several sources: Medical Research Council treatment trials, the United Kingdom Childhood Cancer Study Group, and histopathology review panels (5). The following three diagnostic groups were defined to test the plausibility of the population mixing hypothesis: ALL, NHL, and all other tumors. Two controls were matched on age and sex to each participating case, randomly selected from children registered within the same National Health Service organizational unit (Family Health Services Authority for England and Wales, Health Board for Scotland) as their matched case (5).

Linkage to the Census of Great Britain

Cases and controls were linked via the postcode (equivalent to a zip code) of their residence at the time of diagnosis to the 1991 Census of Great Britain (The 1991 Census, Crown copyright, ESRC Purchase). Every household was legally required to complete the census form, which contained 25 questions. The content ranged from the age and sex of occupants to indicators of affluence such as employment and housing conditions. To maintain confidentiality, data were released at an areal level, with the smallest geographic units being indivisible. The smallest units in England and Wales were the 108,336 Enumeration Districts and, in Scotland, the 38,084 Output Areas, containing an average of 400 persons. These units were aggregated into 9,527 Electoral Wards (England and Wales) and 1,002 Postcode Sectors (Scotland), with an average of 5,000 persons.

The address was assigned a validated postcode and was then linked to a zip code (equivalent to the 1991 Census of Great Britain). The residential local authority identifier was then linked to an Enumeration District or Output Area code. Linked data were available at the following levels: Enumeration District (England and Wales), Postcode Sector level (Scotland), and the “average” person lives but more closely reflects land use and type of region. A more useful measure of the density at which an average person lives is the “population-weighted” population density (7), defined as

\[
d_j = \frac{n_i}{a_j}
\]

where \(n_i\) is the number of residents and \(a_j\) is the spatial area. However, \(d_j\) does not necessarily reflect the density at which the “average” person lives but more closely reflects land use and type of region. A more useful measure of the density at which an average person lives is the “population-weighted” population density (7), defined as

\[
w_j = \sum_{i=1}^{r} d_i \left( \frac{n_i}{n_j} \right)
\]

where \(d_i\) is calculated for each subregion \(i\), derived by substituting \(j\) in equation 1, and \(n_i\) is the number of persons in the smaller region.

Indices of population mixing

The 1991 Census of Great Britain recorded the residential address of all persons 1 year prior to the census date. These data provide, for every Electoral Ward and Postcode Sector, the numbers of persons moving into the area in the previous year broken down by the Electoral Ward or Postcode Sector.
Mixing. Volume and diversity of population mixing were calculated as the proportion of the population with a different address 1 year before the census, excluding those moving within the same Electoral Ward/Postcode Sector. Diversity of population mixing (8, 9) in region j was calculated by using the Shannon index of diversity (10) \( H_j \), where

\[
H_j = -\sum_{i=1}^{s} \left[ p_{ij} \ln p_{ij} \right] - \frac{s-1}{m_j} + \frac{1 - \sum p_i^{-1}}{12m_j^2} + \frac{1}{12m_j^3} \sum (p_i^{-1} - p_i^2).
\]

For each area j, \( p_{ij} \) is the proportion of migrants coming from the ith area as a proportion of all migrants moving into the total number of areas \( s \), and \( m_j \) is the total number migrating to area j. Higher values indicate a higher diversity of originating areas and therefore higher levels of population mixing. Volume and diversity of population mixing were calculated separately for the “all-age” (1 year or older) and “childhood” (aged 1–15 years) populations.

Statistical analysis

The deprivation index was divided into seven categories, with an equal number of census units for Great Britain in each category. The distribution of population mixing volume (both childhood and all age) was highly skewed and was subject to log transformation prior to inclusion in the modeling process (8). Population mixing diversity was categorized into those Electoral Wards/Postcode Sectors below the 10th centile, those between the 10th and 90th centiles, and those above the 90th centile to allow direct comparison with a previous report on population mixing (9). An indicator of rural density was derived by categorizing all Electoral Wards/Postcode Sectors as below (rural) or above (not rural) 1.5 (all-age population) or 0.28 (childhood population) persons per hectare as measured by the population-weighted population density. Conditional logistic regression models were fitted to data for cases and their matched controls. Each variable was fitted individually, and model fit was assessed by using the likelihood ratio test between the null model and the model for each area. Two multivariable models were constructed, one using all age indices and the other childhood indices, with variables chosen from the univariable analysis. Covariates were chosen if either the likelihood ratio test for the univariable model against the null model was statistically significant (\( p < 0.1 \)) or a 95 percent confidence limit for the individual odds ratios did not include unity. The statistical interaction between the index of rurality and the diversity of population mixing was assessed in the multivariable model.

RESULTS

The study enrolled 3,838 cases and 7,669 matched controls. ALL accounted for 38 percent of all cases, NHL accounted for 6 percent of all cases, and the remaining cases had other tumors (see reference (5) for further details). The likelihood ratio test suggested that the index of deprivation was a significant covariate in the model for both the ALL and NHL groups, and this index was included in the multivariable models (table 1). However, this variable was not included in the multivariable model for the other-tumors group.

In the ALL group, the odds ratio was significantly raised for the lowest category of diversity in all-age population mixing (odds ratio (OR) = 1.37, 95 percent confidence interval (CI): 1.00, 1.86). For NHL, an increased risk was observed for the lowest category of diversity in childhood mixing (OR = 2.83, 95 percent CI: 1.15, 7.00). These factors were included in their respective multivariable models. Volume of population mixing was not associated with ALL cases for either the all-age or childhood populations. Volume of all-age population mixing (OR = 0.58, 95 percent CI: 0.32, 1.07) was included in the multivariable model for NHL because of the significant model fit (\( p = 0.079 \)).

There was a marginally significant increased risk of ALL with rural density that improved model fit (\( p = 0.037 \) for childhood and \( p = 0.058 \) for all-age populations). This finding was not replicated for the NHL group. No evidence of association was found between any of the individual census variables and disease for the other-tumors group: no covariates were appropriate for inclusion in the multivariable analysis.

Table 2 shows the results of the multivariable models selected from the univariable analyses (table 1). A significantly elevated odds ratio of ALL was evident for the lowest diversity of all-age population mixing (OR = 1.40, 95 percent CI: 1.03, 1.91). For rural regions, an elevated, but not statistically significant, association was found with ALL in both populations. An elevated odds ratio was observed in the category with the lowest diversity in childhood population mixing for the NHL group (OR = 2.76, 95 percent CI: 1.10, 6.97). No statistically significant interactions were found between population density and diversity of population mixing (results not shown), and there was no significant improvement in model fit after inclusion of the interaction terms for any diagnostic group.

Fitting a separate model for each age group (0–4, 5–9, and 10–14 years) produced no clear patterns, and the results were difficult to interpret. In the ALL group, the strongest effect for the lowest category of diversity in all-age population mixing was observed for the age groups 5–9 years (OR = 1.92, 95 percent CI: 1.01, 3.64) and 10–14 years (OR = 2.06, 95 percent CI: 0.99, 4.29). For NHL, odds ratios for the lowest category of diversity in childhood population mixing were raised for all age groups: 0–4 years (OR = 3.10, 95 percent CI: 0.43, 22.50), 5–9 years (OR = 3.60, 95 percent CI: 0.55, 23.54), and 10–14 years (OR = 1.56, 95 percent CI: 0.33, 7.24). There was no evidence of a significant association between population mixing and the other-tumors group by age.

Because of the possible differences between infant leukemia and leukemia occurring in older children, the ALL category was stratified into those less than 18 months of age at diagnosis and those older. The results for the diversity in all-age population mixing was similar between all cases and those diagnosed at older than age 18 months. There was a similar, but raised odds ratio for those diagnosed at less than
DISCUSSION

The United Kingdom Childhood Cancer Study recruited 3,838 cases with childhood cancer nationally, with 7,669 randomly selected population-based controls available for comparison. The national census counted over 60 million persons and was used to provide an independent and comprehensive picture of characteristics of population movement, density of inhabitants, and material deprivation for the local area in which children were living at the time of their cancer diagnosis. The findings from this investigation do not support the Kinlen population mixing hypothesis (2).

Kinlen (2) proposed that population mixing leads to the mixing of nonimmune and infective children, which subsequently leads to an epidemic of some infection(s). This
infection leads to leukemia and NHL. Refinement of this hypothesis led to it being linked with only those regions in which there was an excess of cases (11). For the Kinlen hypothesis (2) to provide a general mechanism for all cases, we would expect to find an increasing volume of migration to be associated with increased risks of leukemia and NHL. In this study, volume of migration was not significantly associated with either of these conditions, which does not lend support to the population mixing hypothesis as a general explanation for these pediatric cancers.

In this study, low diversity in migrants’ region of origin was associated with childhood ALL and NHL. These associations were consistent in the univariable model, and they were also consistent in the multivariable model after controlling for the potential confounding effects of deprivation. The relation between population mixing and socioeconomic status is not clear, but it is possible that both deprivation and population mixing contribute to the causal pathway of infectious exposure but via different routes that share similar attributes. However, it is unlikely that inclusion of deprivation in the final multivariable model inappropriately modified the risk estimates for population mixing. Population movement leads to mixing of infectious persons with susceptibles, and it acts as a mechanism for transmission of viruses and bacteria through the population (12). Therefore, these results do support a role for infectious disease in the etiology of both ALL and NHL.

In total, 3.7 million persons moved to another census area (Electoral Ward or Postcode Sector) in the year prior to the census, which equates to 7 percent of the population of Great Britain. On average, migrants moving into a region came from 105 other census areas (range, 1–969). The Special Migration Statistics contain an enormous quantity of information, which consists of four dimensions: origin, destination, age group, and sex. There are approximately 10^8 cells in the Special Migrations Statistics, but, in practice, only 10^6 cells contained nonzero data; the rest were redundant. To reduce this information to a meaningful exposure variable, we adopted the approach taken by Stiller and Boyle (9) and calculated two indices to give a measure of the mixing of populations.

The present study did not suffer from the consequences of less-than-full participation in the comparison group because participation was not required. The case-control study design is prone to selection bias when the comparison group does not accurately represent the population from which the cases were sampled.

### TABLE 2. Multivariable conditional logistic model of childhood cancer, with covariates chosen from univariable analysis, for models from the United Kingdom Childhood Cancer Study considering all-age and childhood populations separately

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Acute lymphoblastic lymphoma</th>
<th>Non-Hodgkin’s lymphoma</th>
<th>Other tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratio 95% CI</td>
<td>Odds ratio 95% CI</td>
<td></td>
</tr>
<tr>
<td>All-age population</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model fit, df (p value)†</td>
<td>20.48, 9 (0.015)</td>
<td>13.97, 7 (0.053)</td>
<td>No covariates appropriate</td>
</tr>
<tr>
<td>Deprivation</td>
<td>Included</td>
<td>Included</td>
<td></td>
</tr>
<tr>
<td>Mixing diversity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10%</td>
<td>1.40</td>
<td>1.03, 1.91</td>
<td></td>
</tr>
<tr>
<td>10–90%</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;90%</td>
<td>0.87</td>
<td>0.69, 1.09</td>
<td></td>
</tr>
<tr>
<td>Mixing volume</td>
<td>Log continuous</td>
<td>0.69</td>
<td>0.36, 1.31</td>
</tr>
<tr>
<td>Rural density</td>
<td>1.19</td>
<td>0.89, 1.60</td>
<td></td>
</tr>
<tr>
<td>Childhood population‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model fit, df (p value)†</td>
<td>14.95, 7 (0.037)</td>
<td>17.51, 8 (0.025)</td>
<td>No covariates appropriate</td>
</tr>
<tr>
<td>Deprivation</td>
<td>Included</td>
<td>Included</td>
<td></td>
</tr>
<tr>
<td>Mixing diversity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10%</td>
<td>2.76</td>
<td>1.10, 6.97</td>
<td></td>
</tr>
<tr>
<td>10–90%</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;90%</td>
<td>0.96</td>
<td>0.61, 1.50</td>
<td></td>
</tr>
<tr>
<td>Mixing volume</td>
<td>Log continuous</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural density</td>
<td>1.26</td>
<td>0.94, 1.68</td>
<td></td>
</tr>
</tbody>
</table>

* CI, confidence interval.
† χ² (p value) for likelihood ratio test against null model.
‡ Children aged 1–15 years.
were drawn (13). Distribution of the initial selection of controls in relation to socioeconomic indicators, such as deprivation, was reassuringly similar to that expected from national data (13). In the interview component of the study, it was necessary to contact the parents of the children selected and request permission to conduct a face-to-face interview. Among the parents of controls, 36 percent of those asked refused. The socioeconomic profile of the resulting comparison group differed from that of the original first-choice controls (13).

Use of national census data, collected independently of the study, ensured that disease status of the study subjects did not affect the measures of mixing. Furthermore, certain exposures of interest, such as the relative geographic isolation, population mixing, deprivation, and population density of an area, are measures that relate to a geographically delimited region and not to an individual. These exposures must not be confused with the ecologic study design, which uses the area as the unit of observation. However, the measures of exposure, based on the locality in which the individuals reside, may lead to potential misclassification errors.

Comparison of studies of population mixing

Figure 1 and table 3 summarize risk estimates from all 17 studies known to have investigated the association between leukemia in children aged 0–14 years and residential population mixing. This figure is divided into four sections, each listing studies that have taken one of four different approaches to measuring population mixing; for this reason, no attempt was made to calculate an overall risk estimate. The risk estimates presented are based on the overall estimate of risk for the whole study, ignoring subgroup analyses. Many studies have proceeded to analyze various age and urban/rural subgroups, but these subgroups were not defined a priori as the target population and, as such, offer considerably reduced statistical validity.

Six studies provided a qualitative assessment of the level of population mixing, retrospectively examining unusual events considered to represent high population mixing. These studies, shown in section a of figure 1, reported a consistently elevated incidence compared with the baseline and have been summarized by Kinlen (2), with one exception (14).
The studies included in section b of this figure were based on geographic regions that experienced a rapid growth in population; no account of population turnover due to both inward and outward migration was taken. Kinlen et al. (15) found that mortality from leukemia was significantly raised in new rural British towns during the 1950s and 1960s. Langford (16) found a significantly raised incidence of leukemia in local-authority areas in England with greater than 50 percent growth over the 10 years 1961–1971. Kinlen and John (17) reported that in rural districts receiving a high number of World War II evacuees (of all ages), mortality from leukemia was elevated significantly. A small study from New Zealand found no evidence of increased risk in a rural region with a high and rapid influx of people (18). A study of 121 cases of leukemia in Hong Kong found no evidence of an increased incidence in areas of high population growth (19). Finally, Koushik et al. (20) did not find a significantly elevated incidence rate of ALL for all children aged 0–14 years.

Studies that included a measurement of the volume of inward migration are listed in section c of figure 1. An ecologic analysis of the population-based English and Welsh National Registry of Childhood Tumours, which compared incidence during 1979–1985 with the Great Britain Census, reported an association between higher volume of migration and higher incidence of ALL (9). A study of 61 cases of combined ALL and NHL in Cumbria (northwest England) showed that incidence was not significantly associated with volume of migration in the childhood population (21). In a recent reanalysis of Stiller and Boyle’s work (9), which extended the study period to cover 1966–1987, incidence of NHL and leukemia was associated with an increasing proportion of movers (22). The reanalysis was conducted at a smaller geographic level (the Electoral Ward) than that of the original study, but it applied the single estimate of migration from the 1981 Census to the 22 years of numerator data. A subgroup analysis identified urban regions as contributing most to this effect. Although these findings contrast with those of the present study, restriction of the present study to a 4-year period immediately following the 1991 Census enabled inclusion of subtle shifts in population not available to long study periods and large geographic areas. In agreement with the results from the United Kingdom Childhood Cancer Study, a recent study conducted in three counties of England, with 248 cases, showed a decreased risk of ALL with increasing volume of migration (23).

Section d of figure 1 reports risks derived from studies that assessed diversity of the origins of the migrants. Diversity in population mixing was significantly associated with leukemia incidence in the ecologic analysis of the National Register of Childhood Tumours; risk estimates were not reported in the paper (9) but were obtained from one of its authors (C. Stiller, Oxford University, personal communication, 2002). Dickinson and Parker (21) reported a decreased incidence of ALL and NHL associated with increasing “paternal diversity,” which is in a similar direction to the present study and that of Parslow et al. (23).

The 17 published studies surveyed above do not consistently support the population mixing hypothesis. It is clear that population mixing, acting as a proxy measure for increased exposure to a putative infectious agent, is not a consistently associated risk factor for the general occurrence of leukemia and NHL. However, for ALL, there is some

### TABLE 3. Summary of the studies of population mixing and acute lymphoblastic leukemia in children (risk estimates plotted in figure 1)

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Reference no.</th>
<th>Year of publication</th>
<th>Country</th>
<th>Study design</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alexander et al.</td>
<td>19</td>
<td>1997</td>
<td>Hong Kong</td>
<td>Incidence</td>
<td>261</td>
</tr>
<tr>
<td>Dickinson and Parker</td>
<td>21</td>
<td>1999</td>
<td>England</td>
<td>Incidence</td>
<td>68</td>
</tr>
<tr>
<td>Dickinson et al.</td>
<td>22</td>
<td>2002</td>
<td>Great Britain</td>
<td>Incidence</td>
<td>10,194</td>
</tr>
<tr>
<td>Dockerty et al.</td>
<td>18</td>
<td>1996</td>
<td>New Zealand</td>
<td>Incidence</td>
<td>47</td>
</tr>
<tr>
<td>Kinlen</td>
<td>25</td>
<td>1988</td>
<td>Scotland</td>
<td>Incidence</td>
<td>2</td>
</tr>
<tr>
<td>Kinlen et al.</td>
<td>15</td>
<td>1990</td>
<td>Great Britain</td>
<td>Incidence</td>
<td>23</td>
</tr>
<tr>
<td>Kinlen and Hudson</td>
<td>26</td>
<td>1991</td>
<td>Great Britain</td>
<td>Incidence</td>
<td>297</td>
</tr>
<tr>
<td>Kinlen et al.</td>
<td>27</td>
<td>1993</td>
<td>Scotland</td>
<td>Incidence</td>
<td>101</td>
</tr>
<tr>
<td>Kinlen and John</td>
<td>17</td>
<td>1994</td>
<td>Great Britain</td>
<td>Incidence</td>
<td>90</td>
</tr>
<tr>
<td>Kinlen et al.</td>
<td>28</td>
<td>1995</td>
<td>Great Britain</td>
<td>Incidence</td>
<td>130</td>
</tr>
<tr>
<td>Kinlen and Balkwill</td>
<td>14</td>
<td>2001</td>
<td>Great Britain</td>
<td>Incidence</td>
<td>9</td>
</tr>
<tr>
<td>Koushik et al.</td>
<td>20</td>
<td>2001</td>
<td>Canada</td>
<td>Incidence</td>
<td>1,394</td>
</tr>
<tr>
<td>Laplanche and deVathaire</td>
<td>29</td>
<td>1994</td>
<td>France</td>
<td>Incidence</td>
<td>8</td>
</tr>
<tr>
<td>Langford</td>
<td>16</td>
<td>1991</td>
<td>England</td>
<td>Incidence</td>
<td>81</td>
</tr>
<tr>
<td>Present study</td>
<td>2003</td>
<td>Great Britain</td>
<td>Case-control</td>
<td>1,461</td>
<td></td>
</tr>
<tr>
<td>Parslow et al.</td>
<td>23</td>
<td>2002</td>
<td>England</td>
<td>Incidence</td>
<td>248</td>
</tr>
<tr>
<td>Stiller and Boyle</td>
<td>9</td>
<td>1996</td>
<td>Great Britain</td>
<td>Incidence</td>
<td>162</td>
</tr>
</tbody>
</table>
agreement concerning the protective effects in diverse backgrounds of immigrants.

The Greaves hypothesis

An alternative hypothesis is that common ALL might be a rare outcome of a common infection, resulting from an abnormal immune response or modulation (3). Wiemels et al. (24) provided evidence for a genetic mutational event, occurring before birth, with the creation of a TEL-AML1 fusion gene (24). This event is necessary, but not sufficient, for the development of certain biologic subtypes of ALL and may be relatively common. However, to progress to overt leukemia, a second mutation is required, the probability of which is increased by an abnormal pattern of infection. Immunologic isolation due to geographic or social isolation of a person during infancy may delay exposure to common infections until the second or third year of life, when exposure normally occurs neonatally or in infancy. When common infections are encountered, as an inevitable consequence of going to school and of early social interaction, the immune system may not respond appropriately. The findings from this study, and those included in section d of figure 1, support the Greaves hypothesis since regions relatively isolated from the mixing of infections have a higher risk of ALL. Social encounters with other persons, such as those experienced in the nursery or at school, are sufficient to degrade immune isolation; large-scale population migration is not necessary. However, other aspects of the Greaves hypothesis, such as the initiating gene fusion, were not addressed; therefore, the present study does not provide a definitive test of the delayed infection hypothesis.

Conclusion

This study did not support Kinlen’s population mixing hypothesis (2) as a general explanation for leukemia and lymphoma: no association between disease and an increased volume of mixing was observed. It may be that the hypothesis applies under conditions of an exceptionally high incidence of leukemia and NHL, but these findings were unable to support this possibility. This study, and a survey of other published studies, lend their support most naturally to the Kinlen hypothesis, such as improved hygiene and kindergarten attendance.

ACKNOWLEDGMENTS

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