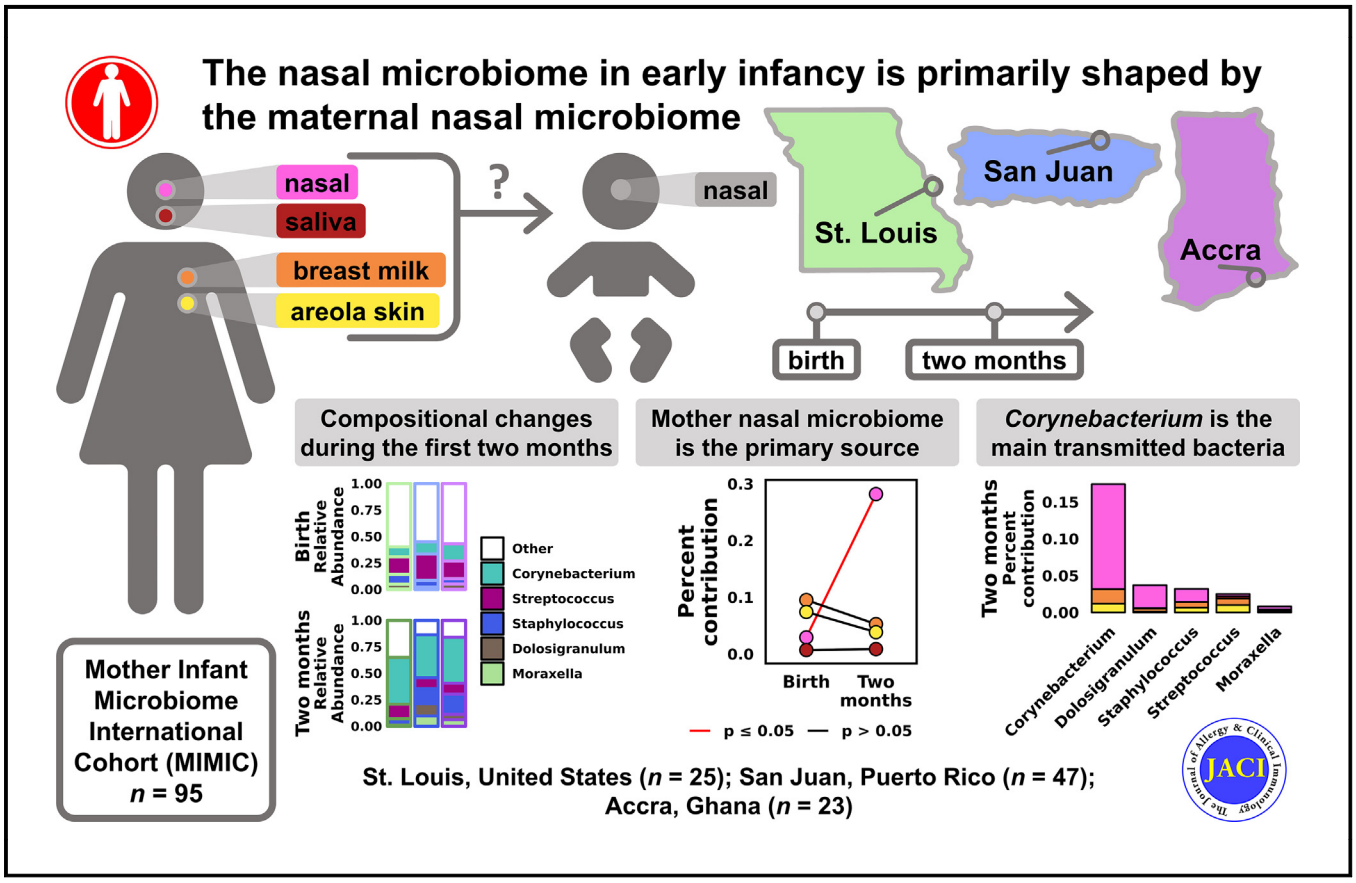
The nasal microbiome in early infancy is primarily shaped by the maternal nasal microbiome

Bailey E. Quinn, BS, José Alejandro Reyes Rodríguez, BS, Emmanuel Kweku Sam, BS, Jasmina Duliman, BS, Elizabeth Denn, MS, Sandra Lee, MPH, et al

GRAPHICAL ABSTRACT



Capsule summary: The maternal nasal microbiome was found to be the primary source that contributed bacteria, particularly the beneficial bacteria *Corynebacterium*, to the offspring nasal microbiome in early infancy. This finding could advance strategies that may shape healthy nasal microbiomes and reduce the incidence of respiratory infections and asthma in childhood.

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The nasal microbiome in early infancy is primarily shaped by the maternal nasal microbiome

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Background: The infant nasal microbiota closely mediates the risks of developing childhood respiratory diseases. However, the primary sources of these early residing bacteria remain largely unknown, preventing the development of microbiome strategies for disease prevention.

Objective: Our aim was to identify the primary maternal source of bacteria found in the early infant nasal microbiome.

Methods: We conducted a birth cohort study titled the Mother Infant Microbiome International Cohort (MIMIC) study. We recruited 95 mother-newborn dyads from 3 sites (St Louis, Mo; San Juan, Puerto Rico; and Accra, Ghana) and collected samples at 2 time points (at the infants' birth and when they were around 2 months old). We performed analyses of 16S ribosomal RNA gene sequencing data to evaluate the maternal microbiomes (nasal, saliva, breast milk, and areola skin) as sources seeding the infant nasal microbiome.

Results: The infant nasal microbiome underwent a major compositional change during the first 2 months of life. The maternal nasal microbiome was identified as the primary source of bacteria in the early nasal microbiome across the 3 study regions. *Corynebacterium* was predominantly transferred from the maternal nasal microbiome. Infants were more likely to harbor a *Corynebacterium*-dominant nasal microbiome if the nasal microbiome of their mother was *Corynebacterium* dominant.

Conclusions: The maternal nasal microbiome is an important source of bacteria in the early nasal microbiome. A large portion of transmitted bacteria from the maternal nasal microbiome belonged to the generally beneficial bacterial genus *Corynebacterium*. The results from this study will aid in the development of early-life intervention strategies aimed at reducing the incidence of childhood respiratory diseases and asthma. (J Allergy Clin Immunol 2025;■■■:■■■-■■■.)

Key words: *Infant nasal microbiome, maternal sources, microbial transmission, childhood asthma, respiratory viral infections,* Corynebacterium*, Puerto Rico, Ghana, Africa, MIMIC*

The early-life nasal microbiota has been repeatedly documented as an important mediator of childhood respiratory health.[1-5] In the nasal cavity, some bacteria such as those from the genus *Corynebacterium,* may play a protective role by decreasing the risks of developing respiratory infections and asthma later in childhood,[6-9] whereas early colonization by pathogenic bacterial species, such as those from the genera *Streptococcus*, *Haemophilus*, and *Moraxella,* may increase the risks of developing diseases.[3,10-13] Therefore, the composition of nasal microbiomes lays an important foundation for the developmental risk of respiratory diseases, and shaping a healthy nasal microbiome is a promising strategy for disease prevention. However, there is limited knowledge regarding the sources of bacteria in the early nasal microbiome, hindering the development of intervention strategies.[14-17]

Early bacterial colonizers in the nasal cavity undergo compositional evolution and play an essential role in defining the developmental trajectory of nasal microbiomes during childhood.[15,18,19] Thus, understanding the primary sources of acquired nasal bacteria during early infancy is crucial for developing effective strategies to foster a healthy nasal microbiome.[18,20] Prior studies have demonstrated that the maternal microbial reservoir is the most important source seeding the infant microbiome at different body sites.[14,21,22] Furthermore, studies of the infant gut microbiome have indicated the maternal gut microbiome as the primary source of the offspring gut microbiome, highlighting the role of ecologic adaptation in microbial vertical transmissions throughout early infancy.[21,22]

Early studies of the infant nasal microbiome have shown both similarities and regional variations across different geographic regions, which may be explained by climatic differences.[1,22] Furthermore, accumulating evidence has shown that environmental exposures, air pollution, and sociocultural factors have the potential to influence the nasal microbiome in infants and adults, suggesting the existence of regional variations.[4,23-27] However, there is a notable absence of studies from regions in Africa and the Caribbean, despite their high burden of childhood respiratory diseases.[28-31] Existing research on the infant nasal microbiome has focused predominantly on samples from a single geographic site, mostly in the United States, Europe, and other high-income countries and regions.[3,14,18,32-36] Therefore, to better understand the generalizability of our findings, it is essential to

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Abbreviations used
ASV: Amplicon sequence variant
IRB: Institutional review board
MIMIC: Mother Infant Microbiome International Cohort
PCoA: Principal coordinate analysis

evaluate potential regional differences in maternal seeding of the infant nasal microbiome across various countries.

To this end, we conducted a birth cohort study called the Mother Infant Microbiome International Cohort (MIMIC) study and recruited a total of 95 mother-newborn dyads across 3 distinct regions (25 from the Washington University School of Medicine and the Barnes-Jewish Hospital in St Louis, Missouri; 47 from San Juan City Hospital in San Juan, Puerto Rico; and 23 from the University of Ghana Medical Centre in Accra, Ghana). We collected infant nasal swab samples as well as samples from multiple maternal body sites, including maternal nasal, saliva, breast milk, and areola skin at 2 time points (at the infants' birth and when they were around 2 months of age). We then performed robust 16S ribosomal RNA gene sequencing to evaluate and identify the maternal sources of the early nasal microbiome. The aim of this cohort study was to evaluate the composition of and changes in the infant nasal microbiome during early infancy and identify the primary source of bacteria found in the early infant nasal microbiome. We hypothesized that the infant nasal microbiome will undergo a significant compositional change during the first 2 months of life, with a shift in the distribution and relative abundance of genera, such that samples collected at birth will differ significantly from those collected at age 2 months. Additionally, we hypothesized that the maternal nasal microbiome would be the primary source among potential maternal sources seeding the infant nasal microbiome in early infancy. To test our hypotheses and explore potential consistencies across the 3 study regions, we performed separate analyses for each region.

METHODS

Cohort sampling and DNA processing

We conducted the MIMIC study across 3 different institutes, with independent institutional review board (IRB) reviews and approvals from each. We recruited mother-newborn dyads between 2021 and 2023 from the Washington University School of Medicine and Barnes-Jewish Hospital in St Louis (IRB approval no. 202103149), San Juan City Hospital in San Juan, (IRB approval no. 00002788), and the University of Ghana Medical Centre in Accra (IRB approval no. UGMC-IRB/MSRC/018/2021). The inclusion criteria were as follows: (1) mother with a healthy pregnancy, (2) full-term birth, (3) passage of meconium within the first 24 hours, and (4) tolerance of feeding by mouth. The exclusion criteria were as follows: (1) premature birth; (2) admission to the neonatal intensive care unit; (3) acute illness at the time of sample collection; (4) identified congenital gastrointestinal, airway, or pulmonary malformation; and (5) identified chromosomal or genetic abnormality. The research coordinators at each institute identified eligible mothers on the basis of the inclusion criteria and contacted them to introduce this study for voluntary participation. All of the participating mothers provided informed consent before enrolling in the study. For each dyad, we collected infant nasal samples as well as maternal nasal, saliva, breast milk, and areola skin swab samples. The first set of samples were collected within 72 hours after the infants' birth, and the same set of samples were collected again between 5 and 9 weeks after birth (during the postpartum appointment). Each sample was then placed into a DNA/RNA Shield lysis tube (Zymo Research, Irvine, Calif) and shipped to the Washington University School of Medicine within 2 weeks of collection. Samples were stored in a freezer at –80°C until processing. In total, samples from 95 families (25 from St Louis, 47 from San Juan, and 23 from Accra) were used in this study. The ZymoBIOMICS DNA Miniprep Kit (Zymo Research) was used to extract microbial DNA from each sample. During the sample collection at both time points, each mother also completed a written questionnaire that included questions about demographics, preexisting conditions, medications, birth type, diet, and exercise.

Sequencing approaches and data processing

Sequencing libraries were prepared from the extracted DNA by utilizing Quick-16S NGS library prep kits (Zymo Research). The V1-V2 region of the 16S ribosomal RNA gene was amplified and barcoded for each individual sample. The barcoded gene fragments were pooled and sequenced using the Illumina MiSeq platform (Washington University Center for Genome Sciences; 2×250 standard run). To characterize and compare the infant nasal microbiomes from the different time points and research sites, all of the infant nasal samples were pooled and sequenced for analyses to avoid bias due to batch effects. Then, the infant nasal and maternal samples from the same family were pooled for sequencing to characterize the potential maternal sources.

The resulting fastq files from the sequencing were imported into RStudio, version 1.4.1717, for processing and analysis with the DADA2 workflow.[37] The reads were filtered and trimmed with forward reads at 240 bp and reverse reads at 160 bp. The amplicon sequencing variances (ASVs) were inferred by using the merged forward and reverse reads. Taxonomy assignments were based on training set 18 of the Ribosomal Database Project.[38] The taxonomy and metadata were used to construct a phyloseq object.

We then performed a 2-step contamination removal procedure. We first used the Decontam package,[39] with a prevalence threshold of 0.1 to remove potential contaminations. Then, an in-house program was used to identify and remove environmental contaminations based on prevalence in negative control samples. If an ASV was prevalent in half of all negative control samples, the ASV was considered a contaminant and removed. Following the contamination removal procedures, any samples retaining fewer than 100 reads were removed.

Statistical analyses

To evaluate whether the infant nasal microbiome underwent a significant compositional change during the first 2 months of life, we conducted both alpha and beta diversity analyses. Alpha diversity was used to evaluate the richness and evenness of bacterial taxa across the samples. We performed alpha diversity analyses based on the number of observed ASVs and Shannon index. Beta diversity measured the differences in microbial composition between samples. We used the weighted UniFrac distance to calculate the beta diversity and then used principal coordinate analysis (PCoA) plots to visualize the results. The

alpha and beta diversity calculations were performed using the phyloseq R-package, version 1.38.0. Statistical analyses comparing the relative abundance of the top genera within infant nasal samples between the 2 time points (at birth and 2 months postpartum) were based on paired 2-tailed *t* tests.

We then evaluated whether the maternal nasal microbiome was the primary source of bacteria found in the infant nasal microbiome. Maternal contributions to the infant samples were calculated using SourceTracker through QIIME2.[40,41] SourceTracker is a bayesian statistics–based computational tool that determines the source of bacteria present in targeted microbial communities. The algorithm uses 16S rRNA sequencing data to compare each bacterial ASV present in the provided infant sample with their corresponding maternal samples (nasal, saliva, breast milk, and areola skin) as sources and evaluate the proportion of its contribution. Analysis was conducted with results aggregated at both the genus and phylum levels. The ASV-level results were also combined to assess the percentages of each of the maternal samples that contributed to the infant sample. To ensure normalized source data in the results from SourceTracker, the maternal data were rarefied to the lowest number of reads present in any of the 4 maternal sample types from each family. The results calculated from SourceTracker were compared between the 2 time points by using paired *t* tests. Additionally, we calculated the number and abundance of shared taxa between each maternal-infant sample pair to compare differences between the maternal nasal sample and each of the other 3 maternal samples, with significance assessed by a Wilcoxon signed rank test. Finally, we compared the relative abundance of shared taxa between each infant nasal microbiome and its own maternal nasal microbiome as well as the average abundance of shared taxa between an infant and all of the other maternal nasal microbiomes, with significance assessed by using a paired *t* test.

We performed the aforementioned analyses separately on samples from each region (St Louis, San Juan, and Accra) to assess potential consistencies across the 3 distinct regions.

Furthermore, we identified the bacteria sourced from the maternal nasal microbiome at the genus level. We then combined the data from the 3 research regions to focus our analysis on *Corynebacterium*, which is the genus transmitted most frequently from the maternal nasal to infant nasal microbiome. First, we plotted the prevalence of *Corynebacterium* in both the infant nasal and maternal samples. Next, we grouped the taxa from *Corynebacterium* by their presence in any of the maternal nasal samples and compared their relative abundance in the infant nasal microbiome. Statistical significance was measured by using a Wilcoxon signed rank test. Finally, we categorized the maternal and infant nasal samples as *Corynebacterium* dominant or *Corynebacterium* nondominant based on the relative abundance of *Corynebacterium* (threshold 0.25). The significance of associations was calculated by using a 2-tailed chi-square test.

RESULTS

The MIMIC study was conducted across 3 research sites, and the samples were sequenced with high quality

Between 2021 and 2023, we recruited a total of 95 mother-newborn dyads across 3 research sites. Of these, 25 dyads were recruited from Washington University School of Medicine and Barnes-Jewish Hospital in St Louis, 47 dyads were recruited from San Juan City Hospital in San Juan, and 23 dyads were recruited from the University of Ghana Medical Centre in Accra. As shown in Table I, of the infants from St Louis, 60% were male, 4% were Hispanic, 68% were White, and 84% were vaginally delivered. Of the infants from San Juan, 62% were male, 100% were Hispanic, 49% were White, and 49% were vaginally delivered. Of the infants from Accra, 48% were male, 0% were Hispanic, 100% were Black, and 50% were vaginally delivered. At 2 months of age, exclusive or partial breast-feeding was noted among 72% of the infants from St Louis, 85% from San Juan, and 91% from Accra.

We first focused on the infant nasal microbiome and sequenced 190 infant nasal swab samples collected from all 3 research sites. After sequencing data processing and contamination removals, 7 samples were excluded because they retained fewer than 100 reads. The number of raw reads, retained reads, and ASVs were assessed by region and time point (see Table E1 in the Online Repository at www.jacionline.org). We then performed dyad-based sequencing to connect the bacteria in the infant nasal samples with those found in the maternal communities. Among these, 14 samples of various types were missing. A total of 936 samples, which included an infant nasal swab and 4 maternal swabs (nasal, saliva, breast milk, and areola skin) from each dyad, were sequenced. After quality control and contamination removals, 31 of the collected samples were removed owing to a low number of reads (<100 reads). The number of raw reads, retained reads, and ASVs for each region, as well as the time point and sample type, were assessed independently (see Table E2 in the Online Repository at www.jacionline.org).

The infant nasal microbiome underwent a major compositional change during the first 2 months of life

We evaluated the composition of the infant nasal microbiome and the changes therein during the first 2 months of life. To assess potential differences between regions, we conducted the analysis for each region separately for comparison. We paired the samples for each infant on the basis of time of collection, and any infants missing a sample were removed from the analysis. At birth, the infant nasal microbiomes from St Louis, San Juan, and Accra appeared to have an even distribution of genera (Fig 1, *A-C*). However, at 2 months of age, each microbiome was dominated by a select number of genera that differed between samples across the 3 regions (Fig 1, *D-F*).

We further evaluated these differences over the first 2 months of life. The number of ASVs present at birth in the nasal microbiomes of the infants from St Louis was similar to the number of ASVs present in the samples collected at age 2 months (Fig 1, *G*), although a significant decrease in Shannon diversity was observed ($P < .01$ [Fig 1, *H*]). The San Juan (Fig 1, *I* and *J*) samples exhibited a similar pattern, with the number of observed ASVs indicating no significant changes ($P = .68$), whereas the Shannon index decreased significantly ($P < .01$). The Accra samples (Fig 1, *K* and *L*) had a borderline significant change in Shannon diversity ($P = .046$), with the same downward trend from birth to 2 months, representing a shift toward an environment dominated by a select number of genera and contrasting with the even distribution seen at birth.

The compositional differences between the 2 time points from each research site were visualized in the PCoA plots based on

TABLE I. Phenotype characteristics by region

Selected characteristics, no. (%)	St Louis (n = 25)	San Juan (n = 47)	Accra (n = 23)
Infant sex male, no. (%)	15 (60.00)	29 (61.70)	11 (47.83)
Infant ethnicity			
Hispanic or Latino	1 (4.00)	47 (100.00)	0 (0.00)
White	17 (68.00)*	18 (48.65)†	0 (0.00)
Black	5 (22.73)*	11 (29.73)†	23 (100.00)
Other	0 (0.00)*	8 (21.62)†	0 (0.00)
Gestational age (y), mean (SD)	38.16 (1.25)	39.23 (2.90)	38.36 (0.90)*
Vaginally delivered, no. (%)	21 (84.00)	23 (48.94)	11 (50.00)*
Breast-feeding at age 2 mo, no. (%)	18 (72.00)	40 (85.11)	21 (91.30)
Presence of pets at home, no. (%)	15 (62.50)‡	26 (55.32)	4 (17.39)

*Percentage of a total of 22 families.
†Percentage of a total of 37 families.
‡Percentage of a total of 24 total families.

weighted UniFrac distances (Fig 1, *M-O*). For all 3 regions, the samples collected at birth were tightly clustered and dispersed at 2 months of age, yielding a significant difference ($P < .01$ for each site). This indicated a general similarity between the infant nasal samples collected at birth before becoming more dissimilar after 2 months. Notably, a compositional shift in maternal nasal samples between the 2 time points was observed and visualized by using PCoA plots (see Fig E1, *A-C* in the Online Repository at www.jacionline.org). The compositional changes were significant and consistent across all 3 research sites (for St Louis, $P < .01$; for San Juan, $P < .01$; and for Accra, $P = .03$). This may be attributed to changes in environmental exposures from the postpartum room at the first collection to the home environment at the second collection.

We further quantified the changes in relative abundance of major genera from the infant nasal samples over the first 2 months of life. The samples collected from all 3 regions experienced a significant increase in the relative abundance of *Corynebacterium* (Fig 1, *P-R*). The trends with regard to other genera, either an increase or decrease in relative abundance, were consistent between both time points across all 3 regions, although the changes in the relative abundance of *Dolosigranulum* indicated significantly different opposing trends in samples collected from San Juan and Accra. These results indicated a fundamental shift occurring in the infant nasal microbiome during the first 2 months of life, from a general infant nasal microbiome with broad similarities and evenly distributed bacteria to one that was more individualized with select dominant genera.

We then compared the infant nasal microbiome at age 2 months across the 3 regions. At 2 months, the samples collected from San Juan had a significantly higher number of observed ASVs than those from Accra ($P = .02$ [Fig 2, *A*]), although there were no differences in Shannon diversity across all 3 regions (Fig 2, *B*). The PCoA plot based on weighted UniFrac distances also indicated a similarity between the 3 regions at age 2 months ($P = .11$ [Fig 2, *C*]). Major bacterial genera, including *Corynebacterium, Streptococcus*, and *Veillonella,* were similarly abundant across the 3 regions (Fig 2, *D*). This further suggested a compositional shift aligning with a non–region-specific development of the infant nasal microbiome.

In addition, we evaluated variables, including sex, birth type, feeding method, and presence of pets at home, which may affect the infant nasal microbiome at age 2 months. We did not find any significant impacts of these factors across any of the 3 research sites (see Figs E2 and E3 in the Online Repository at www.jacionline.org) or when combined (see Fig E4 and E5 in the Online Repository at www.jacionline.org).

The maternal nasal microbiome was the primary source of the infant nasal microbiome

We next attempted to evaluate the maternal microbiomes as potential sources of early-life nasal bacteria. For comparison, the analysis was conducted on a regional basis. The maternal and infant samples were paired by family, and any samples missing a pair were removed from analysis. When SourceTracker was used on the samples from St Louis, 15.71% of the infant nasal microbiome was attributed to maternal breast milk at birth before significantly decreasing to 1.34% at 2 months of age ($P = .01$ [Fig 3, *A*]). Inversely, the percentage of maternal nasal contributions at birth was 1.54%, and it increased significantly to 25.18% at age 2 months ($P < .01$ [Fig 3, *A* and see Table E3 in the Online Repository at www.jacionline.org]). The same increasing trend of the maternal nasal contributions from birth to 2 months was seen in the samples from San Juan (from 2.55% to 31.02% [$P < .01$]) and Accra (from 5.20% to 18.03% [$P < .05$]) (Fig 3, *B* and *C* and see Table E3).

Further evaluations revealed that the maternal microbiomes from different body sites may contribute a similar number of ASVs to the infant nasal microbiome (Fig 3, *D* [*top panel*]). However, the ASVs potentially contributed by the maternal nasal microbiome had a significantly higher relative abundance in the infant nasal microbiome than those from the saliva ($P = .01$), breast milk ($P < .01$), and areola skin microbiomes ($P < .01$ [Fig 3, *D* (*bottom panel*)]). The maternal samples from San Juan were also found to contribute a similar number of ASVs to the infant nasal microbiome, but the relative abundances of ASVs shared between the infant nasal and maternal microbiomes were significantly higher for those potentially transmitted from the maternal nasal microbiome than for those from the maternal saliva ($P < .01$) and breast milk microbiomes ($P = .01$ [Fig 3, *E*]). Likewise, a similar trend was confirmed for the Accra samples, although those results were not significant (Fig 3, *F*).

To further validate intergenerational transmission, we compared the relative abundance of infant nasal ASVs that were shared with their own maternal nasal microbiome samples with the average relative abundance of infant nasal ASVs that were shared between each infant sample and all the other maternal nasal samples. The infant nasal ASVs that were shared with their own maternal samples were significantly more abundant than those shared with other maternal samples. This trend was present across all 3 regions: for St Louis, $P = .01$ (Fig 3, *G*); for San Juan, $P < .01$ (Fig 3, *H*); and for Accra, $P = .03$ (Fig 3, *I*).

We then compared the weighted UniFrac distances between each infant nasal sample and its own maternal samples with the average distance between an infant nasal sample and all of the other maternal samples. The infant nasal samples collected at

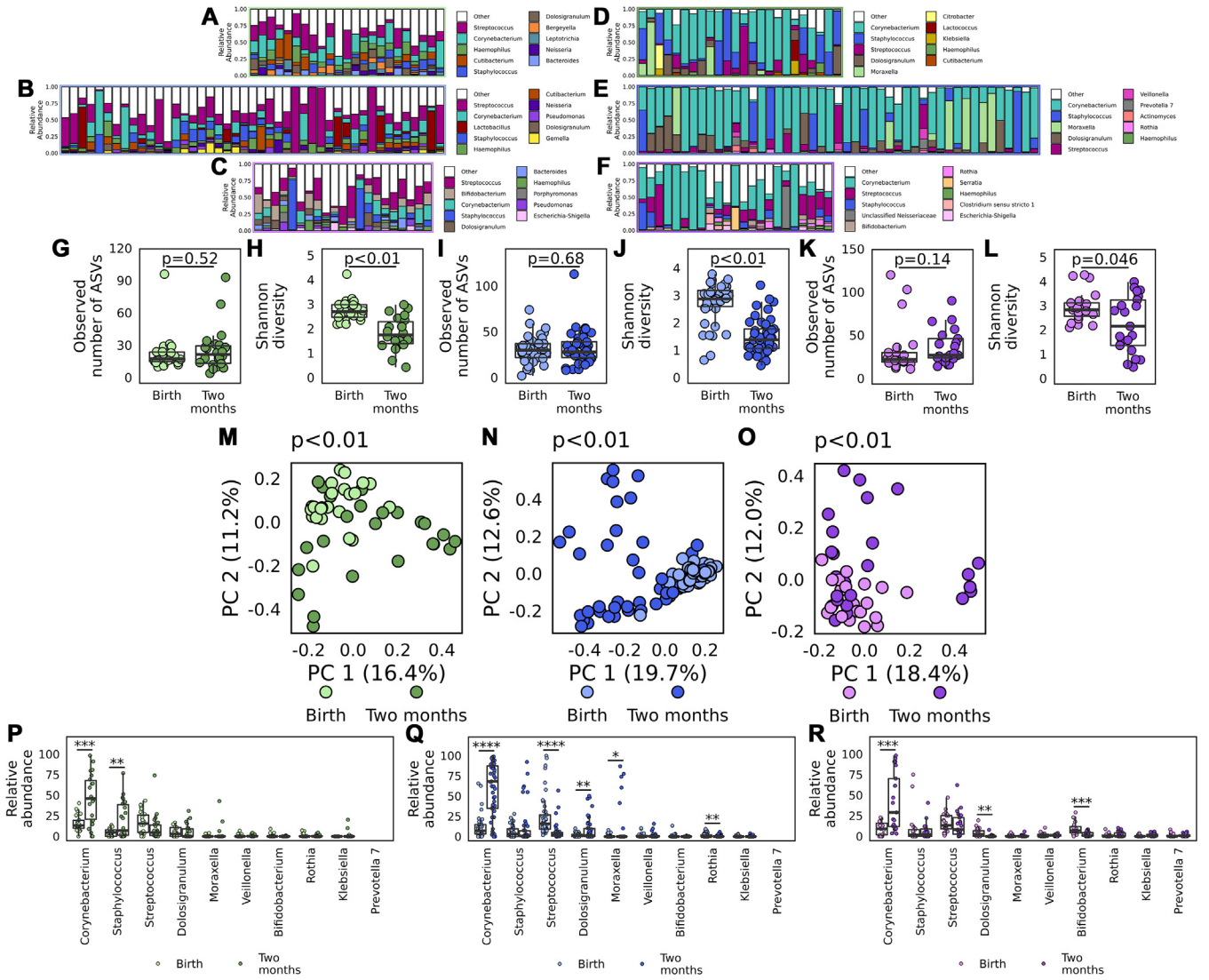

FIG 1. The infant nasal microbiome underwent a major compositional change during the first 2 months of life. **A-C,** The top 10 genera of the infant nasal samples from St Louis (n = 23) (**A**), San Juan (n = 45) (**B**), and Accra (n = 21) (**C**) were used to plot birth samples for each region. **D-F,** The samples collected at age 2 months were plotted in the same manner for St Louis (n = 24) (**D**), San Juan (n = 47) (**E**), and Accra (n = 23) (**F**). **G-L,** Diversity measures were used to evaluate the nasal samples collected at birth and age 2 months. The infant nasal samples were used to evaluate the observed number of ASVs and Shannon diversity for samples collected from St Louis (n = 22) (**G** and **H**), then San Juan (n = 45) (**I** and **J**), and Accra (n = 21) (**K** and **L**). The significance for alpha diversity was measured using a Wilcoxon signed rank test. **M-O,** Beta diversity was assessed using the weighted UniFrac dissimilarity in a PCoA plot, and the significance was measured using analysis of similarities for the samples from St Louis (n = 25) (**M**), San Juan (n = 47) (**N**), and Accra (n = 23) (**O**). **P-R,** The relative abundance of the top 10 genera identified for St Louis were compared between samples collected at birth and those collected at age 2 months (n = 22) (**P**) and then repeated for San Juan (n = 45) (**Q**), and Accra (n = 21) (**R**). The significance for all regions was evaluated by using a paired 2-tailed *t* test.

2 months were significantly more similar to their own maternal nasal samples than to other maternal nasal samples from St Louis (see Fig E6, *A* in the Online Repository at www.jacionline.org), San Juan (see Fig E6, *B*), and Accra (see Fig E6, *C*). This confirmed the existence of a significant familial similarity between the infant nasal and maternal nasal samples, highlighting the maternal nasal microbiome as an important source of the infant nasal microbiome by 2 months of age.

Corynebacterium was the primary bacteria contributed by the maternal nasal microbiome to the infant nasal microbiome

Next, we identified the bacterial taxa contributed by the maternal microbiome to the infant nasal microbiome at 2 months of age in each region. Through use of the SourceTracker results at the genus level for St Louis, the maternal nasal microbiome was identified as the source of a large amount of *Corynebacterium*

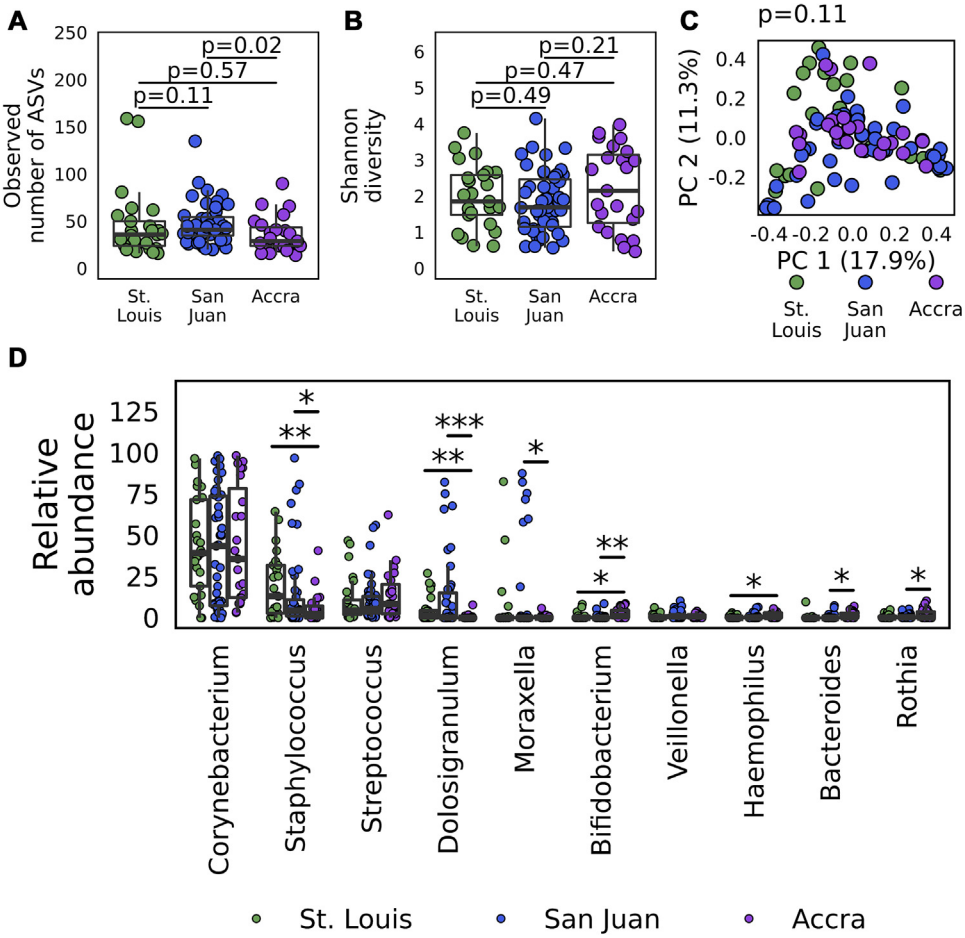

FIG 2. The composition of the infant nasal microbiome was similar across the 3 regions (n = 95). **A** and **B,** Samples collected in St Louis, San Juan, and Accra when the infants were 2 months of age were compared by using alpha diversity measures, observed number of ASVs (**A**) and Shannon diversity (**B**). **C,** Beta diversity was assessed by using the weighted UniFrac dissimilarity in a PCoA plot for samples from infants at age 2 months, with the significance measured by using analysis of similarities. **D,** The top 10 genera present across all 3 regions at 2 months of age were used to evaluate changes in the relative abundance; significance was evaluated by using a paired 2-tailed *t* test.

(Fig 4, *A*), while also contributing some *Staphylococcus* and *Dolosigranulum* to the infant nasal microbiome. Similarly, the samples of maternal nasal microbiome from San Juan primarily contributed *Corynebacterium,* along with *Staphylococcus*, *Dolosigranulum*, and *Moraxella* (Fig 4, *B*), to the infant nasal microbiome, whereas the maternal nasal samples from Accra mainly contributed *Corynebacterium* (Fig 4, *C*). At the phylum level, the maternal nasal samples contributed Actinobacteriota across all 3 regions but contributed Firmicutes only in St Louis and San Jaun (see Fig E7 in the Online Repository at www.jacionline.org).

Because *Corynebacterium* was identified as the predominantly contributed bacterial genus and because it consistently represented a significant portion of the infant nasal microbiomes across all 3 regions at age 2 months, we pooled the samples from the 3 regions for *Corynebacterium* analysis. We identified *Corynebacterium* across all of the sample types collected from all 3 regions, with a total of 494 ASVs represented in a heat map (Fig 4, *D*). Notably, more abundant *Corynebacterium* species were identified in multiple regions. The infant nasal samples from all 3 regions had 98 different *Corynebacterium* ASVs in total, which was the lowest number among all sample types. Of the 98 ASVs, 54 were found in at least 1 maternal sample and 44 could not be identified in any of the maternal samples. The relative abundances of *Corynebacterium* ASVs found in any of the maternal nasal microbiomes were significantly higher than those *Corynebacterium* ASVs not found in any of the maternal nasal microbiomes ($P < .01$ [Fig 4, *E*]). This indicated that *Corynebacterium* species capable of colonizing the maternal nasal microbiome were more likely to thrive in the infant nasal microbiome. We then categorized the maternal nasal and infant nasal samples on the basis of *Corynebacterium* dominance (relative abundance > 25%). The results suggested that a mother with a *Corynebacterium*-dominant nasal microbiome was more likely to have an infant with a *Corynebacterium*-dominant nasal microbiome ($P = .01$ [Fig 4, *F*]).

DISCUSSION

The composition and sources of the nasal microbiome in early infancy are not well understood,[14,33,34] so this study aimed to

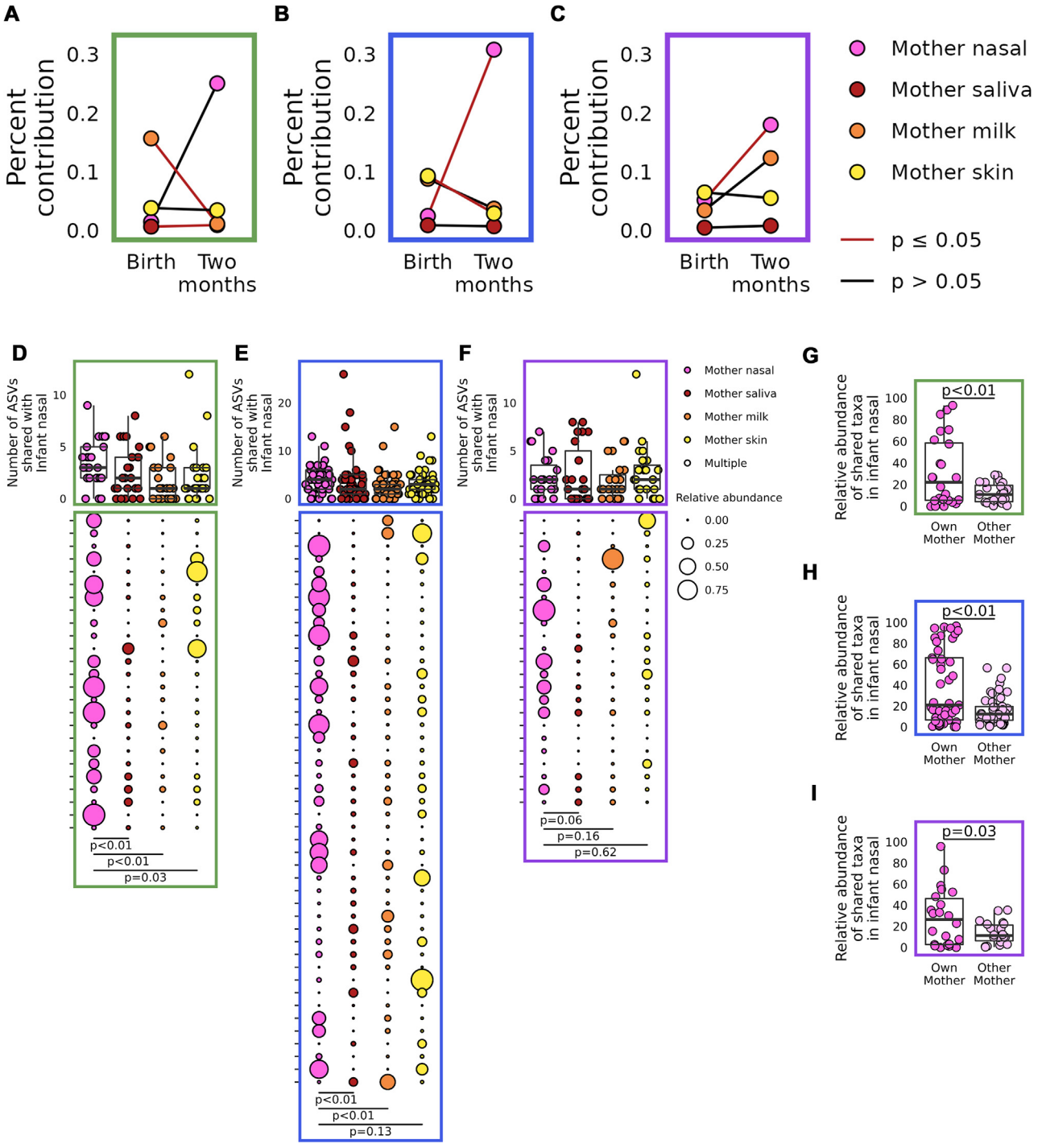

FIG 3. Bacteria acquired by the infant nasal microbiome can be attributed to the maternal nasal microbiome. **A-C,** Changes in the maternal contributions to the microbiome between birth and age 2 months were calculated for the infant nasal samples from St Louis (n = 25) (**A**), San Juan (n = 47) (**B**), and Accra (n = 23) (**C**). Paired 2-tailed *t* tests were used to evaluate the significance. **D-F,** The number of ASVs and relative abundance of ASVs common between an infant nasal sample and only1 maternal sample were compared by using a Wilcoxon signed rank test for St Louis (n = 25) (**D**), San Juan (n = 47) (**E**), and Accra (n = 23) (**F**). The relative abundance of ASVs in an infant nasal sample that were also found in their own maternal nasal sample and other maternal nasal samples were compared by using a paired 2-tailed *t* test for St Louis (n = 25) (**G**), San Juan (n = 47) (**H**), and Accra (n = 23) (**I**).

address these knowledge gaps. We conducted a birth cohort study, the MIMIC study, across 3 distinct geographic regions to test our hypotheses that the infant nasal microbiome undergoes a significant compositional change during the first 2 months of life and that the maternal nasal microbiome is the primary maternal source seeding the infant nasal microbiome. We then

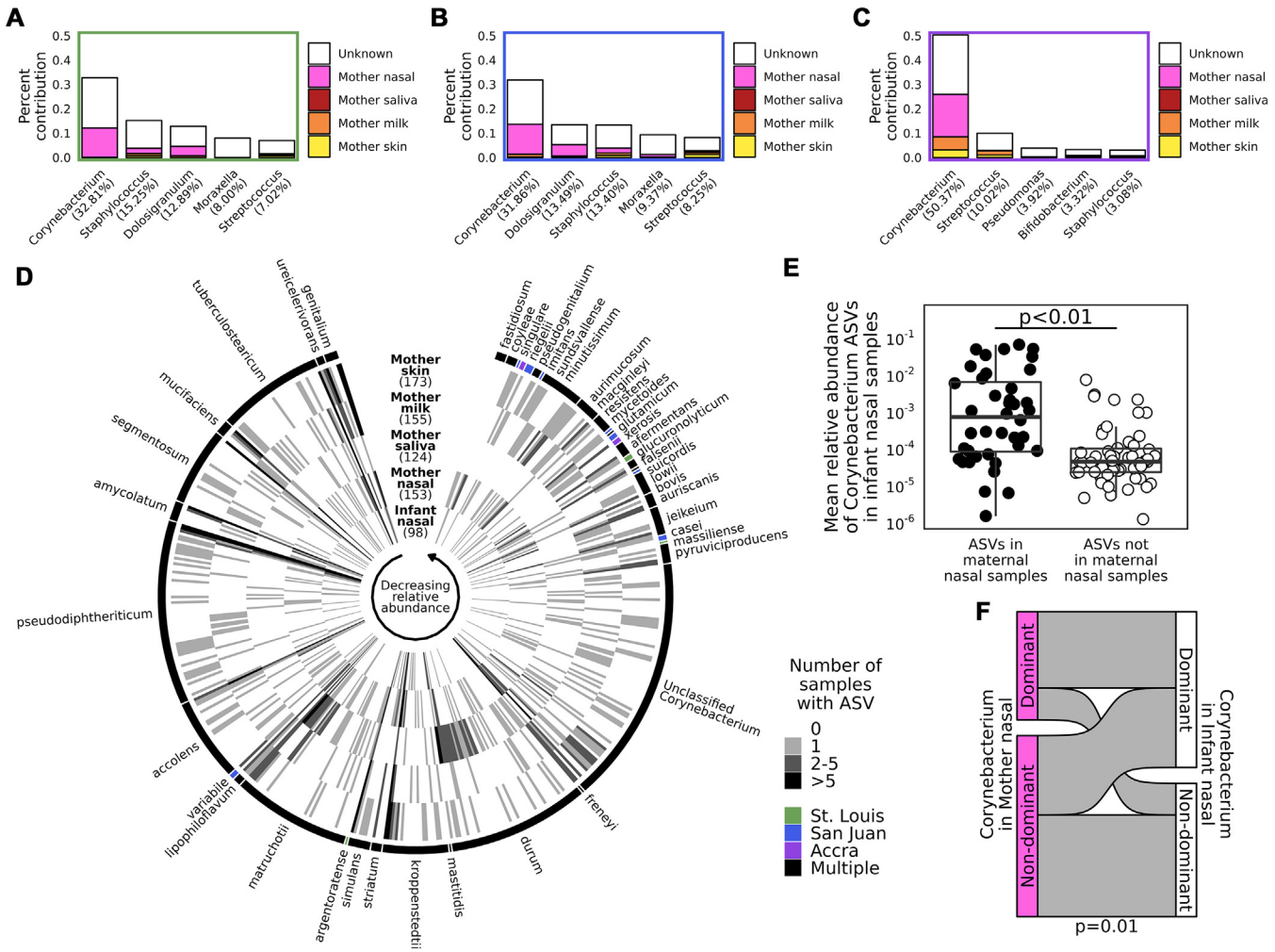

FIG 4. *Corynebacterium* in maternal microbial communities was more likely to thrive in the infant nasal microbiome. **A-C,** The SourceTracker results were averaged at the genus level and then scaled by the relative abundance of each genus in the infant nasal microbiome for St Louis (n = 25) (**A**), San Juan (n= 47) (**B**), and Accra (n = 23) (**C**). **D** and **E,** The prevalence of *Corynebacterium* ASVs in the infant nasal and maternal samples was used to generate a heatmap (n = 95) (**D**). The relative abundance of *Corynebacterium* ASVs was compared between those that were or were not present in any maternal nasal samples; the significance was measured by using a Wilcoxon rank sum test (n = 95) (**E**). **F,** Maternal nasal and infant nasal samples were evaluated within dyads for the relative abundance of *Corynebacterium* and compared in a Sankey plot, and a 2-tailed chi squared test was performed for significance (n = 91).

compared the results from each research region (St Louis, Mo; San Juan, Puerto Rico; and Accra, Ghana).

Our study revealed a rapid development of the nasal microbiome during early infancy. The nasal microbiome at birth consisted of a wide range of bacteria with similar small abundances, resulting in high homogeneity. After 2 months, however, the nasal microbiomes were dominated by a few typical genera, resulting in niche-specific microbiomes as well as increased variations among the samples. This emphasized the importance of identifying the sources of early nasal bacteria for microbial modifications. Our findings identified the maternal nasal microbiome as the primary source of bacteria in the infant nasal microbiome, which aligns with the results from an experimental study involving sows and piglets and reporting a direct vertical transmission route.[42]

We performed separate analyses for each region and found that the infant nasal microbiomes were similar in terms of developmental trends during the first 2 months of life. The maternal nasal microbiome was also consistently found to be the primary source of the infant nasal microbiome across all 3 regions. This indicated that the maternal nasal microbiome is a robust seeding source and that its contribution to the offspring nasal microbiome may not be affected by regional environmental or sociocultural factors. However, our study focused only on the first 2 months of age, a period when environmental factors may not yet play a major role. Therefore, further studies with a longer follow-up period are important to better evaluate regional variations with respect to the composition and maternal sources of the infant nasal microbiome.

In our study, *Corynebacterium* was identified as the primary bacterial genus seeded from the maternal nasal to infant nasal microbiome. Infants were more likely to harbor a *Corynebacterium*-dominant nasal microbiome at age 2 months if the nasal microbiome of their mother was *Corynebacterium* dominant.

Corynebacterium is widely considered beneficial and has been repeatedly correlated with a decreased risk of development of severe respiratory infections and asthma in early childhood.[6,43,44] Therefore, the maternal nasal microbiome may serve as an important source for beneficial bacterial transfer to the offspring nasal microbiome in early infancy, suggesting that a healthy maternal nasal microbiome may play a crucial role in development of a healthy infant nasal microbiome. Importantly, we also observed compositional changes in the maternal nasal microbiome between the 2 time points, highlighting a dynamic feature of the maternal nasal microbiome during the postnatal stage. Further research on the maternal nasal microbiome is needed to understand this essential reservoir and its involvement in shaping the offspring nasal microbiome.

The identified mother-to-offspring nasal microbial transmission suggested that nasal microbial colonization is reliant on niche adaptivity, which is in line with the findings from gut microbial transmissions.[21,22] In addition, we found that the relative abundance of shared nasal bacteria was significantly higher between a mother-offspring pair than between a mother with an infant from another family. This implies that parenting practices may also play an essential role in exposing an infant to the microbiome of their mother, which may be unique to each family. However, shared bacterial taxa between maternal and infant nasal microbiomes may be due to shared environmental exposures or similar mucosal immunity between a mother-offspring pair and not a direct vertical transmission. Studies that include the aerosol microbiome, nasal samples from other family members, and immune biomarkers are needed to further investigate other possible mechanisms.

We acknowledge some limitations of the current study. First, to evaluate the maternal sources, we collected samples from multiple maternal body sites that often have close contact with the infant nose. However, a large portion of the infant nasal microbiome was not attributed to any of the collected samples. This implies that other important sources may have been missed in this study; therefore, future studies that include additional potential source samples, especially environmental samples, could provide a more comprehensive understanding of the sources of bacteria found in the infant nasal microbiome. Second, the vertical transmission of bacteria is a dynamic process.[22,45] Studies with a longer follow-up period after birth would allow us to further track the potential changes of microbial sources over time. Third, environmental and sociocultural differences have the potential to affect nasal microbial compositions in infancy,[46,47] but we did not evaluate and compare these variables across the 3 research regions. It is important to collect relevant behavioral information and consider their role in microbial vertical transmissions in future studies to better understand variations across different regions. Fourth, although we did not observe significant effects of several variables, such as sex, birth type, feeding method, and presence of pets at home, on the composition of the infant nasal microbiome at 2 months after birth, the limited statistical power of these variable analyses in our study may have influenced the findings. Therefore, studies with larger sample sizes are needed to more accurately assess the potential impact of these variables.

In summary, characterizing the early nasal microbiome and understanding the microbial acquisition will aid in the development of early-life intervention strategies aimed at reducing the incidence of respiratory diseases and asthma during childhood. Our MIMIC study highlighted a rapid compositional change in the nasal microbiome and identified the maternal nasal microbiome as a primary reservoir of bacteria in the offspring nasal microbiome during early infancy. Our major findings were consistent across 3 geographic regions, with a large portion of the acquired bacteria found to be *Corynebacterium*, a genus that is generally believed to be beneficial.

Source data

The 16s ribosomal RNA gene sequencing data used in this study can be found in the Sequence Read Archive (SRA) under the BioProject accession number PRJNA1162546.

DISCLOSURE STATEMENT

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Key messages

- **A birth cohort study, the MIMIC study, with 3 research sites (St Louis, Mo; San Juan, Puerto Rico; and Accra, Ghana) identified the maternal nasal microbiome as the primary source seeding the offspring nasal microbiome in early infancy.**
- **The infant nasal microbiome experienced marked compositional changes during the first 2 months of life across all 3 distinct geographic regions studied, indicating a critical window for microbial development and modifications.**
- ***Corynebacterium* was predominantly transferred from the maternal nasal microbiome to the offspring nasal microbiome. Because *Corynebacterium* is associated with lower risks of developing severe respiratory infections and asthma, the maternal nasal microbiome may play an important role in shaping a healthy infant nasal microbiome by seeding beneficial bacteria.**

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