Twenty-year Follow-up of Kangaroo Mother Care Versus Traditional Care

Nathalie Charpak, MD,[a] Rejean Tessier, PhD,[b] Juan G. Ruiz, MD, MSc,[c,d] Jose Tiberio Hernandez, PhD,[e] Felipe Uriza, MD, MSc,[c,d] Julieta Villegas, MD, MSc,[a] Line Nadeau, PhD,[b] Catherine Mercier, PhD,[b] Francoise Maheu, PhD,[f] Jorge Marin, MD,[g] Darwin Cortes, PhD,[h] Juan Miguel Gallego, PhD,[h] Dario Maldonado, PhD[e]

abstract

BACKGROUND AND OBJECTIVES: Kangaroo mother care (KMC) is a multifaceted intervention for preterm and low birth weight infants and their parents. Short- and mid-term benefits of KMC on survival, neurodevelopment, breastfeeding, and the quality of mother–infant bonding were documented in a randomized controlled trial (RCT) conducted in Colombia from 1993 to 1996. The aim of the present study was to evaluate the persistence of these results in young adulthood.

METHODS: From 2012 to 2014, a total of 494 (69%) of the 716 participants of the original RCT known to be alive were identified; 441 (62% of the participants in the original RCT) were re-enrolled, and results for the 264 participants weighing ≤1800 g at birth were analyzed. The KMC and control groups were compared for health status and neurologic, cognitive, and social functioning with the use of neuroimaging, neurophysiological, and behavioral tests.

RESULTS: The effects of KMC at 1 year on IQ and home environment were still present 20 years later in the most fragile individuals, and KMC parents were more protective and nurturing, reflected by reduced school absenteeism and reduced hyperactivity, aggressiveness, externalization, and socio-deviant conduct of young adults. Neuroimaging showed larger volume of the left caudate nucleus in the KMC group.

CONCLUSIONS: This study indicates that KMC had significant, long-lasting social and behavioral protective effects 20 years after the intervention. Coverage with this efficient and scientifically based health care intervention should be extended to the 18 million infants born each year who are candidates for the method.

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[a]*Fundación Canguro, Bogotá, Colombia;* [b]*Université Laval, Québec City, Québec, Canada;* [c]*Pontificia Universidad Javeriana, Bogotá, Colombia;* [d]*Hospital Universitario San Ignacio, Bogotá, Colombia;* [e]*Universidad de los Andes, Bogotá, Colombia;* [f]*Hôpital St Justine, Montréal, Québec, Canada;* [g]*Hospital Universitario Infantil San José, Bogotá, Colombia; and* [h]*Universidad del Rosario, Bogotá, Colombia*

Dr Charpak (Principal Investigator) was responsible for generating the research protocol, processing of the original randomized controlled trial database, oversaw all data collection and analysis, was responsible for writing and revising the manuscript, contributed as a content expert, and was in charge of literature review and state of the art; Dr Tessier (Co-principal Investigator) was responsible for generating the research protocol, writing and revising the manuscript, oversaw specific data collection and analysis, contributed as a content expert, and was in charge of literature review and state of the art; Dr Ruiz (Co-principal Investigator) was responsible for generating the research protocol, data cleaning, writing and revising the manuscript, and contributed as a specific content expert; Dr Hernández (Co-principal Investigator) oversaw the treatment of neuroimages, data cleaning and analysis, revision of the manuscript, and contributed as a specific content expert; Dr Uriza (Co-principal Investigator) participated in the generation of the research protocol, revision of the manuscript, and contributed as content expert; Dr Villegas (Co-investigator) was responsible for processing of the original randomized controlled trial database, oversaw data analysis, was responsible for writing

WHAT'S KNOWN ON THIS SUBJECT: Kangaroo mother care (KMC) is an intervention for preterm and low birth weight infants. Short- and mid-term benefits of KMC on survival, neurodevelopment, and the quality of mother–infant bonding were documented in a randomized controlled trial in 1993–1996.

WHAT THIS STUDY ADDS: This study indicates that KMC had significant, long-lasting social and behavioral protective effects 20 years after the intervention in adolescence and young adulthood. Coverage with this efficient, scientifically based health care intervention should be extended.

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Low birth weight (defined as weight <2500 g) was the direct or associated cause of death in 44% of the estimated 2 763 000 neonatal deaths worldwide in 2013.[1] According to the World Health Organization, 10% of all births worldwide are either low birth weight or premature (ie, birth at <37 weeks of gestational age). Preterm survivors more frequently exhibit neurologic and behavioral impairment,[2] and premature or low birth weight infants (LBWI) later have cognitive deficits, poor academic performance, or attention problems.[3–5] At school age, they are less socially competent and more often victimized than their peers,[6] and, in adolescence, they are more often socially rejected and less attentive.[7]

Kangaroo mother care (KMC) is a human-based technique with well-established short- and mid-term effectiveness and safety, suitable for use in all settings. It is based on 3 components: (1) kangaroo position (ie, continuous skin-to-skin contact between mother and infant), which provides appropriate thermal regulation, among other benefits; (2) exclusive breastfeeding when possible; and (3) timely (early) discharge with close follow-up. KMC was originally developed in Colombia as an outpatient alternative to a neonatal minimal care unit, in which infants remain in an incubator while they gain weight.[8]

In 1993 to 1996, our group conducted a randomized clinical trial (RCT) to compare the original KMC intervention and "traditional" inpatient care. The trial showed that morbidity, mortality, growth, development, and other selected health-related outcomes were at least as good as or better than those obtained with usual care when infants reached term and at 1-year corrected age (CA). The main short- and mid-term results have been reported in international, peer-reviewed journals.[8–11]

The 2 main questions addressed in the present study were whether the documented 1-year benefits persisted up to 20 years and whether the KMC intervention had a long-term protective effect against cognitive, social, and academic difficulties in a randomized block of participants who had weighed <1800 g at birth.

METHODS

Population and Sample

We followed up a cohort of former LBWI who participated in the RCT on KMC 20 years previously. The participants were infants who weighed ≤2000 g at birth, survived the transition to extrauterine life, and were eligible for neonatal minimal care. They were randomly assigned to KMC or to the control group according to birth weight (≤1200, 1201–1500, 1501–1800, and 1801–2000 g). The present study included the randomized sample of infants weighing ≤1800 g at birth, who comprised >90% preterm infants, to allow comparisons with other follow-up studies.

The study protocol was approved by the ethical committee of the Pontificia Universidad Javeriana and the Univerité Laval. Participants were informed and asked to sign a consent form. Anonymity of data was guaranteed.

Twenty years after enrollment, systematic efforts were made to contact and re-enroll all former LBWI known to be alive at 1 year CA. A survival cohort effect was anticipated, and more control infants than KMC infants died during the first year of follow-up, implying a possible imbalance of mortality and other potential confounders. To assess whether the expected imbalance between groups could bias comparisons in the re-enrolled cohort, a Rasch model[12] was fitted to estimate the overall degree of vulnerability (fragility index) due to factors present before allocation. Fifteen unevenly distributed binary indicators were selected to represent injuries that might have occurred during pregnancy, birth, or the neonatal period before randomization (Table 1). The wide span of discrimination estimates confirmed use of a 2-parameter model, and the goodness-of-fit improved ($P < .001$). The index is based on individual factorial scores, on the assumption that a common latent variable measures the nonspecific personal fragility of an infant. The fragility indexes of the 2 groups were similar (Fig 1).

Between January 18, 2013, and December 26, 2014, the same social worker who coordinated the follow-up visits during the original RCT traced the participants using multiple sources of information and located 494 (69%) of the 716 participants in the original RCT known to be alive at 1 year. Of these, 3 had died after 1 year of age, 11 were living outside Bogotá, and 39 refused to participate. The 222 former participants who could not be located were presumed from their civil registry numbers to be alive. Of the original 433 infants who were randomized to treatment and weighed ≤1800 g at birth, 264 subjects (61% of the participants who weighed ≤1800 g at birth) agreed to participate and were re-enrolled (Tables 2 and 3).

Descriptive analyses confirmed that re-enrollment did not introduce bias in the distribution of variables in the overall population ($n = 433$) or in the re-enrolled sample ($n = 264$), with no significant differences in the main baseline demographic variables, potential confounders, or growth or development indices (Table 4). Some differences were no longer statistically significant in the re-enrolled cohort because of loss of statistical power due to attrition of the cohort.

Equally intense efforts were made to track KMC infants and control infants. Once the participating families were identified, telephone interviews were conducted to determine the vital status of the former LBWI and their availability and willingness to participate. A first appointment was then fixed.

General Procedures

Before measurements were made, all the participants were referred to an optometrist and a phonoaudiologist to ensure that they could participate in all tests; glasses were provided or adjusted, as needed. The main outcome variables at 20 years[13–24] are listed in Table 5. In the 3-day evaluation, each participant underwent a full medical examination and a battery of psychological and neuropsychological evaluations; neuroanatomical, functional, and neurophysiological assessments; and house visits, with collection of complete education and work histories.

The exposure was random allocation to KMC or traditional care 20 years previously. The potential confounders were parents' demographic characteristics, education, and socioeconomic status at the birth of the child, and children's antenatal and perinatal anthropometrics and general health at birth and during neonatal adaptation before eligibility.

Data Processing and Analysis

Data were recorded in a standard format both on paper and online. Categorical variables were compared by using χ^2 or Fisher's exact tests; numerical discrete and continuous variables were compared in parametric and nonparametric tests, as appropriate. Alpha P values <.05 were considered significant.

Bivariate analyses were conducted to compare the distribution of potential confounders and effect modifiers according to exposure and each outcome. Stratified and multivariate

TABLE 1 Parameters of the Fragility Index (2-Parameter Logistic Rasch Model) comprising Problematic Events During Pregnancy, Birth, or the Neonatal Period Before Randomization in the Original RCT Cohort

Parameter	Difficulty[a]
Preterm	1.8972291
Intrauterine growth restriction	−0.5855773
Intrauterine growth restriction and preterm	−1.2851473
Gestational age at birth	−0.7523441
Acute suffering at birth	0.3160136
Neonatal reanimation	−1.8858323
Weight at birth <1501 g	−1.7757791
Toxemia during pregnancy	−0.3618344
Primiparous	−0.1795824
Apgar score 5 min <7	−0.6533428
Male sex	−0.1965165
Neonatal sepsis	−1.7442807
Gestational age at randomization	−2.162849
Nosocomial infection before randomization	−1.7062807
Severe jaundice	−0.5502986

[a] An easy indicator (negative value) is any observed fragility; a difficult indicator (positive value) is seen only at the most severe levels.

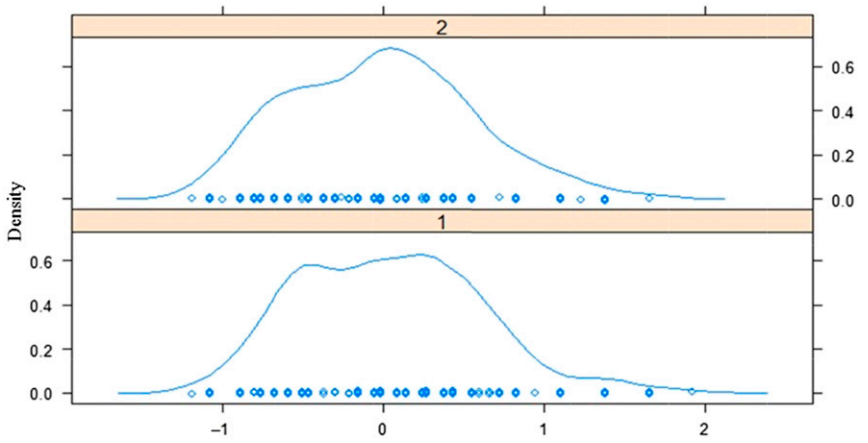

FIGURE 1
Fragility index before randomization in the re-enrolled cohort according to group. Wilcoxon rank sum test with continuity correction, $P = .1968$. Group 1: KMC; group 2: control.

TABLE 2 Path From Birth to 20 Years of the Re-enrolled Cohort (441 Participants)

RCT Re-enrolled Sample	Total Cohort	KMC	Control
Newborns ≤2000 g (September 1993–September 1994)	1084 (100)		
Noneligible newborns	338 (31)		
Transferred to another clinic	129		
Died before randomization	157 (15)		
Congenital malformation or neurologic pathology	52		
Original RCT sample	746	382 (51)	364 (49)
Died during the first year	30	11	19
Survivors at 1 y of CA	716 (96)	371 (97)	345 (95)
Not located at 20 y of age	222 (31)	119 (32)	103 (30)
Located but not re-enrolled at 20 y of age	53 (7)	26 (7)	29 (8)
Died between 1 and 20 y	3	1	2
Refused to participate (6 twins in each group)	39	19	22
Out of scope	11	6	5
RCT re-enrolled cohort at 20 y of age	441 (62)	228 (61)	213 (62)

Data are presented as *n* (%).

TABLE 3 Path From Birth to 20 Y of the Re-enrolled Cohort ≤1800 g at Birth (264 Participants)

RCT Target Sample Re-enrolled for First Analysis and Neurologic Imaging	Total Cohort	KMC	Control
Original RCT ≤1800 g	433	229 (53)	204 (47)
Died during first year	21	7	14
Survivors at 1 y	412 (95)	222 (97)	190 (93)
Not located at 20 y of age	119 (29)	68 (31)	51 (27)
Located but not re-enrolled at 20 y of age	29 (7)	15 (7)	14 (7)
Died between 1 and 20 y	3	1	2
Refused to participate (6 twins in each group)	20	10	10
Out of scope	6	4	2
RCT re-enrolled cohort (≤1800 g) at 20 y of age	264 (64%)	139 (63%)	125 (66%)
Documented MRI in re-enrolled cohort	213 (80%)	115 (83%)	98 (78%)
Interpretable MRI (no brackets, no movement)	195 (74%)	108 (78%)	87 (70%)

Data are presented as *n* (%).

analyses were conducted to assess confounding and interaction and to compute adjusted unbiased estimates of effect for each outcome variable. Analyses were conducted by using SPSS version 19 (IBM SPSS Statistics, IBM Corporation) and R version 3.02 (R Foundation for Statistical Computing, Vienna, Austria).

For an integrated view of individual and grouped multiple outcomes, we developed software that allows visualization of neuroimaging results with outcome according to potential independent variables.[25]

RESULTS

Cumulative Mortality at 20 Years

Overall cumulative mortality after entry into the study was 24 (5.5%) of 433 (95% confidence interval [CI]: 3.4–7.7), with rates of 8 (3.5%) of 229 in the KMC group and 16 (7.7%) of 204 in the control group (odds ratio: 0.42 [95% CI: 0.18–1.02]; $P = .05$). After adjustment for weight and gestational age at birth, the protective effect of KMC against mortality was significant (odds ratio: 0.39 [95% CI: 0.16–0.94]; $P = .04$).

Overall IQ at 20 Years

No overall or specific differences in mean IQ scores were found between the KMC (87.5 ± 13.8) and control (88.4 ± 13.9) groups at 20 years. Measures at 6 months, 12 months, and 20 years, however, showed small but significant differences in the subgroup with transient neurologic examination results at 6 months' CA (used as a proxy for the fragility index in the original RCT), with higher scores for the KMC group (Table 6).

Table 7 displays the statistically significant links between modifications due to KMC in anthropometrics, maternal stress, and the Home Observation for Measurement of the Environment (HOME**)** test at 1 year CA and IQ at 20 years.

Overall Health Outcomes

The frequency of chronic conditions reported at interviews was similar in the 2 groups, except for hypothyroidism (6.5% in the KMC group, 0.8% in the control group)

TABLE 4 Comparison of the Re-enrolled Sample and the Overall Survivor Population (≤1800 g)

Variable	433 Survivors of the Original RCT		*P*	Re-enrolled Sample (264 Young Adults)		*P*
	KMC	Control		KMC (*n* = 139)	Control (*n* = 125)	
Multiple pregnancies, *n* (%)	45 (19.8)	28 (13.8)	.12	29 (20.9)	15 (12.1)	.06
Small for gestational age, *n* (%)	18 (7.9)	21 (10.3)	.40	11 (7.9)	7 (5.6)	.48
Gestational age at birth, median (min–max), wk	33 (26–40)	33 (26–40)	.47	34 (26–40)	34 (27–40)	.80
Gestational age at birth, *n* (%)			.68			.77
<32 wk	114 (49.8)	93 (45.6)		66 (47.5)	56 (44.8)	
33–34 wk	60 (26.2)	52 (25.5)		39 (28.1)	37 (29.6)	
35–36 wk	37 (16.2)	38 (18.6)		23 (16.5)	25 (20.0)	
>37 wk	18 (7.9)	21 (10.3)		11 (7.9)	7 (5.6)	
Female sex, *n* (%)	111 (48.5)	122 (59.8)	.02	72 (51.8)	76 (60.8)	.17
Days in neonatal care unit (including intensive care), median (min–max)	16 (1–64)	23 (1–68)	.00	15 (1–64)	23 (1–57)	.00
Admission to neonatal care unit (including intensive care), *n* (%)	179 (78.2)	140 (68.6)	.02	112 (80.6)	88 (70.4)	.06
Weight at eligibility, median (min–max), g	1590 (930–2000)	1575 (1090–2000)	.40	1575 (930–1980)	1550 (1100–2000)	.06
Age at eligibility, median (min–max), d	10 (1–60)	9 (1–55)	.59	9 (1–60)	10 (1–53)	.87
Days on minimal care after eligibility, median (min–max)	4 (1–31)	7 (1–47)	.00	4 (1–31)	7 (1–33)	.00
Weight at discharge, median (min–max), g	1580 (1025–2000)	1650 (1100–2550)	.00	1575 (1025–1900)	1650 (1100–2000)	.00
Fragility index	0.22 (–1.25 to 1.81)	0.18 (–1.25 to 1.55)	.37	0.30 (–0.88 to 1.55)	0.17 (–1.25 to 1.30)	.69

P, two-tailed χ^2 test. Min–max, minimum–maximum.

TABLE 5 Outcomes Variables, Measures, and Descriptors for the Re-enrolled Sample (≤1800 g)

Mortality and Morbidity at 20 Years	Reported by the Hospital or the family and From the National Civil Registry
General health at 20 y	Relevant medical history, diagnosed illnesses (including epilepsy, cancer, mental illness, chronic respiratory disease, and malnutrition), injuries, physical growth (height-for-age, weight-for-age, weight-for-height, and head circumference); BMI, lean body mass
Productivity, academic and labor data	Preschool and school history (years attended, school grades repeated, age at dropout, maximum level attained), school achievement and performance scores in Colombian national examination, labor force participation status, wages
Sensory motor status	Fine motor skills,[13] including visual motor integration[14]
Cognition	General intelligence (Wechsler abbreviated scale of intelligence),[15] memory (California verbal learning test),[16] attention (test of attentional performance)[17]
Social and emotional behavior	Behavioral and emotional problems (Conners,[18] ABCL[19]), index of parent and peer attachment,[20] self-esteem (Rosenberg test),[21] stress and mental state (life habits), depressive mood[22,23]
Family environment	HOME inventory[24]
Sensorial acuity	Visual acuity: full optometric examination Auditory acuity: tonal audiometry
Neurophysiology and imaging	Transcranial magnetic stimulation, MRI, functional MRI with 5 paradigms, diffusion tensor imaging only in the target group (<1800 g at birth) and in the reference cohort
Metabolic profile	Blood glucose, lipids profile, thyroid-stimulating hormone, insulin, carotid artery intima thickness (in a stratified subsample of participants)

(Table 8). Hypothyroidism was associated with birth via cesarean delivery ($P = .04$), admission to a NICU ($P = .03$), birth weight ≤1200 g ($P = .02$), and gestational age at birth ≤32 weeks ($P = .02$). Those with hypothyroidism tend to have a higher fragility index (0.82) than those without (0.17) ($P = .22$). Neurologic examinations identified cerebral palsy at the same rate in the 2 groups but with more motor functional deficit in the control group (38% vs 12% in the KMC group). Clinical diagnosis of short stature at 20 years was prevalent in both groups. Of participants with intrauterine growth restriction at birth (both preterm and term infants), 47% were short at 20 years, with no difference between groups.

Complete information on distant and near visual acuity was available for 259 participants: 137 of 139 in the KMC group and 122 of 125 in

TABLE 6 Repeated Measures of Developmental and Environmental Outcomes at 6 Months and 1 and 20 Years According to Neurologic Status at 6 Months in the Re-enrolled Sample (≤1800 g)

Measure	KMC		Control		*P*		
	Normal	Transient or Abnormal	Normal	Transient or Abnormal	KMC Versus Control	Neurologic Status	Interaction Between Neurologic Status and Groups
IQ at 6 mo	98.1 ± 10.0	90.0 ± 13.4	99.5 ± 9.2	84.5 ± 12.6	.23	.00	.03
IQ at 12 mo	103.4 ± 6.6	99.4 ± 8.8	103.0 ± 6.7	94.6 ± 10.2			
IQ at 20 y	87.2 ± 13.1	90.2 ± 14.9	89.9 ± 14.9	87.0 ± 12.7			
HOME at 12 mo	39.3 ± 6.8	39.9 ± 5.5	39.7 ± 7.5	35.5 ± 8.0	.11	.12	.02
HOME at 20 y	39.5 ± 7.3	40.5 ± 6.0	40.7 ± 6.6	36.6 ± 5.4			

Data are presented as mean ± SD.

TABLE 7 Outcomes of the Intervention Observed at 12 Months of Corrected Age on IQ at 20 Years of Age in the Re-enrolled Sample (≤1800 g)

Outcome at 1 y	IQ at 20 y		*P*
	IQ <90	IQ ≥90	
Factorial score[a] of weight during first year of CA	−0.16 ± 0.96	0.01 ± 0.89	.01
Factorial score[a] of height increase during first year of CA	−0.24 ± 0.95	0.07 ± 0.97	.01
Factorial score of head circumference during first year of CA	−0.12 ± 0.95	0.15 ± 0.98	.03
Head circumference at 1 y of CA per 50th percentile of expected head circumference for age and sex × 100	97 ± 3.13	98 ± 2.72	.01
Factorial score[a] of maternal feeling of stress			
At 41 wk	0.12 ± 0.93	−0.14 ± 1.15	.04
At 1 y of CA	−0.13 ± 0.90	0.28 ± 0.99	.00
HOME test at 1 y of CA			
All 5 subscales	37.5 ± 6.24	40.4 ± 5.32	.00
Family cognitive stimulation subscale	4.4 ± 2.34	5.6 ± 2.46	.00
Structured environment subscale	5.5 ± 1.49	5.8 ± 1.26	.02

Data are presented as mean ± SD.

[a] Factorial score of weight, height, and head circumference at 40 weeks' CA and 3, 6, 9, and 12 months' CA.

TABLE 8 Social and Chronic Health Conditions in 264 KMC and Control Re-enrolled Participants (≤1800 g)

Condition	KMC (n = 139)	Control (n = 125)	P
Living with parents	134 (96.4)	110 (88.0)	.01
Original family	97 (69.8)	84 (67.2)	.37
Victim of direct violence at school	36 (25.9)	44(35.2)	.07
Working	59 (42.8)	41 (32.8)	.06
In a relationship	61 (43.9)	54 (43.2)	.51
Repeated at least 1 y of school	59 (42.4)	47 (38.2)	.28
Asthma	15 (10.8)	11 (8.8)	.37
Epilepsy	6 (4.3)	5 (4.0)	.57
Frequent accidents (frequent falls)	27 (19.7)	23 (18.4)	.46
Endocrine system alteration	5 (3.6)	5 (4.0)	.56
Hypothyroidism	9 (6.5)	1 (0.8)	.01
Precocious puberty	2 (2.2)	0	.14
Short stature	42 (30.2)	36 (28.8)	.45
Learning disability	31 (23.0)	28 (22.4)	.55
Mental illness	22 (15.8)	18 (14.4)	.44
Physical therapy required	24(14.5)	14 (11.4)	.12
Language therapy required	20 (17.3)	27 (22.0)	.08
Altered neurologic examination	25 (18)	21 (16.8)	.46
Severity of neuromotor abnormality at 20 y			.04
With disability	3 (12)	8 (38.1)	
Without disability	22 (88)	13 (61.9)	

Data are presented as n (%).

TABLE 9 Academic Studies and Productivity of 264 KMC and Control Re-enrolled Participants ≤1800 g

Variable	KMC (n = 139)	Control (n = 125)	Difference	P
Years of preschool	2.52 ± 1.07	2.05 ± 1.04	0.47 ± 0.14	.00
School absenteeism	0.07 ± 0.26	0.17 ± 0.37	−0.09 ± 0.04	.01
Years of school	11.31 ± 1.34	11.50 ± 1.61	−0.19 ± 0.18	.15
School quality, mathematics score	48.22 ± 4.72	48.38 ± 4.26	−0.16 ± 0.65	.40
Standardized mathematics score	−0.17 ± 0.99	0.17 ± 1.02	−0.35 ± 0.14	.01
Standardized language score	−0.12 ± 0.89	0.13 ± 0.85	−0.26 ± 0.13	.02
Wage per hour	4.77 ± 6.65	3.13 ± 2.29	1.65 ± 0.78	.02

Data are presented as mean ± SD. School absenteeism is a dummy variable that takes value 1 if the individual has temporarily dropped out of primary or secondary school. School quality is the school average in the nationally standardized test score in mathematics. Wage per hour is given in thousand Colombian pesos; 1000 pesos is equivalent to US$ 0.40.

the control group. In optometrics, 13 (9.5%) of 137 participants in the KMC group and 6 (4.9%) of 122 in the control group had poor bilateral visual acuity (P = .12). Complete data from the auditory evaluation were available for 264 participants. Eight (4 in each group) patients had external hearing aids, and 1 (in the KMC group) had a cochlear implant; 9.8% of the cohort had a unilateral or bilateral hearing deficit (neurosensory or conductive lesion).

Schooling, Productivity, Academic Record, and Work History

The KMC group had more years of preschool (P = .00), but children had the same number of years of schooling and the same age at completion. Fewer members of the KMC group had been temporarily absent from school (P = .01), and they had higher average hourly wages (P = .01) (Table 9).

The control group had a significantly higher score on "language" in the Colombian national examination (P = .02), and they received more language therapy (21% vs 14.5% in the KMC group) during childhood than the KMC group. The mathematics scores differed significantly between the 2 groups (P = .01); they were lower in the KMC cohort, especially among boys born at ≤32 weeks' gestational age. Nevertheless, of the children who had severe bilateral neurosensory disorders who passed the national examination, 6 were in the KMC group (67%) and 3 in the control group (33%).

Family Environment and Social Behavior

More KMC children in the cohort lived with their parents (P = .01). We constructed a variable to evaluate paternal support that includes all aspects of the father's participation in the care of the infant during the first year of follow-up. This variable had a positive impact on the home environment at 1 year CA.[11] Paternal support in the re-enrolled sample was the same in the 2 groups, but the impact depended on whether the father had carried the infant in the kangaroo position during the neonatal period. Three of the HOME inventory subscales (family companionship, regulatory activity, and learning material at 20 years) were significantly higher in the group in which the

TABLE 10 Social Behavior Outcomes (ABCL and Conners Test) at 20 Years According to Parents (Sample, ≤1800 g)

Mother's Level of Education	KMC, Mean ± SD		Controls, Mean ± SD		*P*		
	Low	Higher	Low	Higher	KMC Versus Controls	Mother's Level of Education	Interaction Between Mother's Level of Education and Intervention
Conners hyperactivity	62 ± 10	65 ± 15	74 ± 14	60 ± 14	.15	.01	.00
Conners aggressivity	54 ± 12	54 ± 11	64 ± 15	53 ± 11	.03	.00	.00
ABCL DSM antisocial	69 ± 16	71 ± 14	78 ± 14	68 ± 16	.29	.09	.02
ABCL DSM internalization	72 ± 26	74 ± 24	82 ± 16	74 ± 22	.23	.42	.18
ABCL DSM externalization	63 ± 24	64 ± 22	79 ± 16	62 ± 23	.09	.03	.00

TABLE 11 Variables Associated With Left Caudate Nucleus Volume at 20 Years (Sample ≤1800 g)

Time	Variable	Slope	*P*
Before intervention	Fragility index	−0.29	.00
During intervention	Duration of kangaroo position	0.25	.00
At 20 y	9-hole peg test	−0.18	.01

Results of linear regression (r^2) = 0.16, F (3.17) = 12.21, P = .00, calculated with Braviz software.[25]

father had carried the infant in the kangaroo position, with a clear relation between paternal support at 1 year and the stability of the family 20 years later (score for paternal support in families without separated parents: 15.3 vs 14.6 for separated families, P = .01).

After control for the father's support, the mean total HOME score at 12 months' CA was 0.590 for the KMC group and −0.235 for the control group, indicating a clear advantage for children in KMC families. Moreover, the 12-month HOME score was clearly related to the score at 20 years (β = 0.302). Thus, independently of paternal support, the families of KMC children were more stimulating and protective at 12 months, up to 20 years. The scores at 12 months and 20 years of the subgroup with transient neurologic status at 6 months' CA were significantly higher in the KMC group (Table 6). We concluded that KMC families were more dedicated to their children and that the effect is permanent.

We could not directly link children's behavior to the family environment. However, the Conners' scores for aggressiveness and hyperactivity and for externalization in the Adult Behavior Checklist (ABCL) test were consistently lower in the KMC group, particularly for less well-educated mothers, and these children were perceived as having less antisocial behavior (Diagnostic and Statistical Manual of Mental Disorders [DSM]) than controls (Table 10).

Neuroimaging Results

KMC participants who weighed ≤1800 g (n = 264) at birth and had good-quality nuclear magnetic resonance (n = 195) had significantly larger cerebral volumes of total gray matter, cerebral cortex, and left caudate nucleus than control participants (Table 11). In a linear regression analysis, the volume of the left caudate nucleus was clearly related to the fragility index at birth (the lower the fragility index, the larger the volume), duration in the kangaroo position (the longer in the position, the larger the volume), and the result of the fine motor skills test (the better the performance, the larger the volume) at 20 years.

DISCUSSION

Numerous data were collected in this long-term follow-up study 20 years after the initial RCT, and only notable overall group differences are presented here; others will be explored later.

The KMC group had slightly less severe abnormal neurologic results than the control group, but we cannot separate the effects of stimulation by the family from a functional or anatomic effect of the intervention on the brain. The predictive role of head circumference at the end of the first year has been described elsewhere[26,27] and is reflected in Table 7, which also shows its association with IQ at 20 years.

Sensorial (visual and hearing) and motor (cerebral palsy) morbidity was comparable between the groups at 20 years, indicating that KMC did not protect children from these conditions, as expected. Our evaluation of audition and visual performance before application of the battery of neuropsychological tests showed that as much as 56% of the cohort needed glasses, and 6.9% had bilateral severe hearing loss. It is difficult to find normal values for these neurosensory sequelae, as they are described only for very LBWI in the literature. Severe neonatal jaundice, ototoxic drugs, neonatal hypoxia, and environmental noise in neonatal intensive care are all risk factors for neurosensory hearing loss in these children, who were hospitalized in a neonatal unit in a developing country in 1990. In both groups, the reduced visual acuity was mainly myopia and myopic astigmatism related to regressive and nonregressive retinopathy of prematurity and other factors.[28,29]

The differences in school achievement between KMC infants and control infants, for both mathematics and language, are difficult to explain. The academic difficulties of the KMC

children resemble those of premature cohorts described elsewhere.[30] Very LBWI (<1500 g) had more difficulty in mathematics, independently of their IQ; the lower scores in the KMC group were confined to the most immature children, who were more numerous in this group than in the control group. Lower IQ is regularly found in preterm infants, mainly in very preterm or LBWI.[31,32] A large meta-analysis indicated that the effect lasted up to 20 years.[3] Our study indicates, however, a smaller effect in the KMC group, particularly for those who were more fragile during the first year.

At 20 years, the young ex-KMC participants, especially in the poorest families, had less aggressive drive and were less impulsive and hyperactive. They exhibited less antisocial behavior, which might be associated with separation from the mother at birth.[33] KMC may change the behavior of less well-educated mothers by increasing their sensitivity to the needs of their children, thus making them equivalent to mothers in more favorable environments.

One of our hypotheses was that changes induced by the KMC intervention measured at 1 year are sustained by anatomic or functional changes in the immature brain during the neonatal period. Thus, KMC might allow better maturation of brain tissues and pathways. Studies of brain volume and development in preterm children have shown that premature transition from the intrauterine to the extrauterine environment can reduce the volume of selected cerebral regions, particularly motor regions such as the caudate nucleus.[34] The difference between groups in the volume of the left caudate nucleus is specific, because the periventricular location of this structure makes it sensitive to prematurity. Our KMC cohort of vulnerable survivors might have undergone compensation or plasticity, helping them to increase the volume of this brain structure.

Daily activities in the home environment have the most direct long-term influence on child development.[35] Family changes are an obvious effect of KMC, which appears to reduce contextual disparities and increases the chance that a child will be stimulated and exposed to a wide variety of experiences. KMC seems to motivate families to become more child-oriented. KMC mothers take their children to preschool earlier and provide support, as reflected in a lower rate of school dropout. Fathers' participation has long been recognized as highly positive in infants' social and cognitive growth.[36] KMC promotes paternal involvement in neonatal care, which affects not only the family structure but also the environment in which the child grows up. In this long-term study, fathers' involvement changed the young adults' cognitive capacity.

CONCLUSIONS

As neonatal technology becomes more accessible worldwide, more immature infants are saved, with fewer severe sequelae; therefore, the detection of "minor" sequelae becomes important. Such minor effects include mild cognitive deficits, lack of fine coordination, poor hearing, myopia, or attention deficit can affect the lives of families but often go undetected, especially in developing countries. Our long-term findings should support the decision to introduce KMC to reduce medical and psychological disorders attributable to prematurity and LBW. Bogotá's KMC program was first designed for use in stabilized infants, who usually remain in a neonatal minimal care unit. This period is key for brain maturation and early attachment relationship. We suggest that both biology and environment together might modulate a powerful developmental path for these children, impacting until adult age. Introduction of KMC immediately after neonatal intensive care, without other developmental programs, motivates families to become more child-oriented and shortens this suboptimal period. We hypothesize that the results would be even more significant if KMC was introduced as soon as the infant could tolerate it, even in ICUs.

This new knowledge must be used to extend KMC coverage to the 18 million preterm and LBWI born each year,[37] who are candidates for KMC. We firmly believe that this is a powerful, efficient, scientifically based health intervention that can be used in all settings.

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ABBREVIATIONS

ABCL: Adult Behavior Checklist
CA: corrected age
CI: confidence interval
DSM: Diagnostic and Statistical Manual of Mental Disorders
HOME: Home Observation for Measurement of the Environment
KMC: kangaroo mother care
LBWI: low birth weight infant
RCT: randomized controlled trial

and revising the manuscript, contributed as a content expert, and was in charge of literature review and state of the art; Dr Nadeau (Co-principal Investigator) oversaw specific data collection and analysis, revision of the manuscript, and contributed as a specific content expert; Dr Mercier (Co-principal Investigator) oversaw specific TMS data collection, data cleaning and analysis, revision of the manuscript, and contributed as a specific content expert; Dr Maheu (Co-principal Investigator) oversaw specific neuroimaging data collection (functional MRI), data cleaning and analysis, revision of the manuscript, and contributed as a specific content expert; Dr Marin (Co-principal Investigator) oversaw specific neuroimage data cleaning and analysis (MRI and diffusion tensor imaging), revision of the manuscript, and contributed as a specific content expert; and Drs Cortes, Gallego, and Maldonado (Co-principal Investigators) were responsible for generating a specific research protocol in reference to the social economics aspects of the paper, oversaw specific data collection and analysis, were responsible for writing and revising the manuscript, and contributed as content experts; and all authors approved the final manuscript.

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Address correspondence to Nathalie Charpak, MD, Fundación Canguro, Calle 44b No. 53-50. Bogotá, Colombia. E-mail: ncharpak@gmail.com

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