Supplemental Table 1 – Summary of the Studies That Evaluated Biomarkers in Infants

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| Author, Year, Country, Purpose and Study Design | Sample Characteristics | Study Procedures and Measures | Main Findings | Strengths and Limitations |
| Castral et al. 2015  Country: Brazil  Purpose: Examine the concordance of SC reactivity between mothers and their stable preterm infants during routine infant HL while in mother kangaroo care (MKC) and to compare SC between groups of mothers with and without PPDA and their infants during HL  Design: comparative prospective design | Sample size - n = 42  Gestational age at birth =  32.5 + 1.8 weeks  % Female = 28.6%  Ethnicity -Portuguese- 100%  Birth weight (g) = 1,795.6 ± 618.4  SNAPPE II score = NR  Apgar score (5/mins) = 9.5 ± 0.7  % Cesarean = 69.0% | Procedure – Infants typically had a HL on days 5 and 30 of post-natal life for neonatal screening. Infants SC was collected prior to and 20 minutes after HL.  MKC duration = 30 mins  Number of MKC sessions = 2  Pre-MKC – SC was collected with infant was lying prone in the incubator.  Saliva was stimulated with 3 drops of 5% citric acid and 0.5 mL of saliva was collected by aspirating saliva from the floor of the mouth using a plastic tube attached to a syringe.  Following a standardized protocol, 10 minutes after SC collection, infants were positioned for MKC for a total of 30 mins (10 minutes before HL, during the HL procedure, and 10 mins after HL).  Trained NICU nurse performed the HL. Infant transferred back to the incubator for 10 mins without manipulation  Post MKC – SC was collected 20 mins after the HL | No differences were found in SC levels between the pre and post HL measures (p *=* 0.73)  No differences were found in SC levels between the pre and post HL measures between infants of mothers with and without PPDA (p *=* 0.55) | Strengths   * Independent and concurrent evaluation of the effects of MKC on both mothers and infants SC during routine infant HL   Limitations   * Small sample size * Lacked a control group of infants without MKC * Convenience sample |
| El-Farrash et al. 2019  Country: Egypt  Purpose: Investigate the effect of KC and its duration on neurobehavioral performance, stress response, breastfeeding success, and vitals signs in premature infants  Design: Prospective double-blinded randomized controlled trial | Sample size n = 120  Gestational age at birth  KC 60 min = 32.5 (+1.0)  KC 120 min = 32.5 (+1.4)  Control = 32.4 (+1.0)  % Female  KC 60 min = 55%  KC 120 min = 40%  Control = 50%  Ethnicity- Egyptian  Birth weight (g)  KC 60 min = 1700.3 (+65.0)  KC 120 min = 1686.5 (+85.0)  Control = 1663.4 (+85.0)  SNAPPE II score = NR  Apgar score (5/mins) = median  KC 60 min = 9 (7-9)  KC 120 min = 9 (8-9)  Control = 9 (8-9)  % Cesarean  KC 60 min = 62.5%  KC 120 min = 70.0%  Control = 60.0% | Procedure – randomized using a computer based randomization program into 3 groups: KC for 60 mins per day (n=40); KC for 120 mins per day (n=40), or control group who received conventional neonatal care (n=40)  Procedures:  KC - infants were placed upright in a prone position with their arms and legs flexed directly on the mothers bare chest  Control – parents could visit their babies and breast feed. No direct SSC.  SCC duration – 0, 60, or 120 minutes depending in group assignment  Number of SSC sessions = once a day for at least 7 consecutive days  Measures:  SC was collected using a sterile pipette placed under the infant’s tongue and close to the cheek  SC pre and post first KC session and at 7 days | No significant differences were found between the groups in terms of maternal characteristics, neonatal demographic characteristics, or anthropometric measures (all, p > 0.05)  No significant differences in SC levels were found among the three groups at baseline.  After the first KC session, SC decreased significantly in the KC groups compared to baseline levels (p < 0.05) with no significant differences between to two KC groups.  On day 7, SC levels decreased significantly in all three groups. However, a greater decrease was found in both KC care groups compared to controls (p < 0.001). No significant difference in SC levels was found between the two KC groups (p = 0.0793) | Strengths   * Three group RCT * Double-blind study * Evaluated a dose response effect for KC * Longitudinal study over 7 days * Saliva samples collected at 9AM at least 30 minutes from the time of oral feeding   Limitations  No long term monitoring of growth, neurodevelopment outcomes over a long period of follow-up |
| Feldman et al. 2013  Country: Israel  Multi site: Two different medical centers with Level 3 NICU  Purpose:  1) Determine whether preterm infants receiving KC would show more optimal physiologic functioning in contact -sensitive systems including autonomic functioning, sleep organization, and HPA activity;  2) Determine whether mother child relationships would be more optimal following KC;  3) Determine whether children who received KC would show improved cognitive skills across childhood, particularly EF that require cognitive flexibility and mental shifting; and  4) Determine whether individual stability will be observed in each domain over time  Design: Randomized controlled trial | Sample size - n = 146  Groups:  KC - n = 73  StC - n = 73  Gestational age at birth  KC = 30.38 + 2.50 weeks  StC – 30.82 + 2.98 weeks  % Female  KC = NR  StC = NR  Ethnicity –  KC = Israeli  StC = Israeli  Race  KC = Jewish  StC = Jewish  Birth weight (g) =  KC = 1245.85 + 328.21  StC = 1213.2 + 358.08  SNAPPE II score = NR  Apgar score (5/mins) =  KC = 8.67 + 1.03  StC =8.50 + 1.14  % Cesarean = NR | Procedure – Infants and mothers were recruited from two hospitals and randomly assigned to one of 2 groups with case-match controls: KC or StC for 14 consecutive days  Infants assigned to the KC group were held skin-to skin on the mother’s chest for a minimum of 1 hour per day for 14 consecutive days  Infants assigned to the StC group remained in the incubator and all their care was given in the incubator.  Infants and families were followed and seen 7 times across the first decade of life: at discharge and again at 3, 6, 12, and 24 months, and at 5 and 10 years of age (age corrected).  SC: Saliva samples were collected at age 10. Samples were collected after arrival at the lab (baseline); 15 minutes after the TSST-C (reactivity), and 15 minutes after the second assessment (recovery).  Saliva was collected by salivette and was assayed using a commercial enzyme-linked immunosorbent assay kit. | KC – stress reactivity (nmol/mL)  Baseline SC = 6.77 + 1.30  Reactivity SC = 6.96 + 1.20  Recovery SC = 6.68 + 1.65  StC – stress reactivity (nmol/mL) Baseline SC = 6.96 + 0.98  Reactivity SC = 7.75 + 2.16  Recovery SC = 7.27 + 1.68  At 10 years of age, premature infants who received KC as neonates showed an attenuated stress response. | Strengths   * Randomized controlled trial * Parents blinded to group assignment * Multiple measures of stress including SC   Limitations  SC were only taken at the 10 year assessment. No data are available on the acute effects of KC on SC |
| Forde et al. 2020  Country: USA  Purpose: Evaluate the effects of KMC on physiologic markers of energy conservation (i.e., Hx, Xa, UA) and oxidative stress (i.e., allantoin)  Design: Randomized controlled trial | Sample size - n = 51  Gestational age  KC = 31.8 (+2.5)  Control = 31.4 (+2.1)  % Female  KC = 61.5%  Control = 36.0%  Ethnicity  KC group  White non-Hispanic = 57.7%  Black non-Hispanic = 23.1%  Hispanic/Mexican = 19.2%  Other = 0.0%  Control group  White non-Hispanic = 20.0%  Black non-Hispanic = 36.0%  Hispanic/Mexican = 32.0%  Other = 12.0%  Birth weight (g)  KC = 1827.0 (+492.0)  Control = 1642.0 (+545.0)  SNAPPE II score  KC = 0.0 (0-49)  Control = 0.0 (0-49)  Apgar score (5/mins)  KC = 8.2 (+1.0)  Control = 7.8 (+1.4)  % Cesarean  KC = 56.0%  Control = 69.5% | Procedure – Infants were randomized to an intervention group (i.e., SSC on day 3 and day 4 of life) or a control group (i.e., incubator care on day 3 and SSC on day 4 of life)  SSC – not described  SCC duration = 60 min  Number of SSC sessions:  Intervention group - 2 sessions  Control group - 1 session  Measures:  Urinary collection of Hx, Xa, UA, and allantoin 3 hours before and up to 3 hours after SSC | Mean urinary allantoin levels were significantly lower in the intervention compared to the control group (p = 0.026)  Median levels in Hx, Xa, and UA did not differe between between the two groups  Xa levels increased modestly over time (p = 0.042)  UA levels decreased over time (p= 0.025) | Strengths:   * Randomized clinical trial * Use of urinary biomarkers * Evaluation of biomarkers for both energy conservation and oxidative stress   Limitations:   * Pilot study * Relatively small sample size * Higher percentage of Whites in the intervention group   Range of gestational ages was wide |
| Janevski et al. 2016  Country: Serbia  Purpose: Measure SC in mothers and newborns before and after SSC in order to assess the effect of SSC on mothers’ and infants’ stress and to estimate the efficacy of collecting saliva samples in newborns  Design: Prospective, descriptive study | Sample size – n = 35  Gestational age – 31 weeks (median; range = 25-37 weeks)  % Female = 57.1%  Ethnicity – Serbian = 100%  Birth weight (g) = 1545 (median; range = 745-2450)  SNAPPE II score = NR  Apgar (5/min) = 8 (median; range = 6-9)  % Cesarean = NR | Procedures – SSC was initiated once the infant was stable. SSC was performed daily for 5 consecutive days, for 2 hours between 10AM and 12 noon.  SSC – not describe  SCC duration – 2 hours  Number of SSC sessions - 5  Measures  SC was measured using an eye sponge without any stimulation  SC was collected prior to and following SSC at enrollment and before and after the first and fifth SSC sessions | During the first SSC, SC levels decreased in 40% of the infants and increased in 60% of the infants (*p* = 0.831)  During the fifth SSC, SC decreased in 45.7% of the infants and increased in 54.3% of the infants(*p* = 0.961) | Strengths   * Controlled the time for sample collection * Demonstrated the feasibility of collecting SC samples in infants using an eye sponge under the tongue   Limitations   * Range of gestational ages was wide   Small sample size |
| Kommers et al. 2017  Country: The Netherlands  Purpose:  Assess the feasibility and obtrusiveness of measuring salivary OT in preterm infants receiving KC.  Analyze possible influential determinants that influence OT responses  Design: A pilot study | Sample size – n = 21  Gestational age – 31 + 3 weeks  % Female = NR  Ethnicity – Dutch – 100%  Birth weight (g) = 1705 + 449  SNAPPE II score = NR  Apgar score (5/mins) = NR  % Cesarean = NR | Procedure – Salivary OT samples were collected on a decided day before and during KC.  Baseline condition – infants lying in bed or incubator in the absence of parental touch before the mother arrived  KC care – described as routine KC for at least 30 minutes  KC duration = 30 minutes  Number of KC sessions = 1  Measures: Salivary OT was collected using cotton swabs | OT concentration increased during KC  Mean overall OT level was 4.79 + 0.86 pg/mL.  Before KC - mean OT level was = 4.34 pg/mL  During KC - mean OT level was 5.24 pg/mL  Mean difference in OT levels was 0.9 + 1.38 pg/mL (p=0.38) | Strengths   * Controlled the time for sample collection   Limitations   * Small sample size * Pooling saliva may introduce bias or an overestimated effect |
| Kommers et al. 2018  Country: The Netherlands  Purpose: Investigate whether KC influences salivary OT concentration in preterm infants and which correlates affect OT response  Design: An interim analysis of a feasibility study | Sample size – n = 22, 11 sets of twins  Gestational age – 226.9 + 19.6 weeks  % Female = 45.5%  Ethnicity – Dutch – 100%  Birth weight (g) = 2123.2 + 269.3  SNAPPE II score = NR  Apgar score (5/mins) = NR  % Cesarean = NR | Procedure – Samples were collected twice a day for five consecutive days  Baseline condition – infants lying in bed or incubator in the absence of parental touch  KC care – described as routine KC for at least 30 minutes  SCC duration = 30 minutes  Number of SCC sessions = 5  Measures: Salivary OT was collected using cotton swabs  Infant state of comfort and parent infant interaction were assessed using an investigator developed Likert scale prior to and during KC | OT concentration decreased during KC (p = 0.03)  State of comfort increased during KC (p = .01)  Changes in parent-infant interaction scores were not significant | Strengths   * Controlled the time for sample collection   Limitations   * Lack of specific description of KC * No description of who performed KC * Small sample size * Pooling saliva may introduce bias or an overestimated effect |
| Mehler et al. 2019  Country: Germany  Purpose: Investigate the effects of 60 mins delivery room skin-to-skin contact (DR-SSC) compared with 5 mins of visual contact (VC) on mother-child interaction, salivary cortisol (SC), maternal depression, stress, and bonding at 6 months corrected age  Design: Single-center randomized controlled trial | Sample size - n = 88  Gestational age at birth  DR-SSC = 29 (+2)  VC = 29 (+2)  % Female  DR-SSC = 52%  VC = 37%  Ethnicity - German  DR-SSC = 100%  VC = 100%  Birth weight (g)  DR-SSC = 1250 (+510)  VC = 1170 (+380)  SNAPPE II score = NR  Apgar score (5/mins) =  DR-SSC = 8  VC = 8  % Cesarean =  DR-SSC = 77%  VC = 77% | Procedure - Randomization was performed 45 mins after birth to either 60 mins of SSC (n=44) or 5 mins of VC (n=43)  Procedures:  SCC – DR-SSC started approximately 45 mins after birth and was performed for 60 minutes continuously. Infants were placed naked on their mother’s cheds in comfort position amd covered with a transparent polyethylene wrap and a blanket.  VC infants visited their mothers for 5 mins after initial stabilization. Mothers were allowed to touch but not kiss their infant’s face and were not allowed to unwarp their infants.  SCC duration = 60 minutes for DR-SSC group or 5 mins for VC group  Number of SSC sessions = 1  Infant measures:  SC was a secondary outcome that was collected at 36 to 40 weeks post-gestational age before and 20 minutes after a heel lance. | No differences in baseline SC levels between VC (0.8 (±0.9) µg/dL) and DR-SSC (0.5 (±0.5) µg/dL) groups (p=.197).  A diminished relative increase in SC after the heel lance was observed in VC infants compared with DR-SSC infants (i.e., 52% vs 76%), but the difference was not statistically significant (p = 0.71). | Strengths   * Randomized trial, prospective study * Long-term evaluation of SC following very brief SSC   Limitations   * No immediate evaluation of the effects of SSC on SC levels * Relatively small sample size |
| Miles et al. 2006  Country: United Kingdom  Two tertiary NICUs  Purpose: Address the hypothesis that mother-infant STS contact improves pre-term infant behavioural and developmental outcomes  Explore mediating pathways, namely maternal psychological state, lactation, and infant endogenous cortisol production.  Design: Pragmatic randomized controlled trial | Sample size - n = 78  StC – n = 32  STS – n = 46  Gestational age at birth  StC = 28.0 (+2.3)  STS = 28.0 (+2.1)  % Female  StC = 34.4%  STS = 41.3%  Ethnicity - British  StC = 100%  STS = 100%  Birth weight (g)  StC = 1133 (+367)  STS = 1086 (+402)  SNAPPE II score = NR  Apgar score (5/mins) = NR  % Cesarean = NR | Procedure - Mothers were approached soon after delivery. Infants were eligible if <32 weeks gestation and <7 days of age.  The two NICUs were randomly assigned to STS or StC and continued the specific intervention to mothers who enrolled for 4 months. A wash out period occurred until all of the infants who received the previous condition were discharged from the unit.  STS group: Mothers were seated on a chair at a 60o angle, wearing an open front blouse, and no perfume. The infant was placed naked except for a nappy and woolen hat, directly on the mother’s chest between the mother’s breasts and covered with a light blanket.  Intention was to perform STS for 20 minutes per day for 4 weeks.  StC group – same level of support as STS group  Plasma cortisol levels were measured from 0.5 ml of blood obtained once a week during the first four weeks after birth  Then, at 4 months and 1 year SC specimens were collected following a single IM immunization injection. Saliva samples were collected by allowing the infant to suck on a cotton dental roll.  At 4 months, SC samples were collected 12 PM and 4 PM.  At 12 months, SC samples were collected at 10 AM and 12 PM. | Duration of STS was highly variable (mean = 507 mins, SD = 414 mins)  No differences were found in plasma cortisol or SC between the two groups at any time point.  STS group – plasma cortisol and SC (nmol/L)  1-4 wks - 333 ± 128  4 mos - 3.25 ± 6.36  12 mos - -0.28 ± 5.78  StC group – plasma cortisol and SC (nmol/L)  1-4 wks - 418 ± 379  4 mos - 5.22 ± 7.48  12 mos - -0.03 ± 5.43 | Strengths   * Pragmatic, randomized trial * Long-term evaluation of cortisol following a brief duration STS over 4 weeks * Sampling times that controlled for diurnal variations in cortisol   Limitations   * No immediate evaluation of the effects of STS on cortisol * Wide variation in the amount of STS given to the infants   Relatively small sample size |
| Mirnia et al. 2017  Country: Iran  Purpose: Investigate the effect of SSC by fathers on SC of the infant.  Design: Randomized clinical trial | Infants  SSC - n = 23  StC – n = 22  Gestational age at birth  SSC - 32.00 ± 2.73  StC- 31.35 ± 2.31  % Female =  SSC = 30.4%  StC = 31.8%  Ethnicity  Iranians = 100%  Birth weight (g) - NR  Weight at the time of study (g)  SSC = 1906.96 ± 465.57  StC = 1788.26 ± 407.75  SNAPPE II score – NR  Apgar score (5min)  SSC = 8.39 ± 1.08  StC = 8.61 ± 0.99  Mode of delivery  SSC = 72.7% Cesarean  StC = 73.9% Cesarean | SSC group – infants were placed in fetal position or flexion on father’s chest while wearing only a diaper and hat. Infants were then covered with a thin blanket.  SSC lasted for 45mins  StC group – interventions and routine care were performed with the fathers watching the infants.  In both groups, saliva samples were collected to measure SC between 3 PM and 6 PM.  Samples were collected between two feedings. Infants’ mouths were rinsed with distilled water.  SSC group – samples were collected at 5 mins before SSC, 45 mins after the start of SSC, and 15 mins after the completion of SCC  StC group – samples were collected at the beginning of the father’s visit, 45 mins after the start of the visit, and 60 mins after the onset of the visit. | Changes in SC levels – While both groups had decreases in SC levels over time, no significant between group differences were found.  Using independent sample t-tests that compared SC levels of the two groups at each time point showed no statistically significant between group differences.  SC levels in SSC group:  Before: 83.48 ± 81.33  During: 65.65 ± 72.91  After: 59.56 ± 59.2  SC levels in StC group  Before: 70.91 ± 62.33  During: 69.09 ± 69.27  After: 66.36 ± 71.22 | Strengths   * Evaluation of effects of fathers use of SSC on infant stress responses * Repeated measures of SC * Comparison with a STC group   Limitations   * Small sample size   Only one session of SSC |
| Mitchel et al. 2013  Country: United States  Purpose:  1. Determine whether stress in preterm infants, measured with SC, decreases after five days of KC compared to five days of StC  2. Determine whether KC provides sustainable pain relief beyond the period of skin to skin holding.  Design: Randomized controlled trial | Sample size - n = 38  Groups:  KC - n = 19  StC - n = 19  Gestational age at birth  KC = 29 weeks  StC – 28.5 weeks  % Female  KC = 57.8%  StC = 42.1%  Ethnicity –  KC = Non-Hispanic = 89.5% Hispanic = 10.5%  StC = Non-Hispanic = 100.0%; Hispanic = 0.0%  Race  KC = Caucasian = 89.5%; African American = 10.5%  StC = Caucasian = 84.2%; African American = 15.8%  Birth weight (g) =  KC = 1311.5 + 216.3  StC = 1213.2 + 186.4  SNAPPE II score = NR  Apgar score (5/mins) = NR  % Cesarean = NR | Procedure – Infants and mothers were randomly assigned to either KC or StC for 5 consecutive days from DOL 5 to DOL 9  KC group - Infants were held skin-to skin on the mother’s/father’s chest for a minimum of 2 hours per day from DOL 5 to DOL 9.  StC group - Infants remained in the incubator but at the parents’ request could be held 15 minutes per day  SC: Saliva samples were collected on days 5 and 10 using an eye sponge. The sponge was held alongside the buccal mucosa or under the tongue for 20-25 minutes until it was moist and evenly puffed up.  Samples were collected at 09:00 on days 5 and 10 | No significant between group differences in SC levels (p = .49)  SC levels decreased over time in both groups (p = 0.02) | Strengths   * Randomized controlled trial * Parents blinded to group * Samples were collected at the same time each day * Repeated measures of SC across time   Limitations   * Small sample size * SC samples had inadequate volumes at the beginning of the study * StC infants were allowed to receive 15 mins of KC per day   Relatively short duration of KC |
| Morelius et al. 2005  Country: Sweden  Purpose: Primary aim was to investigate how SSC influences indicators of stress in the mother and her infant as measured by SC and mood changes. Secondary aim was to investigate whether there is a difference in the stress response between the 1st and 4th SSC, sessions.  Design: Baseline response-paired design | Sample size n = 17  First SSC n =17  Fourth SSC n = 14  Gestational age at birth (median, range)  First SSC = 27 range (25-33)  Fourth SSC = 27 range (25-33)  % Female  First SSC – 41.2%  Fourth SSC – 35.7%  Ethnicity – Swedish – 100%  Birth weight (g; median, range) =  First SSC – 935 range (495-2590)  Fourth SSC - 870 range (495-2590)  SNAPPE II score = NR  Apgar score (5/mins, median, range) =  First SSC – 7 range (3-10)  Fourth SSC - & range (3-10)  % Cesarean =  First SSC = 88.2%  Fourth SSC = 85.7% | Procedure – Prior to being removed from the incubator, 30 minutes after beginning, and 30 minutes after completing the 60 minute SSC session, the infant’s saliva samples were collected during the 1st and 4th SSC sessions.  Infant was gently removed from the incubator and placed on the mother’s chest in the upright position. Infant was wearing only a hat and a diaper and was placed inside the mother’s gown and covered with extra blankets.  SSC duration = 1 hour  Number of SSC sessions = 2  SC was collected using cotton tip applicators | First SSC – 38% of infants had a decrease in SC, 38% had an increase, and 23% had no change. The changes in SC during the first SSC were not significantly different.  Fourth SSC – 36% of infants had a decrease in SC and 64% had an increase in SC.  SC was 60% higher pre-SSC (p = .007) at the 1st SSC compared to the 4th SSC.  SC was 47% higher post-SSC (p = .03) at the 1st SSC compared to the 4th SSC. | Strengths   * Stress response assessed using SC, changes in heart rate, and pain * Longitudinal study design * Changes in SC were assessed in both mothers and infants * Food intake was controlled for prior to specimen collection   Limitations   * Small sample size   Missing data associated with insufficient amount of saliva |
| Morelius et al. 2014  Country: Sweden  Multisite:  2 different NICUs  Level-III  Level-II  Purpose: Evaluate the effects of almost continuous skin-to-skin contact (SSC) after preterm birth on SC, parental stress, parental depression, and breast feeding  Design: Randomized controlled trial | Sample size n = 42  SSC n = 18  StC n = 19  Gestational age (PMA)  SSC - 34 weeks  StC - 34 weeks  % Female  SSC – 38.8%  StC – 68.4%  Ethnicity – Swedish – 100%  Birth weight (g) =  SSC - 2468 + 285  StC - 2512 + 274  SNAPPE II score = NR  Apgar score (5/mins) = NR  % Cesarean = NR | Procedure – Families were randomized to SSC or StC  SSC group - Infant was placed in an upright position on the parent’s chest immediately after birth. Almost continuous beginning in the delivery room and continuing for almost 24 hours per day. Parents alternated until the infant’s discharge.  StC group - both parents had the opportunity to provide SSC if they wanted to do so.  SC samples were collected prior to (baseline) and 30 mins (response) after a videotaped diaper change performed by the mother in a home visit when the infant was one month corrected age.  SC samples were collected prior to (baseline) and 30 mins (response) after a videotaped face-to-face session between mother and infant (i.e., 2 mins interaction, 2 mins still-face, and 2 mins interaction) during a home visit when the infant was 4 month corrected age. | No significant differences in baseline levels of SC between the SSC and StC groups at any time point.  Median baseline SC level in the StC group was significantly higher at 4 months compared to 1 month (p= 0.04)  SC reactivity was smaller for infants in the SSC group compared to infants in the StC group at one month (p = 0.01), but not at 4 months (p = 0.45)  Significant positive correlation between mothers’ and infants’ raw baseline SC levels at 4 months corrected age in the SSC group (ρ = 0.65, p = 0.005) but not in the StC group (ρ = 0.14, p = 0.63) | Strengths   * First study to report SC in infants who experienced an average of 19 hours per day of SSC * Controlled the time of sample collection   Limitations   * Small sample size * No saliva collected from fathers   StC group had an average of 7 hours of SSC |
| Neu et al. 2014  Country: United States  Multisite: 5 NICUs  Purpose: Determine whether kangaroo holding of healthy preterm infants over the first eight weeks of an infant’s life facilitates co-regulation of SC between mother and infant.  Design: Randomized controlled trial | Sample size - n = 79  Groups:  Kangaroo holding - n = 29  Blanket holding - n = 26  Control - n = 24  Gestational age at birth = NR  Inclusion criteria stated 32 to 35 weeks  % Female = NR  Ethnicity - NR  Birth weight (g) = NR  SNAPPE II score = NR  Apgar score (5/mins) = NR  % Cesarean = NR | Procedure – Infants and mothers were randomly assigned to one of 3 groups:  kangaroo holding, blanket holding, or control  Kangaroo and blanket holding groups - mothers were encouraged to hold their infants at least one consecutive hour each day for 8 weeks.  Kangaroo holding - mothers held their infants in SSC between their breasts with their blouse or gown or a blanket covering the infants’ backs and a cap or blanket covering their heads.  Blanket holding – mothers wrapped their dressed infants in a blanket  Kangaroo and blanket holding groups – a study nurse visited these mothers weekly for 8 weeks. During visits mothers were encouraged to hold their infants in the assigned manner. Mothers were educated about early child development and infant cues. Nurse visits lasted ~60 mins.  Control group – mothers were given no instructions or restrictions regarding holding time or style. Nurse visits to this group were for 10 to 20 minutes weekly for 8 weeks to collect holding diaries. In addition, general experiences with their infants were discussed.  At each visit, SC were collected at the time the mother picked up her infant, 30 mins after holding began; and 60 mins after holding began.  SC was collected using filter paper. The filter paper was placed on the infant’s tongue and angled toward the cheek for 30 seconds to 2 mins until ~1 inch of the filter paper was completely wet. | SC levels decreased over the course of each holding session (*b* = -.005, p<.01).  Rate of decline in SC levels did not vary over the 8 weeks (*b* <.001, p=.18).  No significant mother-infant cortisol co-regulation occurred in any group at any holding session or over time. | Strengths   * Randomized controlled trial * Multisite study * Repeated measures of SC within and across time * 8-week longitudinal study with serial measures * Concurrent evaluation of the effects of two holding methods compared to a control group on mother-infant cortisol co-regulation   Limitations   * Small sample size * Sample characteristics were not reported * Inadequate stressor to test HPA function * Waiting 20 minutes after 60 mins of holding may have yielded significant differences in the groups   Only one physiologic measure of stress |
| Srinath et al. 2016  Country: Canada  Purpose: Compare physiological and biochemical responses in stable preterm neonates and their parents following kangaroo mother care (KMC) and kangaroo father care (KFC)  Design: Prospective randomized cross-over design | Sample size - n = 26  Gestational age at birth  28 weeks (±2)  % Female – 46%  Ethnicity - Canadian  Birth weight (g) = 1096 (± 217)  SNAPPE II score = NR  Apgar score (5/mins) = NR  % Cesarean – 65.4% | Procedures – KC was provided by the mother or father of the infant in a random order based on availability.  KC - infants were held naked with only diapers and hats in a chest to chest position, placed upright in a prone position with their arms and legs flexed directly on the mothers bare chest with their head directed sideways.  SCC duration – 60 minutes  Number of SSC sessions = 2  Measures:  SC was collected using oral swabs placed under the infant’s tongue and close to the cheek  SC pre and post first KC session and the next session within the next 3 days.  Temperature, heart rate, blood pressure and oxygen saturation were recorded pre and post KC. | No statistically significant difference was found between the pre-post KC changes in SC levels .(p = 0.19) | Strengths   * Prospective comparative study with same infant acting as his or her own control * Evaluated a dose response effect for KC in infants from both mothers and fathers * Longitudinal study 3-4 days * Controlled for variations in SC by asking mothers and fathers not to smoke, exercise, or drink anything besides water for 45 minutes before and during KC   Limitations   * Mothers had experiences one to two sessions of KC   Very small sample size |
| Vittner et al. 2018  Country: United States  Purpose: Examine changes that occur in infant and parent salivary oxytocin (OT) and salivary cortisol (SC) levels during skin to skin contact (SSC) and whether SSC alleviates parental stress and anxiety while supporting mother-father-infant relationships  Design: Randomized cross over design | Sample size - n = 28  Gestational age at birth =  33.0 + 1.6 weeks  % Female = 32%  Ethnicity  Asian – 7%  Black – 14%  Hispanic – 18%  White – 61%  Birth weight (g) = 1,882.0 ± 416.7  SNAPPE II score = 3.9 ± 7.8  Apgar score (5/mins) = 8.3 ± 1.3  % Cesarean = 61% | Procedure - Triads assigned to one of two sequences: Maternal-SSC (M-SSC) on Day 1 and paternal SSC (P-SSC) on Day 2 or P-SSC on Day 1 and M-SSC on Day 2  SCC duration = 60 mins  Number of SCC sessions = 2  Pre-SSC (15 min) collected parental OT/SC saliva  During-SSC (60 min) saliva samples collected during the last 10 minutes  Post SSC (45 min) Infant returned to incubator and left undisturbed for 45 minutes then parents’ saliva was collected  Infant measures: Salivary OT and SC collected using infant swab method | OT levels:  During M-SSC, infants’ OT levels increased from pre-SSC to during SSC and decreased post-SSC. (*p <* 0.001)  During P-SSC, infants’ OT levels increased from pre-SSC to during SSC and decreased post SSC. (*p <* 0.001)  SC levels:  During M-SSC, infants’ SC levels decreased from pre-SSC to during SSC and increased post SSC (*p <* 0.001)  During P-SSC, infants’ SC levels decreased from pre-SSC to during SSC and increased post SSC (*p <* 0.001) | Strengths   * Established a consistent sampling time (1 to 3PM), approximately 1 hour after infant’s feeding to account for diurnal variations in biomarkers * Evaluation of the effects of SCC both mothers’ and fathers levels of OT and SC   Limitations   * Small sample size * Primarily White and well educated parents * Cross over design   Convenience sample |
| Weber et al. 2018  Country: USA  3 different NICUs  Purpose: Determine whether factors related human milk, touch or stressor exposure are related to plasma OT trajectories in premature infants  Design: Prospective longitudinal design | Sample size - n = 33  Gestational age at birth (mean) = 27.32 ± 1.14 weeks  % Female = 45%  Race –  White = 76%  Ethnicity – English speaking mothers  Birth weight (g) mean = 1,013 ± 255.00  SNAPPE II score = NR  Apgar score (5/mins) = NR  % Cesarean = NR | Procedure  Plasma collection started on day 14 of life and continued weekly until the infant achieved 34 weeks corrected gestational age  Plasma collections occurred between 23:00 and 02:00 to control for diurnal variations in OT. All samples were collected before feeding.  Number of SSC sessions = Total hours the infant was positioned in SSC and total hours the infant was held in swaddled position were measured during the 8 hours prior to plasma collection.  Plasma for OT was collected by HL or central line (i.e., 0.3ml of blood), immediately placed on ice, and transported to the laboratory for centrifugation within 1 hour of collection. Supernatants were stored at -80°C until assayed | Average number hours in SSC or swaddled holding during 8 hours prior to plasma collection was less than 1 hour. Average number of hours per week of SSC was 7.59 ± 5.25 and of swaddled holding was 6.91± 6.48  Plasma OT = In the final regression model, SSC was positively associated with plasma OT levels at 27 weeks corrected gestational age (p=.002) and with a decline in plasma OT levels over time (p = .001). | Strengths   * Evaluation of OT levels over 34 weeks * Controlled for the effect of feeding on OT levels   Limitations   * Small sample size * Lacked of a control group   Did not measure plasma OT reactivity in direct response to SSC or stressor exposure |

Abbreviations: C: centigrade, CI: confidence interval, dl: deciliter, DOL: day of life, DR-SSC: delivery room skin-to-skin contact, EF: executive functioning, g: grams, HL: heel lance, hr: hour, HPA: hypothalamic-pituitary adrenocortical axis, Hx: hypoxanthine, KC: kangaroo care, KFC: kangaroo father care, KMC: Kangaroo mother care, mins: minutes, MKC: Mother kangaroo care, mL: milliliter, M-SSC: Maternal skin-to-skin contact, NICU: Neonatal Intensive Care Unit, nmol/L: nanomoles per liter nmol/mL: nanomole/milliliter, NR: not reported, ns: not significant, OT: oxytocin, pg: pictograms, PMA: post menstrual age, PPDA: post-partum depression and/or anxiety, P-SSC: Paternal skin-to-skin contact, SC: salivary cortisol, SD: standard deviation, SNAPPE II: Score for Neonatal Acute Physiology with Perinatal Extension-II, SSC: skin-to-skin contact, StC: standard care, STS: skin-to-skin contact, TSST-C: Trier Social Stress Test for Children, UA: Uric acid, µg: micrograms, VC: visual contact, wk.: week Xa: xanthine