Published in final edited form as:
*J Adolesc Health*. 2010 March ; 46(3): 284–291. doi:10.1016/j.jadohealth.2009.08.001.

# Adolescent offspring of mothers with chronic fatigue syndrome

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## Abstract

**Purpose—**The goal of this study was to determine if adolescent offspring of mothers with chronic fatigue syndrome (CFS) have higher prevalence of CFS and report more fatigue, greater pain sensitivity, more sleep problems, and poorer cardiopulmonary fitness than comparison offspring with no exposure to maternal CFS.

**Methods—**Twenty-six adolescent offspring of 20 mothers diagnosed with CFS were compared with 45 adolescent offspring of 30 age-matched healthy control mothers. Study measures included structured interviews and medical and laboratory examinations for CFS; tender point examination; maximum oxygen uptake and perceived exertion; dolorimetry pain ratings; and questionnaires on fatigue severity and sleepiness.

**Results—**Compared to offspring of healthy mothers, those who were exposed to mothers with CFS reported higher prevalence of fatigue of at least one month duration (23% versus 4%), fatigue of 6 months or longer (15% versus 2%), and met criteria for CFS (12% versus 2%), although these differences only approached statistical significance. CFS and healthy mothers differed on almost all study outcomes, but offspring groups did not differ on measures of current fatigue severity, pain sensitivity, sleep, mean number of tender points, and cardiopulmonary fitness.

**Conclusions—**The higher prevalence of fatiguing states in offspring of CFS mothers, despite the lack of statistical significance, suggests that familial factors may potentially play a role in developing chronically fatiguing states. Alternately, perturbations in pain sensitivity, and cardiopulmonary fitness may be consequences of CFS. Future studies should focus on examining the impact of maternal CFS and associated disability on offspring psychosocial functioning.

### Keywords

chronic fatigue syndrome; child of impaired parents; pain; sleep; physical fitness

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## INTRODUCTION

Chronic fatigue syndrome (CFS) is a condition of unknown etiology characterized by persistent debilitating fatigue accompanied by a number of somatic symptoms [1]. CFS is mainly a disorder of adults, but studies of adolescents have found a point prevalence of 0.4% to 1.1% for chronic fatigue and 0.1% to 0.5% for CFS using the adult diagnostic criteria [2-4]. Recent investigations have examined broader definitions of CFS in adolescents but have found no significant differences in demographic and clinical characteristics of adolescents who meet the adult versus the broadened criteria [5], suggesting that the adult diagnostic criteria may be appropriate for use with children. The presence of CFS has been documented in children as young as 8 years with the bulk of the studies examining adolescents 11-18 years of age [2,5]. Similar to the impact of CFS on adults, the condition in children and adolescents is associated with substantial impairment, especially in terms of school attendance and functioning. No single cause has been identified and most investigators believe that CFS results from the convergence of multiple factors in a susceptible individual[6].

A growing but relatively fragmented literature suggests that alterations in pain sensitivity, sleep, and exercise physiology and their associated perceptual cues confer a risk for developing CFS [6]. For example, most individuals with CFS also meet the diagnostic criteria for fibromyalgia, a condition of chronic widespread pain [7]. However, findings from experimental pain testing are more consistent with perceptual distortions in assessing pain than with objective indices of pain sensitivity [8]. Likewise, other common symptoms such as disturbed sleep and poor exercise tolerance,[9] have not been consistently associated with abnormalities on polysomnography and aerobic capacity testing [10,11].

Genetic and familial factors also may predispose to CFS. Several twin studies suggest that both genetic and environmental factors contribute to the familial aggregation of fatigue [12,13]. However, these studies had several methodological shortcomings such as restricted age range or self-reported unconfirmed diagnosis. In the only family study [14], first-degree relatives of CFS patients were at greater risk of having CFS than family members of age- and sex-matched control patients with other medical conditions. However, these findings could reflect a potential over-reporting bias since probands reported fatigue and CFS in family members.

To our knowledge, no study has systematically examined the relationship between parental CFS and fatigue and its risk factors in their children. We compared adolescent offspring of mothers with CFS to adolescents with healthy mothers. We addressed the following research questions: (1) Do the offspring of CFS mothers have higher rates of fatiguing states compared to offspring of healthy mothers? (2) Do these offspring differ on measures of fatigue severity, pain sensitivity and perception, sleep, and cardiopulmonary physical fitness? We hypothesized that exposed and unexposed offspring would differ on these possible risk factors for CFS, consistent with a familial or genetic component to CFS.

## METHODS

### Participants

Mothers with CFS were recruited from an academic referral clinic devoted to chronic fatigue and pain. The clinic accepts both self- and physician-referred patients and over 80% of patients are female. A comprehensive examination, intensive battery of questionnaires, and structured psychiatric interview for exclusionary psychiatric diagnoses are used to classify patients as having CFS according to the Centers for Disease Control and Prevention (CDC) case definition [1]. Potential participants were identified from the clinic and contacted to determine interest and eligibility. Twenty women with current CFS who were 25-60 years old with at least one biological child were enrolled. Children were required to be between 12-21 years of age and

living with their mother continuously since at least 12 years of age. The most predominant reason for lack of study eligibility for mothers with CFS was not having children in that age range.

Healthy control mothers living in the greater Puget Sound area were recruited through advertising. Healthy mothers were screened to ensure they were free of fatiguing illness, other conditions associated with fatigue, and the CDC-defined exclusionary psychiatric diagnoses for CFS. Thirty healthy control mothers were enrolled. The age and other inclusion criteria for the healthy mothers and offspring were the same as for mothers with CFS and their offspring. The majority if ineligible healthy mothers did not have children in the 12-21 year age range. CFS and healthy mothers were matched on age within 5 years. The study procedures were approved by the University of Washington Institutional Review Board. Written informed consent from adult participants and written informed assent with parental consent from adolescent participants were obtained. All participants from CFS and healthy families were informed that the study focused on examining the effects of CFS on families and each was compensated $100 for the study visit.

## Procedures

Eligible mothers, their offspring, and if available, biological fathers, were invited for a day-long evaluation in the Pediatric Clinical Research Center. All study participants provided demographic and medical history information, and underwent a physical examination, routine laboratory tests, and a structured psychiatric interview (i.e., the Diagnostic Interview Schedule-IV for adults and the Diagnostic Interview Schedule for Children-IV for children and adolescents), to assess the inclusionary and exclusionary criteria for CFS [1]. Blood tests included the standard recommended battery for CFS [1]. Body mass index was calculated for all participants. Together, this comprehensive evaluation was used to confirm CFS in ill mothers and the good health of control mothers, as well as the fatigue status of all offspring. Fatigue of at least one month duration, fatigue lasting 6 months or longer, and symptoms of CFS were assessed by structured interview of offspring and then confirmed by the mother. The structured interview for CFS symptoms has been used extensively and has acceptable psychometric properties (sensitivity = 73%; specificity = 85-100%). The instrument is similar to those used in the assessment of CFS in adolescents [2]. The Tanner Self-Staging questionnaire for sexual maturity was completed by adolescents [15]. All participants also underwent the following procedures. All assessments were conducted blind to the mothers' fatigue status.

**Cardiopulmonary fitness—**All participants completed the step test of cardiopulmonary fitness [16] alone. The 3-minute protocol consists of stepping up and down on a raised platform at a predetermined rate, which differs for male and female participants, while heart rate is monitored. Oxygen ($O_2$) consumption, estimated from this sub-maximal exertion and the mean exercise heart rate are used to estimate maximum $O_2$ uptake in milliliters/kilogram/minute [17]. The step test correlates 0.92 with directly measured values of maximum $O_2$ uptake and reliably estimates cardiovascular fitness [16]. At the completion of the test, all participants rated peak perceived exertion using the 20-point Borg scale [18]. The step test is a reliable, valid measure of maximum $O_2$ uptake that has been used to study hormonal and cardiovascular response to exercise in adolescents and children as young as 3 years old [19,20].

**Pain Sensitivity and Perception—**All participants underwent a tender point examination for fibromyalgia [7], that is used extensively in adults and has been used previously with children and adolescents [21]. Additionally, a dolorimeter was used to apply pressure to a point 2 inches above the wrist of the non-dominant arm to determine pain threshold and tolerance [22]. Pressure was applied at a rate of one kilogram/second until participants indicated the level

of pain was first noticeable (threshold), the level of pain was so great that they were unwilling to continue (tolerance), or when a maximum pressure of 12 kilograms was reached. Participants also indicated their pain intensity at baseline, threshold, and tolerance on a 10 centimeter visual analogue scale (VAS) with word delimiters at opposite ends indicating "no pain" and "worst pain ever". Measures of pain sensitivity were weights in kilograms applied at threshold and tolerance and those of pain perception were the 3 VAS ratings.

**Questionnaires—**Fatigue severity was evaluated using the *Multidimensional Fatigue Inventory*, that has been validated in several populations including cancer and CFS [23]. The instrument is widely used when fatigue is a prominent symptom and to examine fatigue severity in healthy subjects [24]. This is a developmentally neutral scale with similar characteristics to the PedsQL™ Multidimensional Fatigue Scale that has been used with children and adolescents ages 2-18 years and young adults ages 18-25 [25]. Sleepiness was evaluated using the *Epworth Sleepiness Scale*, which reliably and consistently differentiates fatigue from sleepiness [26]. The instrument is the most widely used self-report measure of daytime sleepiness in a variety of populations including children and adolescents where it has been adapted for use with children as young as 8 years [27]. Additionally, the participants completed self-report measures of psychosocial functioning, the results of which is the subject of another manuscript.

## Statistical Analyses

We assessed if health measures differed among mothers with and without CFS and among their offspring. All analyses were conducted using Stata/SE software, Version 9.0 (StataCorp, LP). Significant p value for all tests were set at 0.05.

**Participant Characteristics—**We calculated mean values of continuous variables and frequencies of categorical variables to summarize the demographic characteristics of mothers and children, both overall and by maternal CFS status.

### Outcomes

**Pain, fatigue, $O_2$ uptake, exertion, and sleepiness:** We used linear regression to model each of these continuous outcomes as a function of maternal CFS. For models of the mothers' data, we controlled for age only. For models of the offspring's outcomes, we controlled for the child's age and sex, and calculated robust standard errors to accommodate correlated measurements for participants from the same family group. To calculate adjusted means for each outcome, we set adjustment variables equal to their mean values within groups defined by maternal CFS status. We constructed 95% confidence intervals for each adjusted mean, and p-values for the differences in those means across maternal CFS status.

**Tender point count:** We modeled the number of tender point counts using Poisson regression, allowing both for correlated counts among members of the same family and for deviation from the Poisson variance assumption. We calculated adjusted mean tender point counts using the same adjustment variables and regression adjustment procedure described above.

**Pain threshold and tolerance:** Because the dolorimetry protocol set the maximum allowable pressure at 12 kilograms, some participants never experienced their actual pain threshold or tolerance. Therefore, we constructed Kaplan-Meier survival curve estimates for threshold and tolerance in both mothers and offspring, stratified by maternal CFS status. We conducted Cox proportional hazards regression to assess the effect of maternal CFS on the hazard of experiencing pain threshold or tolerance as the dolorimeter's pressure increased with time. We addressed deviations from the assumption of proportional hazards by estimating time-dependent coefficients for troublesome variables. Our models estimated the age-adjusted hazard ratio comparing CFS mothers to healthy mothers, and the age-and-sex-adjusted hazard

ratio comparing their respective offspring, allowing for correlations among siblings. For both mothers and offspring, we constructed 95% confidence intervals for the true hazard ratio and the p-value from a test comparing the estimated hazard ratio to one.

# RESULTS

## Participant Characteristics

Table 1 summarizes demographic information for mothers and offspring, overall and by maternal CFS status. Other than employment status, the 2 groups of mothers were similar on all characteristics. Consistent with previous reports of underemployment [28], 50% of CFS mothers were employed at least part time compared to 83% of healthy mothers ($p = 0.02$). The mothers with CFS had experienced fatigue for an average of 10 years.

Offspring of mothers with and without CFS were similar with respect to demographic characteristics, developmental stage, and body mass index. Compared to offspring of healthy mothers, those with CFS mothers reported higher rates of fatigue of at least one month duration (23% versus 4%, $p = 0.11$), fatigue of 6 months or longer (15% versus 2%, $p = 0.07$), and met CDC criteria for CFS (12% versus 2%, $p = 0.13$), although these differences only approached statistical significance after correcting for correlations among siblings. There were too few cases of any fatigue in offspring of healthy mothers to formally examine sex differences, however further examination of the fatigue variables in offspring of mothers with CFS indicated that 50% of those who reported at least one month of fatigue, 25% of those with 6 or more months of fatigue, and 33% of those who met CFS criteria, were male.

## Pain, fatigue, $O_2$ uptake, exertion, and sleepiness

The top portion of Table 2 presents the mothers' adjusted means for the outcome measures by maternal CFS status, and the bottom portion presents similar outcomes for the offspring. Age-adjusted mean scores for the Multidimensional Fatigue Inventory scales for general, physical, and mental fatigue were each about twice as high for the CFS mothers as for healthy mothers (all p values $< 0.01$). These scores indicated a moderate level of fatigue severity in mothers with CFS. Compared with healthy mothers, those with CFS also reported higher levels of pain perception (all p values $< 0.01$), had reduced maximum $O_2$ uptake ($p = 0.03$), and greater perceived exertion on the Borg Scale ($p < 0.01$). The mothers did not differ on Epworth Sleepiness Scale scores.

Conversely, offspring of mothers with CFS did not differ significantly in any outcome measures from offspring of healthy mothers. The difference in maximum $O_2$ uptake during the step test approached significance for the girls ($p = 0.06$) but not for the boys ($p = 0.34$).

## Tender point count

Table 2 also presents the age-adjusted mean number of positive tender points identified during the clinical examinations. CFS mothers had more tender points than healthy mothers (mean = 13.5 versus 7.4, $p < 0.01$). Offspring of mothers with and without CFS had similar mean tender point counts.

## Pain threshold and tolerance

Figure 1 presents Kaplan-Meier survival curve estimates for pain threshold and tolerance for mothers and offspring. Plots *a* and *b* depict the proportion of mothers still at risk of reaching their pain threshold and pain tolerance, respectively. The plots indicate that CFS mothers generally reached their pain threshold and tolerance at lower pressures than did healthy mothers. The age-adjusted hazard of reaching the pain threshold for CFS mothers was approximately 3.7 times that for healthy mothers (95% confidence interval: 2.0 - 7.0; $p < 0.01$).

Similarly, the age-adjusted hazard of reaching pain tolerance was about 3.0 times higher among mothers with CFS than among healthy mothers (95% confidence interval: 1.6 - 5.7; $p < 0.001$). Offspring of mothers with and without CFS did not differ on their pain threshold (plot *c*) or tolerance (plot *d*).

## DISCUSSION

We found that offspring of mothers with CFS reported higher rates of fatiguing states than well-matched offspring of healthy mothers, although these differences only approached statistical significance. Although up to 1/3 of adolescents complain of frequent fatigue and up to 16% report severe disabling fatigue lasting for longer than a month [29], chronic fatigue and CFS in children and adolescents are rare [2-4]. Therefore, our findings that 15% of offspring of CFS mothers reported 6 months of fatigue and 12% met the CDC criteria for CFS, are striking.

These results also are consistent with findings from a family history study of CFS [14]. Together they suggest that familial factors, whether genetic or environmental, may play a role in developing chronically fatiguing states. In this regard, several recent studies have examined potential genetic markers for CFS, such as polymorphisms in the serotonergic system, neuroendocrine system, and genes involved in the inflammatory response [30]. Although not conclusive, initial data support the hypothesis that a genetic component may explain some aspects of CFS [30,31].

On the other hand, the sparse literature on the influence of family environment on developing fatigue-related illnesses is equivocal. For example, one retrospective report suggested that maternal overprotection and depression may be risk factors for CFS in adulthood [32]. Another cross-sectional study found that fatigue and psychological distress in mothers were associated with increased odds of CFS in adolescents [33], while a longitudinal study found no evidence of an association [34]. Anecdotal reports from clinicians suggest that mothers with CFS could be hypervigilant in identifying fatigue in their children. Given the dynamics of emotional interdependence in families, this emphasis may put undue pressure on the offspring to fulfill the mothers' worries. The potential for these naturally-occurring family dynamics has yet to be studied in families of adolescents with CFS and has only been applied to patient-partner relationships in adults with CFS [35]. The family systems framework that allows one to identify and examine the organizational complexity of families and the patterns of interactions, has been fruitful in understanding the interpersonal context of physical illness as diverse as cancer, dementia, and chronic pain as well as in managing the effects of illness within families [36]. Thus, future studies could benefit from applying family systems theory to examine specific hypotheses on the relationship between CFS in mothers and offspring.

We found that mothers with CFS differed from healthy mothers on almost all study measures, but the offspring were surprisingly similar. Thus, our hypothesis that these indices were possible risk factors for CFS were not borne out. However, our findings of differences in mothers but not in the offspring suggest that increased pain sensitivity and reduced cardiopulmonary fitness are consequences of CFS in mothers. Although a large body of research has highlighted the association between these domains and CFS, few studies have been able to establish their temporal relationships. In this regard, a recent 12-year longitudinal study found pressure pain thresholds were normal at baseline but had decreased at follow-up in adults who developed chronic tension-type headache [37]. Similarly, some studies suggest that patients with CFS experience reduced physical activity which can then lead to physical deconditioning and reduced pulmonary function [38].

Two other findings are noteworthy. First, female offspring of CFS mothers tended to have poorer maximum $O_2$ uptake than daughters of healthy mothers. Studies suggest that parental logistic support (e.g., transportation to sports events) and explicit modeling of physical activity are associated with increased physical activity in adolescent girls [39]. Second, the average number of tender points observed in both adolescent groups was higher than the mean reported in normal adolescents and similar to the mean in pediatric fibromyalgia [21]. This finding is at odds with our pain sensitivity data in the offspring that were essentially normal. In adults, tender points have been conceptualized as a marker for psychological distress [40]. It is possible that tender points in adolescents also serve as an indicator of psychological distress and measure a different construct than the pain sensitivity measures. Alternately, although our examiners were trained to criterion [7], the tender point examination might have been influenced by inconsistent application of pressure or perceived demand characteristics.

This study has several limitations. Because ours was the first study to systematically examine the relationship between maternal CFS and fatigue in the offspring, we wanted the methodology to be consistent with previous studies of CFS in children and adolescents that used the CDC-defined adult criteria [1]. Specifically, we did not use the newly proposed definition of CFS for children that requires only 3 months of fatigue [5]. Based on that study, the adult diagnostic criteria may be appropriate for use with children. Another shortcoming, due to limited participation, was the exclusion of data from biological fathers. We anticipated that mothers represented the exposure to CFS and would have the main impact on offspring. Finally, our findings are based on a small sample of offspring of CFS mothers drawn from a tertiary care clinic and healthy community-based control mothers. Although we had exceptional power to detect differences between mothers, post-hoc power analyses indicated that we had low (23%-38%) to medium (52%) power to detect the observed differences in the offspring as statistically significant. This reduced power could explain the lack of statistical significance despite increased rates of fatiguing states in offspring of CFS mothers. The small sample size also prevented us from examining potential sex differences in the offspring. Our findings should be validated in a larger study of offspring from community-based maternal CFS.

### Conclusions

We found higher rates of fatiguing states in offspring of CFS mothers than healthy mothers. Although these differences approached significance, they suggest that familial factors may play a role in developing chronically fatiguing states. As well, we found that mothers with and without CFS differed on measures of pain sensitivity and perception, and cardiopulmonary fitness, whereas the offspring groups were surprisingly similar. These findings suggest that perturbations in pain sensitivity and perception, and cardiopulmonary fitness may be consequences of, rather than risk factors for, CFS. Although difficult to diagnose, our findings suggest that a substantial number of children and adolescents of mothers with CFS experience chronic fatigue and CFS that may require supportive care or symptom management. These findings also highlight the importance of a comprehensive assessment of fatigue in children and adolescents that includes information on family history. Early evaluation of offspring with CFS mothers may provide the opportunity for earlier diagnosis or the implementation of preventive or intervention strategies. Future studies should focus on examining the psychosocial impact of maternal CFS and associated disability on offspring.

## Acknowledgments

This work was supported by NIH AI-038429 to Dr. Buchwald. A portion of this work was conducted through the General Clinical Research Center at the University of Washington and supported by NIH Grant M01RR-00037. Dr. Afari also is supported by NIH grant R01AR051524 and the VA Center of Excellence for Stress and Mental Health. The authors gratefully acknowledge the assistance of Cynthia Evanoff in the conduct of this study.

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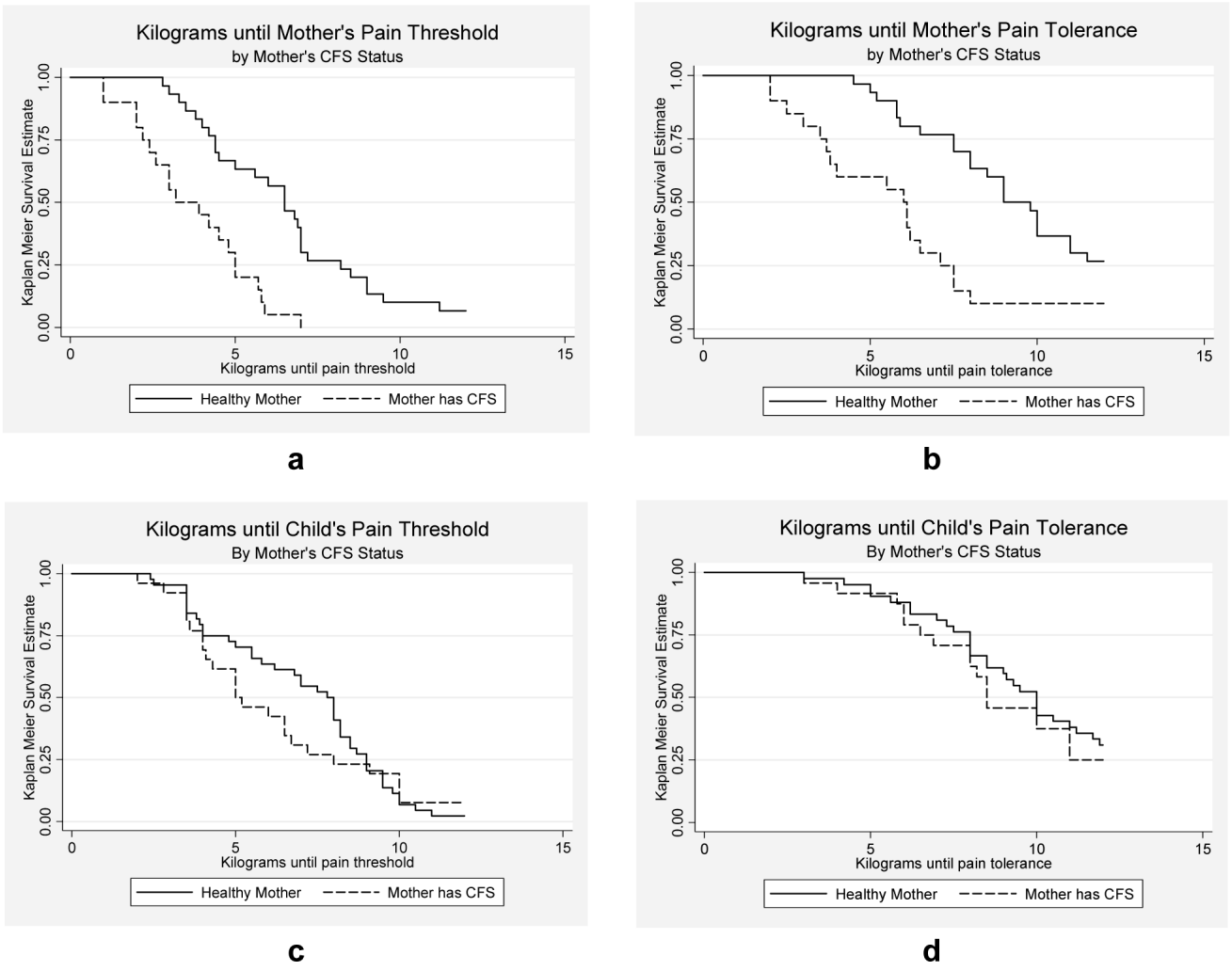


**Figure 1. Kaplan-Meier survival curve estimates for dolorimetry data**

Solid line = healthy mother or offspring of healthy mother; dashed line = CFS mother or offspring of CFS mother. CFS and healthy mothers differed in survival from (**a**) pain threshold ($p < 0.01$) (**b**) and pain tolerance ($p < 0.01$). Children did not differ significantly on (**c**) pain threshold ($p = 0.92$) and (**d**) pain tolerance ($p = 0.31$). Significance tests are based on Cox proportional hazards regression. P-values for mothers are adjusted for age; p-values for children are adjusted for age and sex, and accommodate correlation between siblings.

## Table 1

Participant characteristics

| | CFS Mother | Healthy Mother | Total |
|---|---|---|---|
| ***Mothers*** | ***n = 20*** | ***n = 30*** | ***n = 50*** |
| Age, *mean (sd)* | 45 (4) | 45 (5) | 45 (5) |
| BMI, *mean (sd)* | 27 (4) | 26 (4) | 26 (4) |
| Years of education, *mean (sd)* | 15 (2) | 16 (2) | 16 (2) |
| Children in study, *mean (sd)* | 1.3 (0.6) | 1.5 (0.7) | 1.4 (0.6) |
| Race, % | | | |
| Asian, Pacific Islander | 0 | 17 | 10 |
| Black | 5 | 3 | 4 |
| White | 95 | 80 | 86 |
| Employed full or part time, %* | 50 | 83 | 70 |
| Married, % | 70 | 90 | 82 |
| Years of fatigue, *mean (sd)* | 10 (6) | - | - |
| ***Offspring*** | ***n = 26*** | ***n = 45*** | ***n = 71*** |
| Age, *mean (sd)* | 15 (3) | 14 (2) | 14 (3) |
| BMI, *mean (sd)* | 22 (3) | 21 (6) | 21 (5) |
| Years of education, *mean (sd)* | 8 (2) | 8 (2) | 8 (2) |
| Tanner Stage ≥ G3 / PH3, % | 75 | 80 | 77.5 |
| Female, % | 54 | 44 | 48 |
| Self-reported fatigue of 1 month, % | 23 | 4 | 11 |
| Self-reported fatigue of 6 months, % | 15 | 2 | 7 |
| Meets CFS criteria, % | 12 | 2 | 6 |

*p = 0.02

**Table 2**

Adjusted means and proportions of outcome measures by mothers' CFS status

| | CFS Mother | | Healthy Mother | | |
|---|---|---|---|---|---|
| | ***Mean*** | ***(95% CI)*** | ***Mean*** | ***(95% CI)*** | ***p-value*** |
| ***Mother Outcomes**** | | | | | |
| **Multidimensional Fatigue Inventory**, *score* | | | | | |
| General fatigue | 17.3 | (16.2, 18.4) | 9.6 | (8.3, 10.8) | < 0.01 |
| Physical fatigue | 16.0 | (14.6, 17.3) | 8.1 | (6.7, 9.4) | < 0.01 |
| Mental fatigue | 15.5 | (13.9, 17.0) | 7.6 | (6.5, 8.7) | < 0.01 |
| **Visual Analog Scale for Pain**, *mm* | | | | | |
| Baseline | 27.1 | (18.5, 35.7) | 3.3 | (1.1, 5.5) | < 0.01 |
| Threshold | 41.2 | (32.9, 49.4) | 26.0 | (19.6, 32.4) | < 0.01 |
| Tolerance | 69.0 | (61.2, 76.9) | 49.0 | (39.0, 58.9) | < 0.01 |
| **Tender points**, *count* | 13.5 | (12.0, 15.2) | 7.4 | (5.8, 9.4) | < 0.01 |
| **Epworth Sleepiness**, *score* | 7.8 | (5.8, 9.7) | 6.4 | (5.4, 7.4) | 0.21 |
| **Maximum $O_2$ Uptake from step test**, *ml/(kg.min)* | 15.9 | (14.7, 17.1) | 17.6 | (16.7, 18.6) | 0.03 |
| **Borg Perceived Exertion**, *Borg points* | 14.0 | (12.4, 15.5) | 11.8 | (11.3, 12.3) | 0.01 |
| ***Offspring Outcomes**†* | | | | | |
| **Multidimensional Fatigue Inventory**, *score* | | | | | |
| General fatigue | 9.1 | (7.2, 11.0) | 9.0 | (7.9, 10.1) | 0.62 |
| Physical fatigue | 7.7 | (6.0, 9.4) | 6.9 | (5.9, 8.0) | 0.96 |
| Mental fatigue | 9.5 | (7.6, 11.5) | 8.4 | (7.2, 9.6) | 0.32 |
| **Visual Analog Scale for Pain**, *mm* | | | | | |
| Baseline | 7.3 | (1.8, 12.9) | 6.2 | (3.6, 8.9) | 0.62 |
| Threshold | 24.1 | (18.2, 30.0) | 25.4 | (18.3, 32.5) | 0.81 |
| Tolerance | 48.2 | (40.9, 55.6) | 48.5 | (40.8, 56.1) | 0.78 |
| **Tender points**, *count* | 9.7 | (8.0, 11.8) | 8.3 | (7.1, 9.7) | 0.31 |
| **Epworth Sleepiness**, *score* | 6.6 | (4.5, 8.8) | 5.7 | (4.7, 6.8) | 0.62 |
| **Maximum $O_2$ Uptake from step test**, *ml/(kg.min)* | | | | | |
| Girls | 29.1 | (25.5, 32.6) | 33.4 | (30.5, 36.2) | 0.06 |

| | CFS Mother | | Healthy Mother | | |
|---|---|---|---|---|---|
| | ***Mean*** | ***(95% CI)*** | ***Mean*** | ***(95% CI)*** | ***p-value*** |
| Boys | 54.2 | (49.7, 58.7) | 56.3 | (52.8, 59.9) | 0.34 |
| **Borg Perceived Exertion**, *Borg points* | 11.0 | (9.9, 12.2) | 10.7 | (9.8, 11.6) | 0.80 |

mm = millimeter; ml/(kg.min) = milliliters/kilogram/minute

*Mothers' means adjusted for age via linear regression adjustment, setting age equal to its mean within groups defined by CFS status.

†Offspring means adjusted for age and sex via regression adjustment, setting sex and age equal to theirmeans within groups defined by mother's CFS status.