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Contract No.: HHS 233-01-0012
Contract Amount: $23.78 million

SUPPORTING STATEMENT FOR OMB CLEARANCE

DHHS/ACF/ASPE/DOL
ENHANCED SERVICES FOR THE HARD-TO-EMPLOY (HtE)
DEMONSTRATION AND EVALUATION PROJECT

RHODE ISLAND 15-MONTH PHYSIOLOGY ADD-ON- REVISED

June 7, 2007

Prepared for:

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A. Justification

The Rhode Island site in the Enhanced Services to the Hard to Employ Demonstration and Evaluation Project (the HtE evaluation) is intended to address the effects of telephonic care management on adult depression and employment, and the child component of the study is intended to address the effects of experimentally-induced changes in maternal depression on outcomes for children and adolescents. Two groups of children for whom intervention effects are expected to be strongest are the target of the child add-on study: children 0-5 and children 8-14 at the time of their parents' random assignment to intervention and control gropus. The data collection elements for the main study and for the addition of child assessments to the 15 month follow-up effort have been approved by OMB (# 0970-0276).[1] In this document, we provide the rationale and procedures to add physiological (biomedical) measures to this follow-up to the Rhode Island study. The collection of physiological measures will be fully funded by a grant from the William T. Grant Foundation. Collecting this information will significantly add to this study's contribution to the research literature. Physiological processes can now be examined using simple, non-invasive procedures, collected from participants in their homes by lay interviewers.

A1. Circumstances Necessitating Data Collection

A1.1. Background

A wealth of research has documented the negative effects of maternal depression for children's development (Beardslee, Versage, & Gladstone, 1998; Cicchetti & Toth, 1998; Downey & Coyne, 1990). Early studies found that children of depressed parents were at similar levels of risk as children of parents experiencing other forms of psychopathology (e.g., schizophrenia; Downey & Coyne, 1990). Children of depressed parents show decrements in social behavior and psychological functioning, as well as increased rates of affective disorders like depression (see Cummings & Davies, 1994; Downey & Coyne, 1990; Goodman & Gotlib, 1999, 2002 for reviews). Other work has found that children of depressed parents show a more negative attributional style, resulting in a more negative self-concept (Hammen, 1988; Hammen, Adrian, & Hiroto, 1988). An increasing interest in and recognition of the interplay between individuals' behavior and their physiology has led to a focus on two physiological processes that will significantly add to this prior research: 1) stress physiology, and 2) gene-environment interactions.

A1.2. Stress Physiology: Cortisol

Changes in maternal depression are likely to affect parents' own and their children's physiology, particularly the activity of the stress-sensitive limbic-hypothalamic-pituitary-adrenal axis (HPA). First, we provide an overview of this physiological system. Then we turn to research that suggests a link between changes in depression, the primary target of the current intervention study, and this system.

In response to threat, the hypothalamus increases production of a peptide known as corticotrophin-releasing factor (CRF) that results in the release of adrenocorticotropic hormone (ACTH) by the pituitary. ACTH leads the adrenal gland to release cortisol, which is detectable in saliva. These changes are intended to focus the body's resources on those processes needed to

[1] The authorization to conduct this evaluation and data collection is Section 1110 of the 1993 Social Security Act (see Appendix F).

defend against threat (increasing activity and withdrawal; reducing need for eating, sleeping, and sexual activity; de Kloet, Vreugdenhil, Oitzl, & Joels, 1998; McEwen, 1998; Seyle, 1976). In short, when a stressful event occurs, an individual may experience a series of physiological changes that may involve activation of the HPA axis, and resulting rises in levels of cortisol. Cortisol is an important variable in allostatic load models of stress, in psychobiological models of depression, and has demonstrated effects on health and cognitive systems (Adam, 2006; Chrousos & Gold, 1992; McEwen, 1998).

Interestingly, the HPA axis responds not only to short-term stresses, but exhibits a regular diurnal pattern. Cortisol levels rise with wakening (levels about 30-45 minutes after waking in the morning are higher than at first wake-up) then fall rapidly in the first few hours post-waking, and then continue to fall more slowly across the day, to a low-point in the middle of the night. Interestingly, chronically elevated *and* chronically suppressed average cortisol levels have been considered dysfunctional patterns of cortisol activity (Carlson & Earls, 1997; Gunnar, 2000; Gunnar & Vasquez, 2001). These atypical patterns of cortisol activity are thought to be linked with situations in which the normal stress response has gone awry (McEwen, 1998). In short, chronic stress might lead to frequent and chronic activation of the stress system, or overcompensation by stress systems (and thus chronic underactivity of the stress system), both of which have been associated with emotional and physical health problems (Chrousos & Gold, 1992; Heim, Ehlert, & Helhammer, 2000).

There is evidence to support the hypothesis that the care management outreach and intervention model will affect parents' and children's diurnal cortisol levels. One of the most consistent findings in neurobiology is the link between depression in adults and dysregulation of the L-HPA axis (Beardslee, 2002; Essex, Klein, Cho, & Kalin, 2002; Field, 1994; Nemeroff, 1996; 1998). The typical pattern of high morning-low afternoon levels is disrupted in depressed adults, with hyperactivity found in all levels of the HPA axis, although these patterns are less consistent among depressed children. However, for children, a number of studies have shown that early stressful experiences may alter the typical diurnal pattern of cortisol production. Initial expectations were that early stressors would contribute to increases in cortisol as a result of children's continued response to threat (Gunnar & Vazquez, 2001), although some research has shown a flattened, but also *low* patterning of cortisol production evident in the context of extreme environmental stress (Carlson & Earls, 1997; Gunnar, 2000). While experimentally-induced stressors may lead to elevated cortisol levels, sensitive caregiving has been found to moderate these effects (see Gunnar & Donzella, 2002 for a review). Research on the effects of maternal depression, in particular, on child cortisol has found higher levels of afternoon salivary cortisol as a result of exposure to depression *both* early in development and concurrently (at child age 4.5 years; Essex et al., 2002).

A1.3. Genetic Sensitivity to Intervention Effects

Effects of an intervention focused on parents' depression are likely to differ across individuals. Our baseline assessment of parents and children include a variety of characteristics likely to moderate, or shape, intervention effects, such as severity of depression for parents, and child age and gender. New understanding about the interplay between genes and environments would suggest that understanding the intersection of genetic variation and intervention research will yield important information about the variability of effects across individuals as well.

Tremendous growth in our knowledge about genetic influences has increased our understanding of the consequences of genetic variation. Rather than a simple one-to-one correspondence in which genes determine outcomes for individuals, it is increasingly understood that there is a dynamic process in which the effects of a single gene are influenced by multiple DNA elements, as well as environments (Rutter, Moffitt, & Caspi, 2006). This is especially true of research in the area of psychopathology, including depression. Diathesis-stress theories of depression predict that individuals' response to stress depends on their genetic make-up (in short, is the result of a gene-environment interaction; Caspi et al., 2003; Wust et al., 2004). More specifically, the genes that appear to be associated with mental disorders are normal allelic variations (rather than single mutant genes), for the most part, and thus can be found in a larger proportion of the population than merely those who experience the disorder. These genes appear to predispose individuals to disorders only through their sensitivity to certain high-risk environments.

What does this mean for an intervention focused on reducing depression among parents? The genetic biomarkers of interest for this study measure two things: risk for sensitivity to environmental influences and risk for some of the chemical imbalances that psychotherapeutic medicines can help to address. While an empirical question, those assigned to the program group who have these genetic biomarkers, may be most responsive to the intervention because they are most likely to receive medication management. They also may be most responsive to therapeutic interventions, given their increased sensitivity to the environmental influences. Therefore, we expect that for parents~~For parents~~, treatment strategies may be particularly effective for those with the genetic propensity to experience depression; for children, reducing the environmental risk for their own depression (by reducing the mothers' depression) may be particularly effective for those with the genetic propensity for experiencing the disorder.

Three genetic biomarkers are of critical interest, because they seem particularly strongly linked with depression and stressful life events (and their interaction), and have high enough base rates in the population to observe in our sample: 1) *Serotonin Transporter Polymorphisms: 5HTTLPR short allele (polymorphism of the serotonin transporter gene).* This gene has been found to be associated with greater vulnerability for depression as a main effect, as well as in interaction with negative life events (Caspi et al., 2003). Therefore, those individuals with any "s" allele should have higher rates of depression, but, more importantly, there should also be bigger experimental impacts for those with an s allele. These effects should be even larger for those homozygous for the s allele. 2) *Glucocorticoid Receptor Gene Polymorphisms: N363S (single nucleotide polymorphism).* This gene is associated with increased responses to stress, and therefore should be associated with higher rates of depression and greater susceptibility to life stress (Wust et al., 2004). 3) *BCl1 (restriction fragment length polymorphism).* This gene is associated with diminished cortisol response to stress, and should be associated with lower basal cortisol and lower rates of depression and less susceptibility to life stress (Wust et al., 2004).

A1.4. Research Contribution of Cortisol and Genetic Measures

While the majority of research in this area has focused on the negative effects of maternal depression on children's psychosocial and clinical outcomes, fewer studies have attempted to examine its impact on children's physiology (see Essex et al., 2002 for an exception). Yet, advances in behavioral neuroscience lead us to expect effects on such processes. Examining the neurobiological sequelae of experimentally-induced changes in maternal depression can help us better understand the pathways through which maternal depression alters outcomes for both

adults and children, and for whom it does so. Specifically, while there are a number of studies linking cortisol and adverse life experiences, research investigating whether this system might be sensitive to intervention effects is severely lacking. Therefore, we know very little about how quickly this physiological system responds to changes and how any effects of an intervention might be manifest in physiological as well as behavioral outcomes. Similarly, while there are a number of studies studying the interplay between genes and environments, few if any have examined how genetic variation influences an individuals' sensitivity to intervention effects. For these reasons, adding in physiological assessments to this project can significantly advance the scientific knowledge gained from this research study.

From a policy perspective, understanding the nature and extent of intervention effects requires unbiased assessments of functioning, of which the physiological measures play an important part. In fact, relying on maternal reports for an intervention targeted at their own depression can be quite problematic—if the intervention is effective at reducing depression, it indeed might affect parents' perceptions of their own and others' functioning. Yet, it is not clear whether these perceptions are linked with actual physiological or behavioral change without measuring it directly. These physiological assessments allow for the investigation of exactly this issue.

The assessment of physiology is a burgeoning area of research, and such measures are now being included in national studies such as the National Longitudinal Study of Adolescent Health (ADD HEALTH), National Health and Nutrition Examination Survey (NHANES), National Survey of Child and Adolescent Well-Being (NSCAW) and the Panel Survey of Income Dynamics (PSID), as a means to assess the link between physiological functioning and developmental outcomes in children. In short, the field of behavioral neuroscience has developed to such a point that including physiological measures into large-scale studies is now increasingly common and can significantly advance the scientific contribution of intervention research.

A2. How, by Whom, and for What Purpose Are Data to be Used

We plan to collect physiology data from all sample members in the Rhode Island child add-on study, which includes members of the program group, in which parents are assigned to receive a telephonic care management intervention, and those assigned to the control group, in which parents are assigned to receive "usual care".

More specifically, the target population for the study includes Medicaid recipients in Rhode Island who are receiving Medicaid through a managed care provider, United Behavioral Health (UBH), and who are working-age parents identified with untreated or inadequately treated depression. Individuals identified as having elevated risk for depression were contacted by UBH clinical care managers, who confirmed their level of depression. For those who were depressed, the care managers explained the random assignment study and requested consent from the individual. Once the individual consented, the care manager randomly assigned the individual to either the telephonic care management intervention (program) or to the usual care group (control). The usual care group receives standard care available from UBH which includes much of the same treatment as the program group (should they decide to seek it), but without telephonic care management. The child add-on component is targeted at parents and two specific age groups of children: those 0-5 and those 8-14 at the time of their parents' random assignment. A broad set of prior research would suggest that the intervention will be strongest on these two age groups of children.

The physiology data described here will be linked with the other sources of data already approved for collection for this site. This will allow the study to address the following research questions:

1) What are the effects of a care management outreach and intervention model targeted at parents' depression on parents' and children's stress physiology? How do effects on stress physiology line up with effects on parents' and children's reports of emotional and behavioral outcomes?
2) How do the effects of a care management outreach and intervention model targeted at parents' depression differ for those with differing genetic propensities to experience psychopathology?
3) How do the effects on young children and adolescents of a care management outreach and intervention model targeted at parents' depression differ for children with differing genetic propensities in their susceptibility to negative life events?

A3. Use of Information Technology for Data Collection to Reduce Respondent Burden

Currently, no use of technology has been incorporated into the data collection design to reduce burden. However, non-technology efforts to reduce burden include the choice of procedures for collecting these data that are least invasive to individuals. For the DNA collection, for example, prior methods included finger blood pricks, and cheek swabbing. In our study, we are proposing the use of a very simple saliva collection (described in procedures in Section B) that merely requires respondents to spit into a collection unit. Other techniques to reduce burden include training interviewers extensively in order to ensure the most efficient and least intrusive administration of the collection, and limiting the data collection to the age groups of children most likely to be affected by the intervention, with a maximum of two children per family.

A4. Efforts to Identify Duplication

The physiology assessments allow us to collect information that cannot be found in administrative records, surveys, or the direct assessments of children. They will facilitate the collection of data on parents' and children's stress physiology and their genetic sensitivity to intervention effects, both of which complement the information collected from other sources.

A5. Burden on Small Business

Does not apply. All respondents are individuals.

A6. Consequences to Federal Program or Policy Activities if Data Collection is not Conducted

If this physiology data are not collected, we will not be able to evaluate the impact of the Rhode Island site on parents' and children's stress physiology, a critical complement to the information provided in the surveys and direct assessments of children. The analysis of the impacts of the care management model being examined in Rhode Island would benefit from an understanding of the effects on physiological systems underlying individuals' behavior. And, the genetic information can provide important information about the subsets of individuals for whom this intervention has the strongest effects. In addition, this data has never been collected in a randomized experiment; therefore, the scientific contribution of the research will be far-reaching.

A7. Special Data Collection Circumstances

No such circumstances.

A8. Form 5 CFR 1320.8(d) and Consultations Prior to OMB Submission

The 60-day Federal Register notice soliciting comments for the RI Physiology Add-on was posted in the Federal Register on September 20, 2006 (Volume 71, Number 182, Page 54992-54993. The 30-day was posted on the Federal Register on January 3, 2007, Volume 72, Number 1, Page 134-135. Copies of the 60-day and 30-day Federal Register notices are located in Appendix E.

OMB was briefed on October 24, 2006 about this submission. Comments received on the data collection effort are addressed in this current supporting statement.

A9. Justification for Respondent Payments

Parents who agree to participate in the survey that includes measures of children's functioning will receive payments of $50 in total ($20 for the completion of the core survey and $30 for the completion of the child add-on). Adolescents will receive a gift card valued at $20 for their participation in the Audio-CASI survey. Younger children who attempt the direct child assessment will also receive a toy valued at $10 as incentive for participation. These incentives were included in the prior OMB submission approved for the child add-on to this study.

Parents and children will be offered an additional incentive for choosing to participate in the physiological data collection. A total of eight saliva samples will be collected. The first two will occur in the home when the interviewer is present. As described, a cortisol saliva sample and a DNA saliva sample will be collected then. The remaining six will occur across two follow-up days (three per day), and two daily diaries (one per day) will be collected to supplement the saliva samples. Participants are instructed to mail everything back together (six samples and two diaries) to only require one mailing per person. Families will be given $20 ~~per person~~ for ~~this~~ the parents' samples ~~mailing~~ and ~~will receive~~ $10 for each of ~~their~~the children's ~~mailing~~samples (if applicable). This incentive will be paid to parents (for her own mailing and for completing the mailing for her young child) and to the older children or their parent for ~~their~~ the older children's~~own~~ mailing, once received by the survey firm for analysis. The incentives will be sent, regardless of the condition of the saliva samples.

The purpose of these payments is to improve response rates by decreasing the number of refusals, enhancing respondent retention, and providing a gesture of goodwill to acknowledge respondent burdens. Although many of the techniques suggested by OMB to improve response rates have been incorporated into our data collection effort and are described in Section B3, it has been our experience that small monetary incentives are useful when surveying hard-to-employ populations as part of a complex study design.

The best statement of current thought on incentives is the Symposium on Providing Incentives to Survey Respondents convened in October 1992 by the Council of Professional Associations on Federal Statistics (COPAFS) for OMB. COPAFS asked Richard Kulka of NORC to write a review of the literature in light of what was learned at the symposium. Kulka concluded, "the greatest potential effectiveness of monetary incentives appears to be in surveys that place unusual demands upon the respondent, require continued cooperation over an extended period of time, or when the positive forces on respondents to cooperate are fairly low." Kulka also wrote, "there is evidence that increasing the size of a monetary incentive will result in increases in survey response and/or response quality, although there is also consistent evidence that this

benefit may rather quickly reach 'diminishing returns', whereby large incentives no longer result in appreciable increases in survey response (Kulka, 1992)." We have based the amount of the incentive to be paid for these data collection elements on prior research conducted in this area, and MDRC's and the survey firm's prior experience interviewing similar populations.

A10. Confidentiality

A10.1. Consent

As indicated in the attached consent and assent forms, parents will be given the opportunity to agree to participate in the physiological assessments separately from their agreement to participate in the other portions of the 15 month follow-up effort. Parents will also be asked to provide consent for their children to participate and older children will be administered an assent form prior to the administration of any survey or the collection of physiological data. Parents and children will be given the opportunity to participate in some portions of the physiological data collection and not others (cortisol collection separate from DNA collection, and separately for the use of these data for other research purposes). Consent and assent for this portion of the project will be obtained following their participation in the other components of this follow-up visit, to ensure that this data collection component does not interfere with the core and child add-on components of the study. Consent and assent forms approved by MDRC's IRB are included in the appendix to this document (see Appendices A). Participants will be ensured the confidentiality of the physiological samples, will be told that these samples will be destroyed upon analysis, and provided with clear information about the information that will and will not be collected from these samples (see Appendix C for a question and answer form provided to respondents to address additional questions they may have). As indicated on these consent and assent forms, we have obtained a Certificate of Confidentiality for these data.

A10.2. Protections for Individuals' Confidentiality

Once samples are collected in the home, interviewers will mail back the samples to HumRRO, the survey firm managing the data collection effort for this follow-up study, at their New Jersey office. Participants will also mail back samples to HumRRO directly after the collection on follow-up days. Once the samples are received, HumRRO will enter the ID, time, date, and sample number into an Excel file. The cortisol samples will then be assigned a unique cortisol ID number or barcode to each. The same will be done for the DNA samples. These unique ID numbers will be written on top of each vial in fine tip permanent marker. The labs will use these unique ID numbers to identify the sample. HumRRO will serve as the nexus to link the labs' data with MDRC's data. The mailed material will not have personal identifying information, as the samples will only be identified by ID number.

HumRRO will store all samples, cortisol and DNA, in a locked freezer at their office until they are ready for shipment to the lab for analysis, and subsequent destruction.

All questionnaire and physiological data files will be maintained on the local network at HumRRO's New Jersey office. The network is password protected. These data files will contain no unique information that would allow identification of any study participant. Names, contacting information, case identification and Social Security numbers will be excluded from these data files. Study data files will contain a linking identification number that can be used to match records from one data file to another, for example, linking the physiological information

to the questionnaire responses. The sample management database constructed for the study is the only place that the linking ID number and personal identifiers are stored together. The sample management database is password protected and available only to staff members working on the project.

A Certificate of Confidentiality was issued by NICHD to the Rhode Island site of the Hard to Employ Evaluation on March 26, 2007. With this certificate, we can increase the confidentiality protections of these sensitive data.

A11. Questions of a Sensitive Nature

The collection of these physiological data are potentially "sensitive" for respondents. The data we have proposed were selected in part because they have been widely used in previous research and are respected among experts. Also, a "frequently asked question" list will be provided to respondents to address questions before they are posed. Finally, respondents will be informed by program staff prior to the start of the interview that the information they provide are confidential, that they may refuse to participate in any portion of the data collection, that results will only be reported in the aggregate, and that their responses will not have any affect on any services or benefits they or their family members receive. As mentioned in Section A10, MDRC and its contracted survey firms employ numerous safeguarding procedures to ensure confidentiality.

A12. Estimates of the Hour Burden of Data Collection to Respondents

See Section A15 about changes in burden with this added data collection effort.

A13. Estimates of Capital, Operating, and Start-Up Costs to Respondents

Not applicable. The follow-up physiology data collection will be conducted by a subcontracted survey firm.

A14. Estimates of Costs to Federal Government

The estimated cost for designing, administering, processing, and analyzing this physiological data is $227,875. These costs are being paid for by a grant from the William T. Grant Foundation to a researcher involved in the HtE evaluation, Pamela Morris, at MDRC. There are no costs to the federal government for this data collection effort.

A15. Changes in Burden

We estimate that the saliva samples will constitute an additional 10 minutes per respondent for the in-home samples (5 each for the DNA and cortisol samples) plus an additional 5 minutes for each of the sample collections conducted after the interview visit. Assuming a response rate of 80%, the total number of respondents for parents (400), older children (242) and young children (160) at 15-months were multiplied by the average length of the assessment (5 minutes per sample), divided by 60, then summed to determine the total burden in number of hours. These estimates are based on current proportions of children in each group. The response burden breakdown for the physiological data collection is shown in the table below. The first eight instruments shown below have already been approved by OMB. In this submission we are only seeking approval for the physiological add-ons to the Rhode Island 15-month survey.

Instrument	**Expected Number of Respondents**	**Number of Responses per Respondent**	**Average Burden per Response**	Total Burden **(Hours)**

Rhode Island 6-month	734	1	38 minutes or .63 hrs	464.87
Rhode Island 15-month	734	1	45 minutes or .75 hrs	550.50
New York City 12-month	1000	1	32 minutes or .53 hrs	533.33
Philadelphia 12-month	750	1	25 minutes or .42 hrs	312.50
Kansas/ Missouri 12-month	680	1	45 minutes or .75 hrs	510.00
RI 15-month, parent survey add-on	400	1	45 minutes or .75 hrs	300.00
RI 15-month, youth survey add-on	242	1	45 minutes or .75 hrs	181.50
RI 15-month, direct child assessment add-on	160	1	45 minutes or .75 hrs	120.00
RI 15 month parent initial physiological component	400	2~~8~~	7.5~~5~~ minutes or .125~~08~~ hrs	100~~256~~.00
RI 15 month parent follow-up physiological component	400	6	5 minutes or .08 hrs	192.00
RI 15 month youth initial physiological component	242	2~~8~~	7.5~~5~~ minutes or .125~~08~~ hrs	60.50~~154.88~~
RI 15 month youth follow-up physiological component	242	6	5 minutes or .08 hrs	116.16
RI 15 month young child initial physiological component	160	2~~8~~	7.5~~5~~ minutes or .125~~08~~ hrs	40.00~~102.4~~
RI 15 month young child follow-up physiological component	160	6	5 minutes or .08 hrs	76.80
TOTAL PERSON HOURS				3558.16~~4 85.98~~

A16. Analysis and Publication Plans and Schedule

The HtE evaluation- Rhode Island Site incorporates a random assignment analytic design. The addition of the physiology data allows us to estimate the effects of the telephonic care management model on parents' and children's stress physiology. The addition of the genetic data allows us to address questions about how intervention effects might vary across individuals. Notably, because this is a nascent field, and we are far from understanding the precise meaning of variations in outcomes in either of these measures, these analyses should be viewed as

exploratory. That is, they help us to begin to understand the nature and extent of intervention effects on parents' and children's physiology, and the potential for genetic variations to moderate intervention effects; future research that builds on these findings will be critical.

A16.1. Analysis Plans

***Estimating Overall Impacts*.** Although the use of a randomized design will ensure that simple comparisons of experimental and control group means will yield unbiased estimates of program effects, the precision of the estimates will be enhanced by estimating multivariate regression models that control for factors that also affect the outcome measures. Such impacts are often referred to as "regression-adjusted" impacts. Examples of factors that may affect outcomes are prior depression severity, and baseline demographic characteristics.

The analyses of overall impacts on levels of cortisol will result in estimation models that, in their basic form, can be expressed as follows:

(1) $Y_{ij} = F(T, X_{ni}, U_{ij})$, where:

Y	is a vector of outcomes (e.g., cortisol levels at various times of the day, area under the curve for diurnal pattern of cortisol)
T	is the treatment variable indicating whether the individual is a member of the HtE intervention group
X	is a vector of baseline characteristics to be controlled (e.g., baseline depression severity)
U	is a vector corresponding to the residual (error) term
i	is the subscript designating the individuals in the sample
j	is the subscript designating the outcome of interest
n	is the subscript designating the various personal characteristics to be controlled.

Subgroup analyses. Experimental analysis will be conducted to examine the moderating role of genetic variation on the relation between the intervention and outcomes for adults and children. Differences in subgroup impacts will be tested by conducting split sample regression analyses and estimating differences using an HT statistic. The HT statistic is the weighted sum of squares of the impact estimates for the subgroups and has a chi-squared distribution (Cooper & Hedges, 1994; Greenberg, Meyer, & Wiseman, 1993). Unlike more standard interaction terms, split sample approaches have the advantage of not assuming homogeneity of variance across the subgroups examined. Differences in impacts based on genetic variations may help to tease out differences in effects of the intervention on parents who might be more amenable to treatment, or on children who have higher sensitivity to environmental influences, while still maintaining the strength of the experimental design.

Non-experimental analyses. Non-experimental analyses can help complement the estimation of the experimental analyses. These analyses can test whether experimentally induced changes in depression can be linked statistically with changes in physiological outcomes (Gennetian, Morris, Bos, & Bloom).

Analyses beyond those linked to intervention effects. In addition to the set of analyses presented here, a number of other questions might be addressed with these data. The following questions are of interest: how are levels of cortisol linked with the course of parents' depression across time, in either the control or program group? How are levels of cortisol in parents linked

to differences in parenting practices? How are differing parenting practices linked to cortiol levels among children? With regard to the genetic information, are differing genetic profiles among parents linked to differential sensitivity to environmental influences? Are differing genetic profiles of children linked to differential sensitivity to parental influences (ie., do children with differing genetic profiles more likely to show negative behavioral outcomes as a result of harsh parenting?

Notably, any questions to be addressed would be reviewed by an oversight committee (described below) for their scientific contribution. And, these data will not be used to examine the relation between genetic variation and the receipt of public assistance benefits. These data will be used to advance the kinds of research questions posed above, and not for policy purposes.

Review and oversight.

All analyses and write-up of the results of this study will be overseen by the set of mentors identified for Dr. Morris (the principal investigator leading the collection of this physiology data) as part of her William T. Grant scholars award. The mentors have a defined role in the William T. Grant scholars award: they are identified as experts in the field and have committed to providing scientific oversight of this portion of the project. These mentors are: 1) Adrian Angold, an Associate Professor of Child and Adolescent Psychiatry at Duke University; 2) Megan Gunnar, a Professor at the Institute of Child Development at the University of Minnesota; and 3) Sandra Danziger, a Professor of Social Work and Director of the Michigan Program on Poverty and Social Welfare Policy; and 4) Sheldon Danziger, the Henry J. Meyer Professor of Public Policy and Senior Research Scientist at the Population Studies Center. Gunnar is an expert in developmental neurobiology and has written extensively on the effects of early stressful experiences on the neuroendocrine system, as measured by salivary cortisol; Angold is an expert in the area of child and adult psychopathology and provided the initial guidance on the collection of genetic information in this study. The Danzigers are experts in depression and employment among welfare-recipient parents.

If further analysis of these data is conducted after the conclusion of the William T. Grant Scholars award period, a similar scientific review panel will be created to oversee the scientific contribution of the proposed analyses, and will review the interpretation of any findings that emerge.

A16.2. Publication plans and schedule.

The physiology add-on will be administered along with the 15 month follow-up survey. Fielding will last up to 18 months after the last cohort was randomly assigned, beginning as early as March 2006 and will end as late as March 2008.

Findings from the follow-up physiological data collection will be part of the impact analyses. The results will be published in a series of papers based on the results. These papers will be produced during 2008-2009. Notably, these data will be used for research and not policy purposes. This area of research is a nascent field, and we see this work contributing to the body of knowledge in this area. –

A17. Reasons for Not Displaying the OMB Approval Expiration Date

Not applicable. We intend to display the OMB approval number and expiration date on all survey materials.

A18. Exceptions to Certification Statement

Not applicable. We have no exceptions to the Certification Statement.

B. COLLECTION OF INFORMATION USING STATISTICAL METHODS

B1. Sampling

As indicated in the OMB submission for the 15 month survey add-on, the follow-up sample size for the parents with children in the focal child age groups will be 400 parents. Dependent on whether a mother has one focal child, two focal children in a group, or one focal child in both groups, the estimated sample size for the older children is 242 and for the younger children is 160. This follow-up sample estimate is based on the assumption that physiological data will be collected on 80 percent of the research sample, and on both program and control groups in the research sample.

B1.1. Follow-up Survey Sample Sizes

Survey Efforts/Sites	Fielded Research Samples	Follow-Up Samples
Rhode Island 15-month Parent physiology	500	400
Rhode Island 15-month older child physiology	303	242
Rhode Island 15-month young child physiology	200	160

The evaluation literature often discusses the appropriateness of the sample size for a study by focusing on the smallest program impacts that are likely to be detected with a specified level of confidence, assuming a sample of a given size and characteristics. These are usually called the program's "minimum detectable effects" (MDEs). Analysis of MDEs is also referred to as "power analysis," as it estimates the study's power to measure the effects it was designed to find.

As a guide to determining appropriate sample sizes, the following table projects the statistical power of sampling plans for a two-group impact estimate using results for children aged 11-16 years in the New Hope 5-Year Follow-Up (Huston et al., 2005). This table reports MDEs, the minimum program impact that a sample has an acceptable chance of detecting (with a .10 significance level, and .80 power) for four child outcomes, and for samples of different sizes.

B1.2. Minimum Detectable Effects for Key Outcomes in Effect Size Units

Size of Program and Control Group	Positive Behavior Scale	Externalizing Behaviors	Internalizing Behaviors	Achievement
75/75	.21	.28	.26	.44
100/100	.18	.24	.23	.38

150/150	.15	.20	.18	.31
200/200	.13	.17	.16	.27

Evaluation literature is sorely lacking to allow us to do the same kind of analysis with any confidence for the physiological outcomes proposed to be collected here. Because we see these analyses as exploratory, however, a small sample size may still allow us to build hypotheses about the effects of interventions on physiological outcomes.

Meta-analyses of the randomized clinical trial literature on the treatment of outpatients with major depression suggest that post-treatment depression symptoms between active treatment and control groups are on average about 1 standard deviation (Agency for Healthcare Policy and Research, 1999; DeRubeis et al., 1999; Gaffan, Tsaousis, & Kemp-Wheeler, 1995; Gloaguen et al., 1998; Joffe, Sokolov, & Streiner, 1996; Moncrieff, Wessely, & Hardy, 1998). Given that these are efficacy trials in controlled clinical settings, an effectiveness trial such as the current study may result in an expected effect size on depression of .66 standard deviation, based on prior work on the effects of care management as used in the current study (Katzelnick et al., 2000; Wells et al., 2000). Given that these effectiveness trials have found stronger effects in low-income samples (Miranda et al., 2003), this may be a conservative estimate for this study. This same assumption was made in a related NIH grant application testing this same intervention on a working population (P. Wang, Principal Investigator; Kessler and Simon, co-Principal Investigators).

Longitudinal research on the effects of depression on outcomes for children finds effect sizes ranging from .36 (based on rates of Major Depression Disorder (MDD) in a four-year follow-up of a community sample of parents, some of whom had affective disorders (Beardslee et al., 1993) to .6 found in a 10-year follow-up of clinically-referred parents (Weissman et al., 1997). Assuming the average of these two estimates (.48), and combining this with a .66 treatment effect size on symptom severity, we expect an expected effect size of this intervention effort of on children's diagnosis of depression of .32 (.66 * .36). In order to detect an effect of .32, the total sample of children must at least be 242. Fortunately, our sample for the older age group of children will be able to detect this level of impact. Unfortunately, as with computations of minimum detectable effects, it is very difficult to determine reliable estimates for a power analysis on physiological outcomes that would be analogous to those presented here for depression risk outcomes. However, we present them because they indicate that the sample size for this study is sufficient for some set outcomes that are directly tied to the intervention. Given the strong associations in the literature about the relation between depression and cortisol levels for parents (Nemeroff, 1996; 1998), and between early deprivation and cortisol for children (Gunnar & Donzella, 2002), we are hopeful that the sample will be sufficient to address the effects on these physiological outcomes as well. In fact, if we are to observe associations of the size that were found in a prior study of the effects of depression on children's cortisol (in which effect sizes were in the range of 4.0; Essex et al., 2002), our sample sizes are more than sufficient to find these effects.

B2. Procedures for Collection of Information

Both the cortisol and the genetic data can be collected from participants in very simple, non-invasive procedures in which mothers and children are asked to spit saliva into specific collection kits. As described in detail in the attached documents (See Appendix B), salivary

cortisol will be collected from parents, older focal children and younger focal children (over the age of 2 at the time of follow-up) in the home while the interviewer is present. The interviewer will demonstrate the saliva collection, but parents and older focal children will collect their samples themselves. Parents will collect the saliva from their young focal children. In a similar process, DNA samples will be collected from parents and focal children in the home while the interviewer is present. As with the salivary cortisol samples, the interviewers will model the collection of the samples, but the parents and the children will collect the samples themselves.

In addition to the cortisol and DNA samples collected on the interview day, participants will be asked to collect salivary cortisol samples on two follow up days after the interview is completed in the home (See Appendix C). Parents and older focal children will collect saliva on three times on each of the two days: 1) upon waking up; 2) 30 minutes after waking up; and 3) at the end of the day prior to going to bed. Parents will be asked to collect saliva samples from their young focal children over the age of 2 on two mornings and two afternoons when nothing unusual is going on. Even without external monitoring, good compliance (80-90% of samples taken on time) has been achieved in prior ambulatory cortisol studies in community samples using even more complicated (5-6 samples per day) protocols (Kudielka et al. 2003; Jacobs et al. 2005). However, vials will be equipped with a "compliance cap" that records time and date of sample to ensure adherence to protocol.

Parents and older focal children will be asked to complete a short diary prior to taking their last sample of the day, with information on sleep, mood, and potentially important confounding influences on cortisol, while parents will complete a similar diary on the young focal children (see Appendices D). A couple of points of note in the review of these diaries: 1) It would be ideal to collect information on sleep and wake times in the morning and the mood indices at the end of the day; however, in an effort to reduce respondent burden parents and youth will be asked to complete the diary only one time per day, reflecting back on the prior nights' sleep. This technique has been used in other studies with success (Adam, Hawkley, Kudlieka, & Cacioppo, 2006). 2) Some information on confounding influences on cortisol is omitted from the youth diary, but retained for the parent diary (i.e., information on alcohol and nicotine use). Research has found effect of these substances on cortisol levels (Field et al., 1994; Canals, Colomina, Domingo & Domenech, 1997); given these findings, we opted to collect this information on the adult diary. Fortunately, we have information on the youth survey that is conducted in an Audio-CASI format with the youth about regular alcohol and cigarette use. However, because the information on that diary cannot be necessarily kept confidential from parents (parents may see the diaries completed by the youth since they are conducted when the interviewer is no longer in the home), we opted not to collect that information on the diary. What we miss by not asking it in the diary is the use of alcohol and cigarettes on that particular day. Our expectation is that regular use and use on that day are highly related and the information collected in the survey, while not ideal, will be sufficient to control for these effects.

For the collection of cortisol data, children and youth will be instructed to mouth salivate (a form of cotton) for approximately two minutes. To facilitate the stimulation of saliva, younger children (ages 2 years and older at the time of the assessment) will be given a very small amount of Kool Aid to sweeten the end of the cotton and stimulate saliva flow (if parents indicate that the child is not allowed to have the Kool Aid, the procedure will not be attempted). Post-collection, parents and youth will be asked to place wetted salivate, collected according to the schedule described above, in a vial and return to the interviewer in envelopes. Envelopes will be

provided for families to mail back the samples for analysis, for those samples taken after the interview day.

For the collection of DNA samples, participants will be asked to merely to spit into a special vial, called an Oragene DNA self-collection kit. A small amount of sugar will be offered to stimulate saliva flow, but is optional. The vial resembles a contact-lens holder and has a preservative that allows for room-temperature storage until analysis of the sample can be conducted.

B2.1. Analysis and Destruction of Salivary Cortisol Samples

The Technical University of Dresden's Biological Psychology Laboratory will process the cortisol samples in Germany. This lab is lead by Professor Clemens Kirschbaum, the most well known cortisol researcher in the world.

HumRRO will be responsible for sending the samples to the lab in two groups, one to check the data (to make sure that the data is being entered correctly and values are in the appropriate ranges) and the second for the remaining samples. Kirschbaum's laboratory is known for their quick turnaround (as quick as one weekend); they make use of robotic equipment. Once the samples arrive at the lab in Dresden, they will store the samples in freezers that are located in a locked room. For the past 10 years, not a single sample has been lost or stolen.

Once the data results are sent back to HumRRO, the lab will contact MDRC requesting what should be done with the samples. Once the data has been checked for errors, MDRC will instruct the lab to destroy the samples. There will be no way to link the unique cortisol ID numbers with the participant information without the involvement of HumRRO.

B2.2. Analysis and Destruction of DNA Samples

The Center for Genetic Medicine will process the DNA samples in Chicago, Illinois. The Center is a joint venture of Northwestern University, Northwestern Memorial Hospital, Children's Memorial Hospital, and Evanston Northwestern Healthcare. Our contact person there is Nadereh Jafari, Research Assistant Professor/Core Facilities Director.

HumRRO will be responsible for sending the samples twice during the course of the project to the lab, one to check the data and the second for the remaining samples. The samples will be stored in the locked freezer at HumRRO until the shipment is ready.

The Center has a security system in place at the lab and only accepts samples that have an ID on them (no names or other identifying information). Once the data has been checked for data entry errors, MDRC will instruct the lab to destroy the samples. Samples will be autoclaved (heated to above boiling point and sterilized) which destroys the DNA. There will be no way to link the unique DNA ID numbers with the participant information without the involvement of HumRRO.

B3. Maximizing Response Rates

The goal will be to achieve an 80 percent response rate for this data collection component. Procedures for obtaining the maximum degree of cooperation include:

- Conveying the purposes of the data collection to respondents so they will thoroughly understand the purposes of the data and perceive that cooperating is worthwhile;

- Providing a toll-free number for respondents to use to ask questions about the survey and the survey firm's staff;
- Providing a Frequently Asked Questions list to respondents to respond to some of their common concerns;
- Training site staff to be encouraging and supportive, and to provide assistance to respondents as needed;
- Hiring interviewers who have necessary skills for encouraging respondent cooperation;
- Training interviewers to maintain one-on-one personal rapport with respondent; and
- Offering appropriate payments to respondents.

B4. Pre-testing

Pre-testing was conducted with 9 households to explore any changes to the data collection methods presented here that should be considered. Seven of the nine families returned the samples on the subsequent days as requested. This high level of response rate bodes well for the collection of these data in this study.

B5. Consultants on Statistical Aspects of the Design

We consulted with a number of researchers to assist us in thinking about this data collection effort. 1) We contacted Mary Bruce Webb, who provided information to us regarding the collection of cortisol for NSCAW. Her comments included information gathered from Edith Nottelman at the National Institute of Mental Health and other leading academic researchers who are experts in these data collection efforts. 2) Emma Adam, an Associate Professor at Northwestern University, has served as a formal consultant on the Rhode Island add-on study, offering her guidance and expertise on the protocols and administration of the physiological measures. She is a William T. Grant Scholar and a leading expert in the integration of physiological measures into large scale studies (including the NICHD ADD HEALTH study). She has conducted many of her own experiments using similar measures, and leads training efforts in the collection of these data at CS2 (Cells to Society) a center at Northwestern University. 3) Adrian Angold, an Associate Professor of Child and Adolescent Psychiatry at Duke University, and Megan Gunnar, a Professor at the Institute of Child Development at the University of Minnesota, are experts in this field and serve as two mentors for Pamela Morris' William T. Grant scholars award, the grant that is supporting this data collection effort. (see section A16 above about how these mentors will provide scientific oversight of this portion of the study). Gunnar is an expert in developmental neurobiology and has written extensively on the effects of early stressful experiences on the neuroendocrine system, as measured by salivary cortisol; Angold is an expert in the area of child and adult psychopathology and provided the initial guidance on the collection of genetic information in this study. 4) Avshalom Caspi, a professor in the Social, Genetic, and Developmental Psychiatry Research Center at the Institute of Psychiatry, King's College London has been contacted about this effort. He has written extensively on gene-environment interactions, and has written the leading article on the interaction of the serotonin-transporter gene and life stress in predicting depression, published recently in *Science*.

~~There were no consultants on the statistical aspects of the design.~~