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Title: Unemployment as a chronic stressor: A systematic review of cortisol studies

Objective: Unemployment is a type of chronic stressor that impacts human health. The reasons for how the stress of unemployment effects health is still a matter of discussion. One of the pathways from chronic stress to ill health is mediated by cortisol, and so we set out to compile extant data on how its secretion is affected by unemployment. **Design:** A systematic literature search was conducted to establish the cortisol dysregulatory effects of this stressor. **Main Outcome Measures:** Only studies that specifically examined the effects of unemployment on cortisol excretion, and were written in English were included. **Results:** Ten reports were obtained and synthesised to determine the severity and complexity of the effect of unemployment on cortisol secretion. The resulting combined evidence is mixed in terms of degree or dynamic of relationship. **Conclusions:** The differences between the cumulate findings of the studies can be understood in the context of the lack of both standardised methodology and an absence of consensus on unemployment definition. We propose existing methodologies may be strengthened by acknowledging and accounting for the individual characteristics that may be relevant to the stress experience of unemployment.

Keywords: Chronic Stress; Cortisol; Stress; Systematic Review; Unemployment

Introduction

Unemployment is a stressful life event comprising the loss of both latent and manifest benefits associated with employment. This can be from financial limitation, stigma, reduced social connectedness and social support; and social identity disadvantage by harming self-perception, as well as the absence of self-esteem increases associated with a working life (e.g. productivity, goals and achievements etc.) (Åslund, Starrin, & Nilsson, 2014; McKee-Ryan, Song, Wanberg, & Kinicki, 2005; Shamir, 1986; Takahashi, Morita, & Ishidu, 2015). Not only is it a psychosocial stressor, adding worry and strain to many dimensions of daily living; the consequent effect it has on financial freedom and social connectedness also means the stress experienced by unemployment is furthered still by reducing the ability to remain resilient.

Unemployment has been linked to cardiovascular disease (Dupre, George, Liu, & Peterson, 2012; Herbig, Dragano, & Angerer, 2013), inflammation (Hughes, McMunn, Bartley, & Kumari, 2015), increased health-damaging behaviours (Roelfs, Shor, Davidson, & Schwartz, 2011), depleted immune function (F. Cohen et al., 2007), and mortality (Garcy & Vågerö, 2012). Further, it has been associated with enduring health effects, resulting in an increased risk (11%) in overall mortality for up to 20 years after (Browning & Heinesen, 2012). Not only has unemployment been associated with poorer health on the individual level, this association is also seen geographically at both the regional and national level (Bambra & Eikemo, 2008). One of the pathways by which chronic stress contributes to decreased health is through the persistent activation of the hypothalamic-pituitary-adrenal (HPA) axis, and the over-production of steroid hormones, causing changes to immunity and fatiguing allostatic processes that maintain the precision balance of the body's various systems (Juster, McEwen, & Lupien, 2010; Miller, Chen, & Zhou, 2007).

Cortisol, a steroid hormone of the HPA axis, is elevated during times of stress, and its diurnal rhythms are dysregulated during chronic stress (S. Cohen et al., 2012). Prolonged stress results in the blunting of the diurnal rhythm of cortisol; causing a less pronounced awakening response, and a more shallow

slope of decline across the day (Chida & Steptoe, 2009; Miller et al., 2007). The dysregulation of diurnal rhythms of cortisol secretion has been related to caregiving (Stalder et al., 2014), prolonged temporary employment (Gustafsson, Janlert, Virtanen, & Hammarström, 2012), burnout (Pruessner, Hellhammer, & Kirschbaum, 1999), and work stress (Kunz-Ebrecht, Kirschbaum, & Steptoe, 2004). Elevated levels of cortisol are associated with many health concerns including metabolic syndrome (Stalder et al., 2013), atherosclerosis (Hajat et al., 2013), acute myocardial infarction (Pereg et al., 2011), and cardiovascular mortality (Steptoe & Kivimaki, 2012). On the cellular level, cortisol has also been related to changes within the immune system; contributing to systemic illness, disease vulnerability, and poor general health (Phillips, Ginty, & Hughes, 2013; Segerstrom & Miller, 2004). The relationship between unemployment and these health outcomes, therefore, would appear to be shared with those of cortisol; providing a possible biomechanistic process by which unemployment causes ill health. Unemployment has been associated with an increase in negative health behaviours, and a decrease (by financial deprivation) of the means to stay healthy (Hollederer, 2015; Kalousova & Burgard, 2014), thus it is important to examine more direct means by which unemployment may contribute toward ill-health; via the chronic stress cortisol pathway.

Although unemployment has fallen under the auspices of life events stress (Linn, Sandifer, & Stein, 1985; McKee-Ryan et al., 2005), in biobehavioural research it has been considered a chronic stressor in its own right, primarily due to its temporal effects that can extend for weeks, months and even longer, and (particularly in cases of economic recession) its uncontrollability (Miller et al., 2007). Indeed, there are associations between a longer duration of unemployment and decreases in both psychological and physiological functioning described across the broader literature (Aguilar-Palacio, Carrera-Lasfuentes, & Rabanaque, 2015; Dupre et al., 2012; Griep et al., 2016). In a large population study, examining differences between short- and long-term (e.g. <12 months>) unemployed and employed groups (permanent or temporary), it was found that those unemployed long-term reported worse health than all other groups (Griep et al., 2016). However, those who were insecurely employed reported worse health than those who were unemployed short-term (Griep et al., 2016), showing that

the experience of unemployment may well be changeable, and relevant to context. Further, although unemployment has been shown to be damaging to health, there have been inconsistent associative patterns with health outcomes (McKee-Ryan et al., 2005; Roelfs et al., 2011), including cortisol (Claussen, 1994; Ockenfels et al., 1995). However, the reasons underlying these inconsistencies have yet to be reviewed.

One reason could be that the conceptualisation of “unemployment” as a single phenomenon is highly problematic, and is perhaps the largest issue of contention within the collected literature on the subject. A status of being without gainful employment is in itself not one single entity, but rather is a complex spectrum of social situations, including: (as well as being out of, and wanting/needing work) being retired, a homemaker, on a study break, out of work but not wanting/needing work, working voluntarily without pay, or being out of work through incapacity. The experience of unemployment will likely vary greatly between these discreet groups of people, along with the feelings of stress or dissatisfaction that may be experienced. The International Labor Office (ILO) defines unemployment as those that are out of work but would be available to work *and* are actively seeking work; with those outside of that bracket being considered “inactive” (Brandolini, Cipollone, & Viviano, 2006). This definition is principally oriented to the monitoring of economic activity, however it would seem to encapsulate the “stressful” experience of unemployment; seeking, wanting and/or needing work, but being unable to obtain it. Unfortunately, in the fields of research outside of economics and politics the lines of this definition become somewhat blurred. By and large, the body of literature in the field of behavioural medicine would seem to classify unemployment as simply being without gainful employment, without the context of the individual’s activity or capacity within this status. As will be discussed, most of the researchers in this field have recruited a mixture of “unemployed” and “inactive” participants, to use the parlance of the ILO; and it is this lack of clear definition that causes significant problems with the interpretation of their findings.

Alongside the issues inherent with categorising unemployment, there are further complications when considering the variance of circumstance within those who are unemployed. The issue of control or volition would seem to be important in not only our definitions of unemployment, but also its consequences and subjective experiences. Recent data examining whether employees opt for redundancy in a failing business showed that those who chose redundancy fared better than those who remained employed in terms of both psychological and somatic health (Snorradóttir, Tómasson, Vilhjálmsson, & Rafnsdóttir, 2015), suggesting that those who are unemployed voluntarily could be distinct from those who become unemployed involuntarily. This is supported elsewhere in findings that those who experience voluntary redundancy fare far better than those who experience involuntary redundancy in terms of their mental health and their feelings of being able to regain employment (Waters, 2007). This latter point is particularly salient, as those who choose redundancy may well do so as a more favourable alternative (as opposed to the stress caused by the uncertainty of unstable employment); and there are some that may also choose to become or remain unemployed for other reasons, whom again may not experience the same level of stress than someone who has involuntarily lost their job.

The purpose of this review

Given the links between unemployment and health, the present systematic review sought to compile the available information considering the study of cortisol and unemployment, to extend the current knowledge of the biological mechanisms underlying this phenomenon. Further, we sought to draw out common themes within the available data to better understand the nuances of this stressor, with the view to informing future research protocols. To our knowledge this is the first review to examine cortisol and unemployment specifically, and will provide a foundation for understanding how unemployment affects human health by synthesising the current knowledge, delineating methodology and limitations, and summarising the findings with a view to advancements in the field.

Materials & Methods

Literature Search

A computer-based search was carried out from November 2014 to March 2015, employing the following databases: NCBI PubMed, Web of Science, and EBSCOhost EJS (databases: MEDLINE, PsycARTICLES, Psychology and Behavioural Sciences Collection, and PsycINFO); using the key search terms of “unemployment” or “job loss”. These principle terms were used in conjunction with the Boolean operator AND with the secondary term “cortisol” (e.g. unemployment AND cortisol, or job loss AND cortisol). One additional article (Gallagher, Sumner, Muldoon, Creaven, & Hannigan, 2016) was included after the search period, as this was authored by our group. Reference lists from each paper were screened for potential additional relevant papers not captured in the electronic search. We initially set out to establish the level of extant data that examined the relationship between unemployment and other biomarkers (e.g. using the additional secondary search terms “dehydroepiandrosterone”, “immunity”, “lymphocyte” amongst others), however the data pertaining to other biomarkers of interest was even less abundant than that relating to cortisol. Given these results we decided to focus on cortisol alone, however the relative paucity of biomarker data relating to unemployment is of concern and the field clearly merits further expansion. The PRISMA method was employed for selection and reduction of papers for the review, see Figure 1 for a process diagram. There were no limitations set for date of publication. Any studies that examined cortisol in unemployment via any statistical or research method were considered for inclusion. Articles were excluded if they were not in English, or if they were analysing cortisol in clinical populations as cortisol itself is affected by a broad swathe of chronic illnesses and medications (Kudielka, Hellhammer, & Wüst, 2009), and as such is difficult to compare between clinical and non-clinical groups. As this review was to be the first to examine this subject we sought to retain as much direct comparison between the included studies as possible, in order that an overall picture of the relationship between unemployment and cortisol could be ascertained. As we set out to understand how unemployment

may alter levels of cortisol; any studies that recruited unemployed participants but did not use this status as an independent variable (or level thereof) were not included (Smyth et al., 1997). Due to the very small number of available studies in the area it was decided that no further exclusion criteria should be implemented to avoid substantially limiting the scope of the review exercise. Potential future data syntheses, after further much-needed research has been carried out, may be beneficial to examine the themes highlighted herein. It is important to note that no restrictions on the conceptualisation of unemployment were in place for this exercise. Whilst it is our position that “unemployment” is not one singular concept, this is an issue that has either been difficult to control during data collection, or has not been considered to its fullest extent. If we were to exclude any studies that recruited any participants other than those out of, but actively seeking, work, there would be no studies to review. To outline the extent of the difficulty in conceptualising unemployment, Table 1 details the types of groups included in the reviewed studies. Not all studies provided a detailed outline of exclusion/inclusion criteria, however it can be seen that whilst some studies have been able to retain a reasonably narrow definition of unemployment, no studies have been able to solely capture the “unemployed but seeking” demographic.

[Insert Table 1 around here]

Two potential articles were excluded as they reported preliminary protocol data (Levi et al., 1984a; Smyth et al., 1998) of larger studies reported later (Brenner & Levi, 1987; Ockenfels et al., 1995). As we established “unemployment” as a broad category of those who are not in education, training, employment, or retirement, another potential article was excluded at data extraction stage (Feller et al., 2014). This paper was excluded as the analysis examined unemployment as a grouped factor with both retirement and retraining, therefore not providing a distinct conceptualisation of unemployment. Effect size analysis of the included studies was not possible due to the lack of sufficiently reported data in many of the studies.

[Insert Figure 1 around here]

Results

From the systematic search, ten articles concerning cortisol and unemployment were included. The studies comprise several methodologies, and different aspects of cortisol secretion. It is important to note that a key finding of this exercise is that there are few studies that examine cortisol in the unemployed, particularly as compared to other chronic stressors. For example, a selection of recent reviews or meta-analyses examining the association between cortisol and other chronic stress factors have yielded the following: 62 articles on psychosocial stress (Chida & Steptoe, 2009); and 84 articles on caregiving (Pinquart & Sörensen, 2003). Of those studies that compared (un)employment groups, two studies described higher overall cortisol in unemployed versus employed participants (Arnetz et al., 1991; Dettenborn, Tietze, Bruckner, & Kirschbaum, 2010); one described higher cortisol in long-term (over 12 months) versus short-term unemployment (Maier et al., 2006); two described no difference in overall cortisol between employed and unemployed groups (Claussen, 1994; Ockenfels et al., 1995); and one described only cortisol diurnal rhythm dysregulation in the unemployed, with overall levels being lower than in the employed (Gallagher et al., 2016). A summary of the reviewed studies can be found in Table 2.

[Insert Table 2 around here]

[Insert Figure 2 around here]

The collated data are inconsistent, and often contradictory. A basic consideration here is the timeline of the studies, ranging from 1987 to 2016. Cortisol assessment methodology has advanced a great deal in this almost 30-year period, so it is possible that discrepancies may be being driven by methodology rather than anything else. This is captured by our risk of bias checklist (see Figure 2), where we have attempted to evaluate each study in terms of basic methodological concerns that will apply to this type of analysis in this group of people. Whilst the checklist is not exhaustive, and cannot be proportionally weighted, it is a simple rubric with which we can quickly evaluate the quality of the

present studies. The checklist includes variables that pertain to the measurement of cortisol, such as whether more than one sample was taken, or more than one attribute of cortisol is used; and those that pertain to the participants, such as whether they were all unemployed for the same reason (e.g. redundancy), or whether unemployment is in any way defined. Those variables that were not applicable for the particular study were scored positively so as not to penalise for more robust methodology. For example, the Dettenborn study (2010) used cortisol derived from hair, and would therefore not be subject to issues of timing of sample, nor participant compliance. As can be seen from these scores, there are no studies free from common bias, however it is encouraging to see that this is improving over time.

To better understand whether cortisol may be a chronic stress pathway, we selected only those studies that compared employed to unemployed ($N=7$). Table 3 shows a summary of these studies. Of these studies, just four supported the notion that being unemployed was related to changes in cortisol excretion, either in total output (Arnetz et al., 1991; Brenner & Levi, 1987; Dettenborn et al., 2010) or in slope (when controlling for age) and awakening response (Gallagher et al., 2016). As not all studies were in agreement, and the sub-section of studies spanned such a broad period of time, we were interested to consider whether the concordance between physiological and psychological stress changes as time goes on, and research methodologies improve. It can be seen that all of the studies aside from one in this sub-section detail that the unemployed participants report higher levels of psychological stress, but it is important to note that this single study measured stress through the recording of life events rather than perceived stress, and did also find that their unemployed participants reported higher levels of depression (Hall & Johnson, 1988). The methodology for the studies does improve over time, with the Ockenfels (1995) study being the first to take measures across more than one day to control for extraneous situational factors, a method that is now considered to be best-practice (Stalder et al., 2016). The results prior to this point are therefore less reliable as they do not exert a high level of control. Continuing, the last two studies (Dettenborn et al., 2010; Gallagher et al., 2016) apply strict exclusion criteria to their participant recruitment, and collect

data to cover covariates, such as the use of hormonal contraceptives. This is, again, in accordance with current best-practice guidelines (Stalder et al., 2016), providing a little more weight to the two most recent studies, although we cannot draw any substantial conclusions from just these studies.

[Insert Table 3 around here]

As we were not able to directly answer whether or not cortisol is affected by unemployment, we looked further into the research to understand what consistencies did exist, and how best these can be drawn out and expanded upon in future research. Two key themes emerge from the accumulated data that are pertinent to both understanding the current knowledge, and establishing future directions.

Temporal differences

Several studies herein capture changes across the course of unemployment, either from before job loss, or during unemployment. An exemplar of these temporal differences comes from an early study, where participants were followed across the course of their unemployment (Brenner & Levi, 1987). A pattern of change is observed over time that shows an anticipatory phase of stress before redundancy, followed by a “honeymoon effect” of decreased cortisol output until 12 months (Arnetz et al., 1991; Brenner & Levi, 1987). This is further supported by description of marked differences in cortisol secretion between long-term (>12 months) and short-term (<12months) unemployed people (Maier et al., 2006). This suggests that physiological stress is experienced differently across unemployment, and that 12 months may represent a critical point of change a suggestion with partial support from the psychological stress data from this group of studies (Arnetz et al., 1991) and elsewhere (McKee-Ryan et al., 2005). This is in line with contemporary knowledge whereby chronic stress is characterised in two different patterns of cortisol secretion; hypercortisolism in the acute stage at stressor onset, and hypocortisolism over time as the body attempts to counter-regulate (Miller et al., 2007). An important cultural contextual note here is that at that time in Sweden, where three of the included studies were based (Arnetz et al., 1991; Brenner & Levi, 1987; Hall & Johnson, 1988), 90% of an

unemployed person's previous earnings was provided by the state in unemployment benefit in the first 12 months only, decreasing thereafter (Hall & Johnson, 1988; Levi et al., 1984b). This could explain why cortisol levels appear to peak at this point for these studies; however this does not account for the similar findings of the Maier (2006) study, as their research was conducted elsewhere. Another study in the set described levels of hair cortisol decreasing over time in long-term unemployed (>12 months) participants (Dettenborn et al., 2010). One of the studies (Gallagher et al., 2016) collected data on unemployment duration, and found no cortisol differences between categorical levels of unemployment (<12months>), but this could be because the sample was skewed toward long term (mean 27.1 months). The transitioning from short- to long-term unemployment itself may result in some significant psychological shifts in terms of self-appraisal, as well as the appraisal of the individual's social world, which could either cause or alleviate substantial distress depending on personal dispositional factors. However, exactly when this transition from short to long-term is, may differ in the perception of the individual. Taken together, these discrepant findings highlight the importance of the methodology employed in this research, and how much this can influence the findings and interpretations.

Differences between men and women

The literature appears to hint at differences between the sexes; however these differences could either be due to physiological differences in sex, or the psychosocial aspects of gender. One study specifically examined differences between unemployed men and women; finding that men expressed higher levels of cortisol than women both in general, and in reaction to experimental stress (Grossi, Åhs, & Lundberg, 1998). However, these findings could be related to the way the sampling was carried out, and the lack of control for confounds – particularly those relating to gender. Later, detailing a nexus between financial strain, sex/gender, and cortisol secretion; females high in financial strain showed differences in slope as compared to those with low financial strain; and no such relationship was observable in men (Grossi, Perski, Lundberg, & Soares, 2001). This finding is interesting, as others have reported that men suffer more than women from financial deprivation in unemployment

(Waters & Moore, 2002). Crucially, no control was taken over the use of hormonal contraceptives or hormonal medications in the sample; an issue pervasive through the majority of the literature. As hormonal contraceptives and hormone replacement therapy are both known to alter cortisol secretion (Kajantie & Phillips, 2006; Kirschbaum, Pirke, & Hellhammer, 1995), this is an important factor to consider and control for. Only three studies examining cortisol in unemployment have considered oral contraceptive use (Dettenborn et al., 2010; Gallagher et al., 2016; Ockenfels et al., 1995), and only one reported testing comparisons between men and women (Gallagher et al., 2016) with no significant differences. There is conflicting evidence on the psychological distress experienced by the unemployed, with some studies suggesting that there are little or no gender differences (Creed & Watson, 2003), and others that there are (van der Meer, 2014; Waters & Moore, 2002). The final study (Gallagher et al., 2016) excluded homemakers from their sample, and did not find differences between men and women.

Discussion

Limitations of the extant research

Across this small, rather dated body of literature there are several limitations that would need to be addressed in future research, and may well help to account for the discrepant cumulative findings. Of primary concern is the need to conduct more work using best-practice methodology, as it is difficult to even understand whether cortisol is affected by unemployment with the research base methodology being as outmoded as it is. Cortisol sampling in this cohort of studies was inconsistent, and - in the majority of cases - below the standard that would now be considered to be acceptable – which is likely a reflection of the age of the studies themselves. Three studies took just one sample from their participants (Claussen, 1994; Hall & Johnson, 1988; Maier et al., 2006), meaning that variations in cortisol secretion from daily stressors, sleep, or lifestyle may have contributed to their findings. Other studies report taking one sample per day over several points to track the trajectory of

change (Arnetz et al., 1991; Brenner & Levi, 1987), or at several points across just one day (Grossi et al., 1998; Grossi et al., 2001). Two studies employed multiple sampling across two days (Gallagher et al., 2016; Ockenfels et al., 1995), however one of these did not employ exclusion criteria, or attempt to standardise the methods of collection (i.e. ensuring participants to not eat/drink before etc.) to ensure minimum confounds (Ockenfels et al., 1995). The one remaining study employed hair cortisol sampling (Dettenborn et al., 2010), which provides an aggregated retrospective assessment of cortisol excretion. This novel methodology would constitute a reliable measure of cortisol, however is constrained to retrospective analysis only.

Another aspect of the applied methodology is the lack of control for variables that may affect cortisol secretion, autonomic functioning, or behaviours that may modulate the experience of stress; although this is being improved. Several studies reported that assessments of behaviours likely to affect cortisol were taken, but either did not delineate how/if they were used in analysis (Brenner & Levi, 1987; Claussen, 1994; Levi et al., 1984a), or omitted them from analyses all together (Grossi et al., 1998; Grossi et al., 2001). Several studies reported no exclusions for factors related to cortisol secretion, such as physical health or use of medications (Arnetz et al., 1991; Brenner & Levi, 1987; Claussen, 1994; Grossi et al., 1998; Grossi et al., 2001; Hall & Johnson, 1988), or only limited exclusions (Maier et al., 2006; Ockenfels et al., 1995). This is problematic as the participants may have been taking medications that could alter their autonomic nervous system communication (e.g. antihistamines, sympathomimetics), or affect their mood (e.g. antidepressants, oral contraceptives), thereby impacting on both their cortisol secretion, and their subjective appraisals of stress. Only two studies (Dettenborn et al., 2010; Gallagher et al., 2016) have thus far detailed a stringent level of confounder and covariate control.

Moreover, it is abundantly clear that further control over the definition and context of unemployment is required. An important limitation of the collected evidence is the lack of a standardised definition of unemployment, and the potential inclusion of those who are economically

inactive, but may not necessarily be classed as unemployed (e.g. homemakers, those on study breaks). As can be seen from Table 1, the majority of studies ($N=6$) have either actively included, or potentially failed to exclude, those people that may not technically be “unemployed” in its strictest sense. The roles of homemaker or student are a critical point to consider in unemployment research, as it could be argued that these may be a form of employment or vocation, and as such may not comprise a status of chronic stress. Equally, there are doubtless different experiential factors involved with being unemployed but otherwise able to work, and being unemployed through disability or enforced retirement where there may be no future prospects of re-employment. Further, those that are unemployed from a government perspective (as they do not earn money) may still see some of the benefits of working if they engage in voluntary work, making their experiences distinct also.

Three of the earliest studies in the group were able to in some way standardise their sample of unemployed as they recruited from factories that were due to close, or were carrying out large scale redundancies due to downsizing (Arnetz et al., 1991; Brenner & Levi, 1987; Hall & Johnson, 1988). Although this cannot account for the participants’ future engagement in job seeking activities (and therefore control for a degree of control or volition experienced in sustained unemployment), it does provide a means to understand the impact of job loss. The final study in the set excluded any participants that were in education, that were retired or were homemakers, or who were unemployed but were not able to work (for whatever reason) (Gallagher et al., 2016). This allowed the selection of a sample of people that were unemployed but otherwise able to work, however could not exclude those that were not actively seeking work. The issue of seeking work is complicated, particularly in the setting of this study as it was undertaken following the most recent global recession in a country with relatively high rates of unemployment (Gallagher et al., 2016). Whilst not seeking employment could be suggestive of less dissatisfaction with (un)employment status, higher job seeking activity has previously been associated with increased distress (McKee-Ryan et al., 2005), so not actively seeking work may, in fact, be a way of attempting to diminish the stress experienced in unemployment. Of these four studies, only the most recent study was carried out with what are considered to be

recommended methods for cortisol assessment, making the conclusions of the first three difficult to interpret, and leaving us with only one study that both has a definition of unemployment that is somewhat stable and utilised recommended cortisol assessment methods.

Future directions – A conceptual model of unemployment stress

The collated literature on unemployment and cortisol has some interesting indications; however, it is largely not contemporary, and is therefore incongruous with the methods and considerations of other areas of chronic stress that we see today. To understand unemployment as a biomechanistic process of chronic stress, it is important not only to refine rigorous methodology, but also to account for those variables that we understand to modulate human psychological and biological stress responses. Of utmost importance is the rigorous and sound assessment of cortisol; with multiple measures being taken over multiple days to establish a reliable cortisol output. Further, we propose standardising methodology in this field in terms of: definition of unemployment; control for confounding variables; and the account for contextual elements of stress experience.

As previously outlined, the definition and context of unemployment is an important one, which has been overlooked in this field. Future studies in the area should ensure that participants who identify as unemployed both financially and vocationally, and do not identify as homemakers, retired, unable to work, or on a study break. Moreover, the classification of discrete “types” of unemployment may be beneficial to further understand the complex and differing experiences of this group. For example, a record of the cause of unemployment, such as whether this was through redundancy, and whether or not this redundancy was voluntary etc., will doubtless uncover further nuances that may help us to “unpack” the chronic stress experience of joblessness. Related to both the definition and context of unemployment is the implication of the “social norm effect”, whereby the stigma of unemployment may be far less in areas where it is seen as more normal, which will doubtless have an effect on the subjective stress experienced by those who are unemployed (Clark,

2003). This is of relevance both in times of high unemployment due to economic recession, or local job market collapse (such as due to large plant closure); and in social circumstances or cultures where the impetus to work is less highly valued. A population level study using the World Values Survey has detailed that life satisfaction of the unemployed differs between countries according to their cultural values attached to employment (Stavrova, Schlösser, & Fechtenhauer, 2011), and it is conceivable that this may also apply on a smaller scale also. Similarly, those who have never worked may present a different profile to those out of work, with some studies from Spain showing that those who have never worked exhibit better mental health and report less frequency of negative health behaviours than those that are out of work (Aguilar-Palacio et al., 2015; Urbanos-Garrido & Lopez-Valcarcel, 2015). It is therefore essential that future research accounts for the social context of its participants, where possible. One study in the collated group detailed that this may play a part in their findings, as - at the time of data collection – the unemployment rate was relatively high across the country where data collection took place (10-11%) (Gallagher et al., 2016). During times of global recession, as seen in in the last decade, it is possible that this may be less important as other stressors rise (such as economic inflation and austerity) (Cooper, 2011). This could plausibly abrogate any social norm benefits during such times; and it will likely be of key concern during “boom” times, where these other stressors are lessened, and social “reasons” for unemployment are also decreased, thereby decreasing any social norm from the national/international level to the local level. Moreover, the concept of employability may be a meaningful way to understand individual appraisals of unemployment and job security; with studies suggesting that perceptions of employability highly mediate the relationship between unemployment and wellbeing (Green, 2011), and that employability itself affects attitudes to unemployment (Dunn, 2010).

To disentangle the influence of sex and gender, future studies will need to account for both biological and psychosocial variables. A bare minimum for this would be to account for the use of hormonal medications, and the exclusion of homemakers. This latter point would allow for a more straightforward definition of unemployment. It has been suggested that irrespective of marital status

that women fare better than men psychologically in unemployment (van der Meer, 2014), however this relies on an idea that women do not find identity centrality from a work role, which is culturally and individually relevant (Mannheim, 1993; Warr, 2008). Additionally, there is the suggestion that women may experience less stigma during unemployment than men, due to the gender role of woman as homemaker (van der Meer, 2014). However, other studies have found no sex differences in stigma in unemployed samples (O'Donnell, Corrigan, & Gallagher, 2015). Socioeconomic status (SES) is also interestingly absent as an influence in the synthesised literature. Although the associations between SES and cortisol have been equivocal, there are suggestions that lower SES may be more consistently associated with blunted cortisol secretion across the day (Dowd, Simanek, & Aiello, 2009). As is common with a collection of studies, there was not a single measure of SES, but a few measures that can be used as an index of SES (such as income or education). Within the accumulated works only two studies were able to report any differences between their sample groups or associations with their outcome. The Dettenborn group (2010) reported that their unemployed sample were less educated than their employed controls, but this was not related to cortisol; and our group (Gallagher et al., 2016) reported that income was lower in the unemployed as compared to the employed, but there was no significant difference in education between groups. All of these considerations warrant further investigation in order to establish a contextual framework for unemployment stress.

All interdisciplinary health research is burdened with the difficulty in balancing what is rigorous and what is practical in terms of methodology, and this is equally the case here. There are some key areas that should be attended to in research design and implementation in the future so that they may be adequately accounted for. Any research employing biological analyses must attempt to exclude any major confounding variables (such as illness or use of medications), and control for common behavioural factors that will also impact the analyte (e.g. use of stimulants, amount of sleep, health behaviour). Further, research into the complex area of human stress must also account for a multitude of contextual factors, whose pertinence to both subjective and objective measures of stress are increasingly important. Recent meta-analyses carried out examining unemployment and mental

health (Paul & Moser, 2009), and unemployment and mortality (Roelfs et al., 2011) outline a number of factors that may moderate the effects of unemployment. Moreover, duration of unemployment may well also hold categorical differences in terms of stress experience, and there is reason to examine this as a moderator between unemployment and cortisol dysregulation.

In summary, we propose that future studies should include only those who identify as unemployed and seeking work, and ensure that adequate exclusion and covariate controls are implemented in the design. We posit that there are likely categorical differences between those who are short- and long-term unemployed (delineating these at the 12-month mark); and that wider contextual factors may identify those who are vulnerable, and those who are resilient, to the stress of unemployment.

Conclusions

The overarching conclusion from the literature is that the chronic stress experienced by the unemployed is complex, and requires close and careful evaluation to understand. There is a need for new research with standardised methodology, a clearly defined concept of unemployment, control for confounds, and the consideration of broader contextual factors. In order to understand how the stress of unemployment is experienced biochemically we suggest that future studies carry out analyses across the spectrum of short- and long-term unemployment, as well as different types of and reasons for joblessness to better understand the variation across the out of work group. Overall, we do not believe that the existing data is an accurate reflection of what is likely the case in unemployment. It is inconsistent with the broader literature, where there are far more clear associations between unemployment and both physiological and psychological health (McKee-Ryan et al., 2005; Roelfs et al., 2011). It is curious that the subject has not been studied in more detail, particularly in recent years; and we posit that with more careful methodology that far more robust findings will be discoverable.

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Figure 1. PRISMA flow diagram of article search and selection

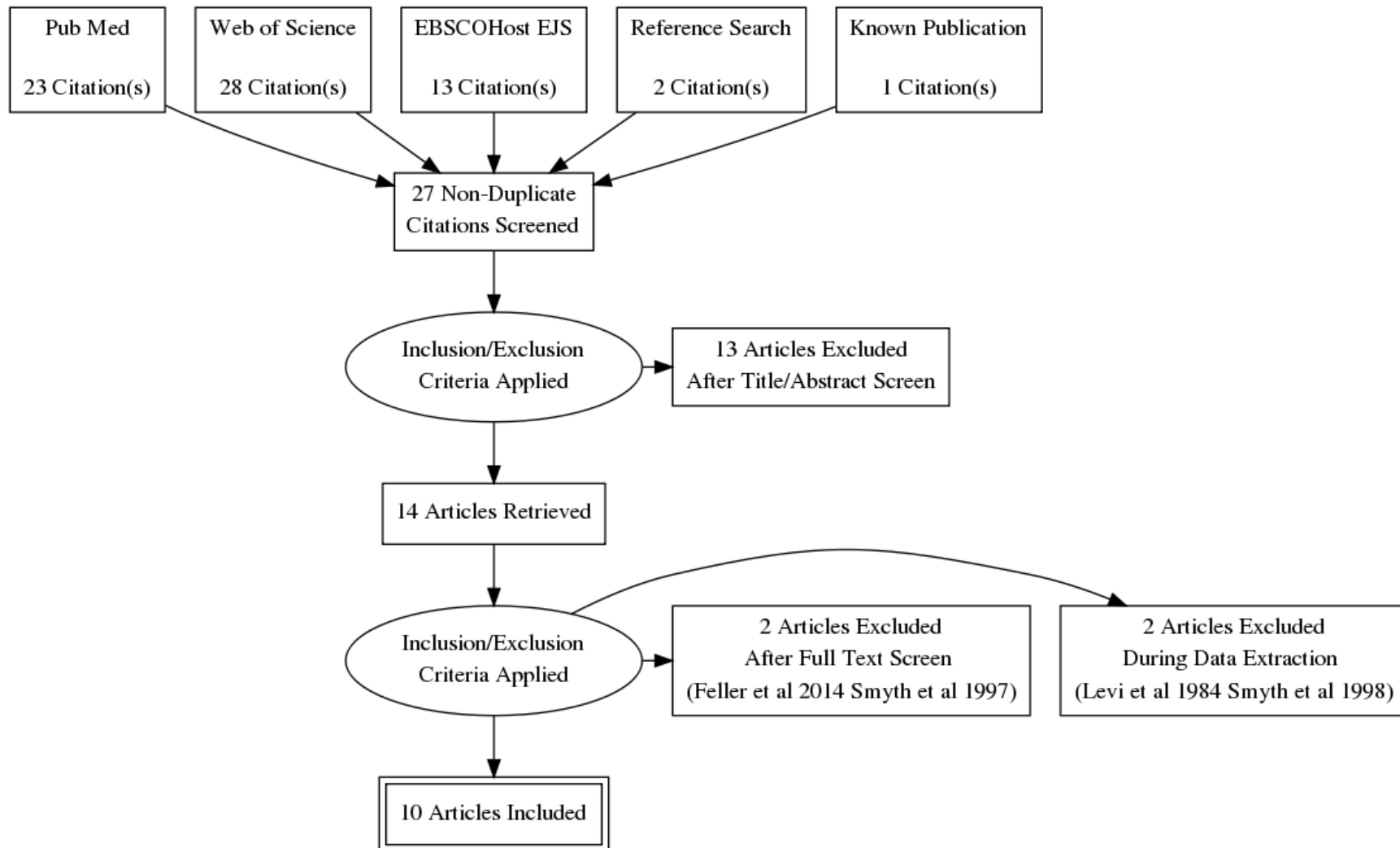


Figure 2. Risk of bias checklist items

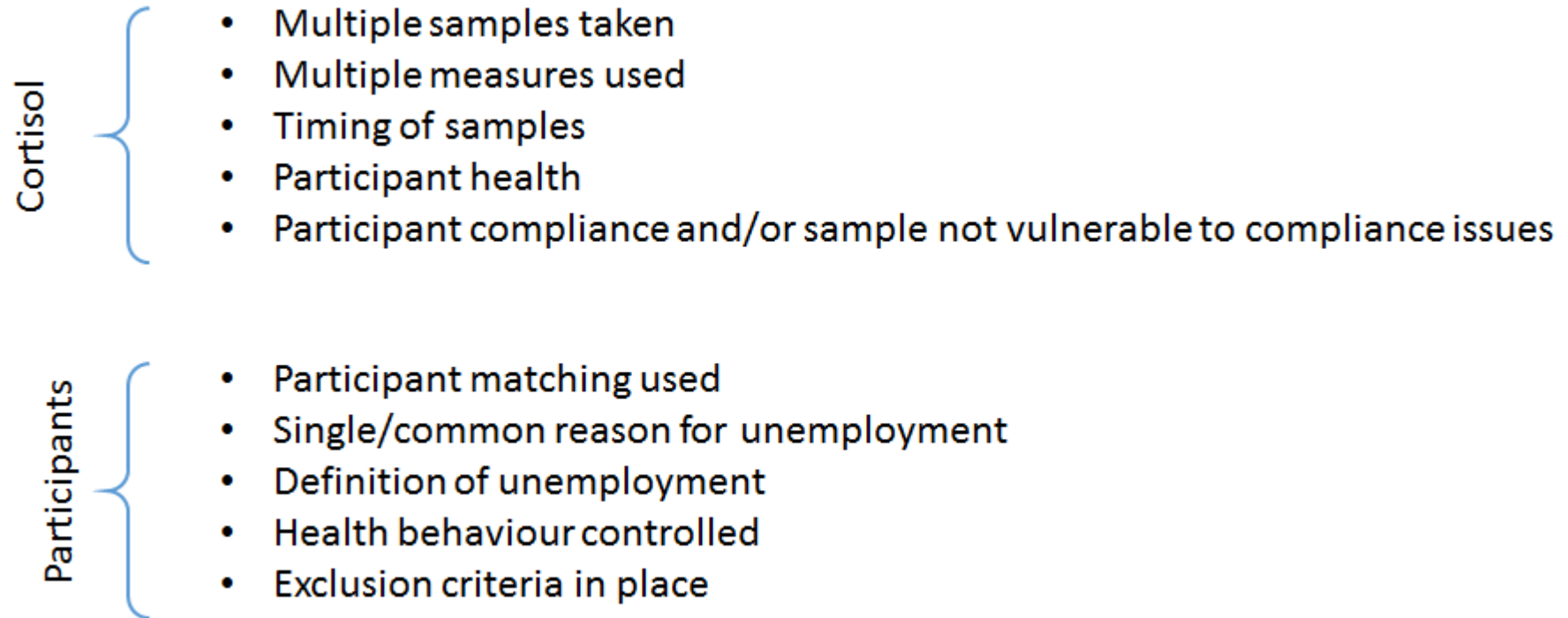


Table 1. Details of the unemployment categories included in studies

	Unemployed			Homemakers	Retired	Study Break	Voluntary Sector
	Seeking/able	Not seeking	Not able				
Brenner & Levi, 1987	✓	✓	✗	✗	✗	✗	✗
Hall & Johnson, 1988	✓	✓	✗	✗	✗	✗	✗
Arnetz <i>et al.</i> , 1991	✓	✓	✗	✗	✗	✗	✗
Claussen, 1994	✓	✓	✗	?	✗	✗	?
Ockenfels <i>et al.</i> , 1995	✓	✓	?	?	✗	?	?
Grossi <i>et al.</i> , 1998	✓	✓	?	?	✗	?	?
Grossi <i>et al.</i> , 2001	✓	✓	?	?	✗	?	?
Maier <i>et al.</i> , 2006	✓	✓	✗	✓	✗	?	?
Dettenborn <i>et al.</i> , 2010	✓	✓	?	?	✗	?	?
Gallagher <i>et al.</i> , 2016	✓	✓	✗	✗	✗	✗	✗

Unemployment & Cortisol

Table 2. Overview on studies on the associations between unemployment and cortisol

Paper	Sample	Cortisol Method	Cortisol Response	Design	Cortisol Group Differences	Bias checklist score	
						Cortisol	Participants
Brenner & Levi, 1987	400 participants (89% female, 89% between 30-50 years old: from Levi <i>et al.</i> , 1984) Group 1: Pre-unemployed (1 month before to 24 months) Group 2: Unemployed (4-18 months) Group3: Insecurely employed Group 4: Securely employed	Blood	Single-sample cortisol level	Prospective, Quasi-Experimental, Within-Subjects	Anticipatory phase of jobloss (1 month prior) shows elevated cortisol that decreases by 1 month after. Cortisol reaction varied highly. Cortisol peaks at around 12 months after redundancy, then decreases up to 24 months.	1/5	2/5
Hall & Johnson, 1988	147 participants (100% female, of working age – Sample drawn from Brenner & Levi, 1987) 96 unemployed (made redundant) 51 employed (similar industry)	Blood	Single-sample cortisol level	Cross-Sectional, Quasi-Experimental, Between-Subjects	No significant difference in cortisol levels between the two groups. Further analysis comparing high and low cortisol across depressed and non-depressed subgroups also showed no significant difference. Mean cortisol slightly higher in unemployed.	1/5	2/5
Arnetz <i>et al.</i>, 1991	354 Employed participants of working age Group 1: <i>n</i> =150 (89.3% female) from plant about to close Group 2: <i>n</i> =62 (83.9% female) insecurely employed Group 3: <i>n</i> =112 (53.6% female) securely employed	Blood	Single-sample cortisol level	Prospective, Quasi-Experimental, Between-Subjects	Cortisol higher in unemployed than employed groups. Largest cortisol changes seen during the first year of unemployment and then normalise. Increased levels of cortisol occur during anticipatory phase of losing employment.	1/5	0/5
Claussen, 1994	310 long term unemployed (>12 weeks); for cortisol	Blood	Single-sample cortisol level	Prospective, Observational,	No significant differences between employed and unemployed, or	3/5	2/5

Unemployment & Cortisol

	measurements 276 at baseline (42% female), 221 at follow-up (44.3% female). Age range of sample pool 16-63 years. 90 employed controls at follow-up (17.7%)			Between-Subjects	unemployed and re-employed. Cortisol was positively associated with prolactin levels and rating of psychosocial stress. Changes in cortisol across time were small, as were changes from unemployed to re-employed.		
Ockenfels et al., 1995	120 unemployed and employed participants (70.8% female; 50% unemployed; mean age 33.72±11.44, 39.70±11.93 years, respectively)	Saliva	Single-sample cortisol level; Slope; Stress Reactivity to natural daily stressors	Cross-Sectional, Experimental, Between-Subjects	No difference between groups on overall cortisol or stress reactivity. Cortisol not related to length of unemployment. Unemployed showed higher morning and lower evening cortisol compared to employed.	5/5	1/5
Grossi et al., 1998	59 long term unemployed (>6 months) (37.2% female; mean age 42±10 years)	Saliva	Stress Reactivity to lab stressor (log-transformed value of change T2-T1)	Cross-Sectional, Experimental, Within-Subjects	Stress reactivity increases in cortisol for all; effect carried by male participants. Baseline cortisol higher among men. Length of unemployment not related to baseline cortisol or reactivity. Age differed significantly across reactivity groups, and was negatively associated with cortisol.	3/5	1/5
Grossi et al., 2001	85 long term unemployed (>6 months) (56% female) Mean ages for women: low financial strain 41±8 years, high financial strain 44±10 years; Men: low financial strain 43±9 years, high financial strain 42±9 years	Saliva	Total cortisol output (sum of log-transformed values across the day); Slope (log-transformed values)	Cross-sectional, Observational, Within-Subjects	No significant differences in men on cortisol relating to health behaviours or financial strain. In women, cortisol levels were higher in those reporting high financial strain. Differences in diurnal rhythm observed related to financial strain, controlling for anxiety and number of cigarettes smoked.	4/5	1/5
Maier et al., 2006	173 unemployed; 71 short-term (<12 months), 102 long-	Blood	Single-sample cortisol level	Prospective, Observational,	Cortisol levels increased prospectively in the short-term unemployed; men showed	2/5	0/5

Unemployment & Cortisol

	term (42.3% and 39.2% female, mean age 39.5±9.7, 44.7±9.5 years, respectively)			Between-Subjects	continuous prospective increase, women showed increases in the first 6 months and then decreased. Higher baseline levels seen in older participants – increased in first 6 months and then stabilised. Continuous increases in younger unemployed participants, becoming comparable with older participants after 12 months. Cortisol levels higher in long-term unemployed.		
Dettenborn et al., 2010	59 participants; 28 employed (57.1% female; mean age 36.74±11.04 years), 31 unemployed (96.8% female; mean age 32.55±9.28 years).	Hair	Hair cortisol concentration	Retrospective, Observational, Between-Subjects	Unemployed participants exhibited higher levels of cortisol in first and second hair samples (preceding 6 months) than employed participants.	5/5	2/5
Gallagher et al., 2016	110 participants; 59 employed (69.5% female, mean age 39.8±11.91), 51 unemployed (68.6% female, mean age 35.4±12.67)	Saliva	Total cortisol output (AUC _G), Awakening Response (T2-T1, controlling for T1. Log-transformed values), Diurnal Rhythm (log-transformed values)	Cross-Sectional, Observational, Between-Subjects	Overall cortisol output higher in employed participants. Blunted awakening response in unemployed even when controlling for confounds. Larger cortisol:DHEAS ratio in the employed.	5/5	3/5

Table 3. A summary of studies comparing cortisol output of employed and unemployed participants

Paper	Cortisol affected by unemployment?	Stress affected by unemployment?	Other cortisol/stress findings?	Number of samples per day, Number of days per participant	Design	Appropriate methodological controls and risk of bias
Brenner & Levi, 1987	Yes	Yes	After the first year of unemployment biological stress reaction is more uniform.	1 2-7 (depending on group)	Prospective	No cortisol controls mentioned Age- and sex-matched controls. Other variables controlled for (self-rated cigarette and alcohol use)
Hall & Johnson, 1988	No	No	Higher proportion of unemployed participants in the “high cortisol” group. Unemployed had higher levels of depression and lower social support. No difference in stressful life events.	1 1	Cross-Sectional	No cortisol controls mentioned. Confounding factors assessed. Standardised unemployment reason (redundancy).
Arnetz <i>et al.</i>, 1991	Yes	Yes	“Mastery has a positive effect on cortisol” Cortisol in the unemployed reduced after the first year	1 Up to 7 across 2 years	Prospective	No cortisol controls mentioned. No participant controls mentioned.
Claussen, 1994	No	Yes	Depression and anxiety scores significantly higher for unemployed, but no significant difference in cortisol.	1 1-2	Prospective	Time of day for cortisol sampling varied, however time since 8am was accounted for. Reference samples were age and gender standardised. Extensive physiological, demographic and individual

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						confounders controlled for.
Ockenfels <i>et al.</i>, 1995	No	Yes	Perceived stress and trait anxiety higher in unemployed, but no significant difference in cortisol. Length of unemployment and trait anxiety not related to cortisol. Perceived stress related to higher cortisol.	6 2	Cross- Sectional	Cortisol taken over two weekdays to control for elevation due to novel stimulus. Diary taken to record health behaviour that affects cortisol. Anticipation controls made. Pregnant & nightshift workers excluded.
Dettenborn <i>et al.</i>, 2010	Yes	Yes	Cortisol concentration was slightly lower in the most recent three months. Perceived stress was higher amongst unemployed.	N/A	Cross- Sectional	Strict exclusion criteria. Hair used for cortisol measurement; aggregate measure not affected by extraneous conditions. Confounds controlled for
Gallagher <i>et al.</i>, 2016	Yes	Yes	Lower overall in unemployed than employed. CAR lower in unemployed. Perceived stress higher in the unemployed.	4 2	Cross- Sectional	Strict exclusion criteria. Two days' worth of cortisol taken. Appropriate cortisol controls taken.