JCN Journal of Clinical Nursing

Journal of Clinical Nursing

DISCURSIVE PAPER

Allostatic load: a useful concept for advancing nursing research

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Aims and objectives. To elucidate the historical development of the allostatic load concept, alongside its use in nursing research, and to explore how allostatic load has been investigated among two stress-vulnerable populations.

Background. 'Stress' is a prominent term in understanding the development of disease. Allostatic load is among several approaches undertaken to quantify the magnitude of stress and understand how stress can affect health.

Method. We explored the advent of allostatic load including its antecedents, and consequences. We used an exemplar case to apply the concept. We reviewed studies that used allostatic load among workers and women of childbearing age.

Results. There remains a need to consolidate a common definition and operationalisation of allostatic load. Despite this need for further work, allostatic load is a good fit for nursing science which focuses on the client, environment and health. Only 12 studies explored allostatic load among workers ($n = 6$) and women of childbearing age ($n = 6$). In some studies, allostatic load was used as a predictor while in others it was used as an outcome. None of the studies considered it as a mediator.

Conclusions. The concept of allostatic load holds promise for nursing researchers to operationalise a holistic view of multiple stressors and to quantify their effects on health. Studies are needed to affirm the role of allostatic load as a potential mediator between multiple stressors and outcomes. Longitudinal studies are also needed to demonstrate a causal pathway from stressor exposure to tertiary outcomes such as chronic conditions and morbidity.

Relevance to clinical practice. Allostatic load is a useful concept for nurses working with stress-vulnerable populations. With the use of an interpretable allostatic load index, nurses will be able to intervene at various stages of the allostasis–adaptation process (stress-response) and adjust interventions accordingly.

What does this paper contribute to the wider global clinical community?

- Nurse researchers and clinicians working with stress-vulnerable populations need clear points of intervention and ability to determine impact of the interventions in the short term.
- The concept of allostatic load is useful at broader levels, including further developing measurement of multiple levels of stress that could take structural inequalities, toxic and traumatic stress into account as predictors in all studies. This concept is also useful in advocating for policies that decrease stress and allostatic load as a way to build a culture of health and decrease burden, morbidity and costs of stress-related disease.
- In the future, nursing is well positioned to place the concept of allostatic support within the theoretical framework and operationalise it – in research and in practice.

Key words: allostatic load, biomarkers, concept analysis, nursing research, stress, vulnerable populations, women of childbearing age, workers

Accepted for publication: 20 January 2017

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Aims

Nursing's meta-paradigm defines the basis of nursing's work as focused on the person, environment, health and nursing (Fawcett 1984). Stressors are a ubiquitous aspect of 'environment'. Types of stressors that must be taken into account include those at each eco-social level which are cumulating and interacting, including social determinants, marginalised identities, socio-economics and interpersonal and intrapersonal factors (Juster *et al.* 2010). The literature is replete with evidence supporting a strong relationship between socio-environmental stressors and health outcomes (National Center for Health Statistics 2012, Cohen *et al.* 2013). Nursing care includes health promotion and risk reduction interventions that address this stress diathesis. These are necessarily complex because the stressors and adverse effects are complex while the clients are diverse. Nursing research could be enhanced by a theory that elucidates a mechanism for assessment of the near-term impact of our interventions (i.e. have a valid proxy endpoint) without having to await the long-term endpoint of morbidity or mortality. The theory of allostasis, and the core concept of allostatic load are excellent candidates for this purpose. The aim of this discursive paper was to provide a concept analysis of 'allostatic load' to advance its use in nursing research.

Background

McEwen (1998) proposed the concept of allostatic load (AL) to explicate how chronic life stressors, including toxic and traumatic stress, impact individuals' health via the physiological responses to such chronic stressors. The concept of AL has been applied in research across various disciplines and findings have generally confirmed that cumulative effects of social and environmental stressors increase the risks for physiological dysregulation and ill-mental and physical health, especially among vulnerable groups (Seeman *et al.* 1997, 2014, McEwen 2000, 2004, Read & Grundy 2012). The clinical value of this concept is that it could serve as a signal of health risk early enough (i.e. when the physiological dysregulation is still subclinical) to lead to interventions that may prevent further deterioration of health and thus prevent future associated morbidity and mortality. For research purposes, it could also serve as a near-term proxy outcome or endpoint in clinical health promotion and risk reduction studies (Juster *et al.* 2010). Despite its promise, AL remains underused in nursing research.

There may be several reasons for underuse of this concept (McEwen & Wingfield 2010, Read & Grundy 2012). A recent systematic review by a nurse researcher exploring the concept of AL among 58 studies indicated the lack of homogeneity in the operationalisation and measurement of AL (Beckie 2012). Beckie (2012) also noted inconsistencies in the study results. For example, some studies were able to show a strong relationship between socio-economic status (SES) and AL biomarkers (Seeman *et al.* 2004), while others did not (Dowd & Goldman 2006). There were also variations in the selection and number of indicators used in operationalising the concept, which usually are added together into an AL index (Juster *et al.* 2010). There's also a lack of consensus about how best to score the AL index (Beckie 2012). Thus, work remains to advance this promising concept into one that can be broadly and consistently used for health research.

Design and method

In this discursive paper, we extend Beckie's (2012) work. Having selected a concept and determined the aim, we will follow the rest of the steps outlined by Walker and Avant (2005). The work to identify uses of the concept and determine defining attributes has been accomplished by others (McEwen & Seeman 1999), but we will summarise. We will identify antecedents and consequences. The concept has already been situated in a theoretical framework (Beckie 2012), but we will illustrate this with a model case. We will discuss issues related to empirical referents. Finally, we will extend focus on cases by looking at two small sets of studies that used AL to research stress effects on health of workers and childbearing women.

Evolution of the concept

Homeostasis

In 1932, Cannon introduced the term homeostasis to describe the tight regulation of physiological and biochemical function (Cannon 1932). Homeostasis involves the maintenance of balance within the bodily systems. With self-correcting negative feedback actions, it could reduce variability and maintain constancy from those systems where invariability is a characteristic of a healthy system (Sterling & Eyer 1988). Those physiological systems work in concert to re-establish the body's initial conditions whenever one or more of the systems exhibited perturbation. As such, homeostatic systems are those where a narrow physiological range is indicative of health and deviance from this range is an indication of pathology [e.g. an elevated body temperature (Carlson & Chamberlain 2005)]. However, the homeostasis concept of stable states and feedback loops is

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insufficient to capture the complexity of physiological systems or account for the variability of integrative networks of adaptation to environmental stressors (Goldberger *et al.* 2002). Hence, the theory of allostasis was developed.

Allostasis

Allostasis refers to the mechanisms through which physiological systems adapt to a changing environment or to stressful challenges (Sterling & Eyer 1988, Karlamangla *et al.* 2002, McEwen 2002). The resting points change according to dynamic biological processes. Variability is a healthy adaptive mechanism in response to environmental demands, which is in contrast to homeostasis which supports stability (Carlson & Chamberlain 2005). Sterling and Eyer (1988) proposed allostasis as the process of achieving stability through change.

AL and allostatic overload

McEwen and Stellar (1993) elucidated the concept of AL as a multisystemic approach to understand the cumulative effects of stress on health as the body responds to stressors that are chronic or severe enough to force adaptation. This central concept, AL, refers to the accumulation of wear and tear on interacting physiological systems from the adaptation process (McEwen & Seeman 1999). This physiological wear and tear is a natural consequence or the price paid for the adaptation. Variation in AL among individuals may reflect individual differences in exposure to stressors and/or the ability to adapt to environments and challenges (Lipowicz *et al.* 2014). It may also reflect allostatic supports they find or receive, which can be multiple and synergistic (Friedman & McEwen 2004). In essence, given stressors and physiological responses to them, if the allostatic load is not too high and adaptation occurs, health is likely to be maintained. If the allostatic load is too high (i.e. if there is allostatic overload), the price paid is dysregulation across multiple systems which leads to disease development. Read and Grundy (2012) defined (high) AL as 'a sub-clinical dysregulation state, resulting from the body's response to stress' (p.1). Allostatic overload is a more extreme form of AL. Allostatic overload, which is AL at the pathological level, can result from sustained, severe or repeated stress, the failure to habituate to repeated challenge, the inability to shut off allostatic responses and inadequate allostatic responses (McEwen & Wingfield 2010).

Antecedents and consequences

Antecedents refer to the events or attributes that must precede the occurrence of a concept (Walker & Avant 2005). Antecedents that occur prior to AL include psychosocial factors (e.g. low socio-economic status, stressful life events including trauma) and individual factors (e.g. post-traumatic stress, isolation or maladaptive coping). These can be thought of as occurring at all eco-social levels (Bronfenbrenner & Morris 2006) and so would include structural inequalities and time-specific stressors, such as exposure to a disaster, war or famine.

A variety of types of stressors have been considered as antecedents. For example, in the National Health and Nutrition Examination Surveys, the antecedent, race, was associated with AL. Blacks had higher AL index scores than did Whites at all ages (Geronimus *et al.* 2006). The differences in AL index scores increased with age. Black women, in particular, had higher AL index scores compared with either Black men or White women. Lower SES (lower education, occupational status, income) and greater social challenges (recent widowhood, high demands) have been reported to be highly correlated with higher AL (Weinstein *et al.* 2003). A study in Alzheimer patients' caregivers showed a greater number of negative life events related to higher AL (von Kanel *et al.* 2003). Among the older, ties with close friends and/or neighbours have been reported in relation to lower AL for both men and women (Seeman *et al.* 2004). Type A personality traits were associated with higher AL in a large sample (Sun *et al.* 2007). Inactivity and poor diet have also been reported in relation to higher AL (Juster *et al.* 2010).

Consequences refer to the events that result from the occurrence of a concept (Walker & Avant 2005). Consequences that could occur as a result of AL include the leading causes of death for vulnerable populations whose stress levels are higher by definition. Consequences of AL include negative health outcomes such as cardio- and cerebrovascular disease, cognitive deficits, weaker physical performance, depression and premature mortality (Seplaki *et al.* 2004, Szanton *et al.* 2009). In the MacArthur Studies of Successful Aging, AL index score explained 35% of socio-economic variation in mortality (Seeman *et al.* 2004).

Theoretical framework and model case

The British Economic and Social Research Council's National Centre for Research Methods Working Paper elaborated a conceptual framework with three stages in the allostasis–adaptation process (Read & Grundy 2012, p. 3). The primary mediators between stress and outcomes are neuroendocrine responses (i.e. stress regulation hormones such as cortisol, oxytocin or catecholamines). Secondary outcomes are (potentially still subclinical) dysregulations that can be seen in immune, metabolic, cardiovascular and anthropometric indicators (i.e. C-reactive protein, glucose,

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blood pressure, hip–waist ratio). Tertiary outcomes are the clinical manifestations that develop as dysregulations accumulate [i.e. poor subjective health, cognitive decline, disease states and premature death (Read & Grundy 2012)]. The premise and promise of AL is that a cumulative index that captures levels of multiple biomarker or anthropometric indicators can signal overload in time to provide a clinical response and prevent adverse outcomes.

A model case scenario can illustrate this allostasis–adaptation process (see Fig. 1). Imagine first, a scenario where overload occurs. A 22-year-old Latina immigrant hotel housekeeper gave birth by Caesarean to an infant with a genetic anomaly who was admitted to the NICU. The stressors are young age, immigration status, non-native English speaker, low wages, surgical delivery and separation from the infant. Primary mediators involve elevated cortisol and dysregulated oxytocin. Secondary outcomes appear as sleep alterations with changes in insulin levels, altered immune and inflammatory responses and mildly elevated blood pressure. The tertiary outcomes manifest as near- and long-term outcomes. In the near term, she experiences fatigue, weight gain, delayed bonding and slow Caesarean wound healing. In the longer term, she develops type 2 diabetes, depression, chronic pain from adhesions and hypertension. Her adaptation to motherhood is not fulfilling to her, and she chooses not to risk having any additional children, especially given depression and early ill health. It would have been possible, however, to have allostasis and adaptation be the result without adverse outcomes. Imagine an alternative scenario in which her stress had been reduced with a regular Spanish interpreter in the NICU, ability to Skype with her mother in Mexico, adequate insurance to prevent worry, maternity leave to accommodate the slow recovery from surgery and the need to be with the infant, as well as nursing home visiting to support her maternal development, monitor her low mood and provide health promotion interventions to support her in regaining healthy sleep and diet until her blood glucose and blood pressure normalise. Her adaptation to mothering a child with chronic health needs becomes a source of pride, and she channels some of her healthy energy into becoming an interpreter in the hospital's NICU.

Empirical referents

Empirical referents are the measurable ways to validate the occurrence of a concept (Walker & Avant 2005). To operationalise AL, measurement of biomarker and anthropometric indicators chosen to represent the primary mediator response

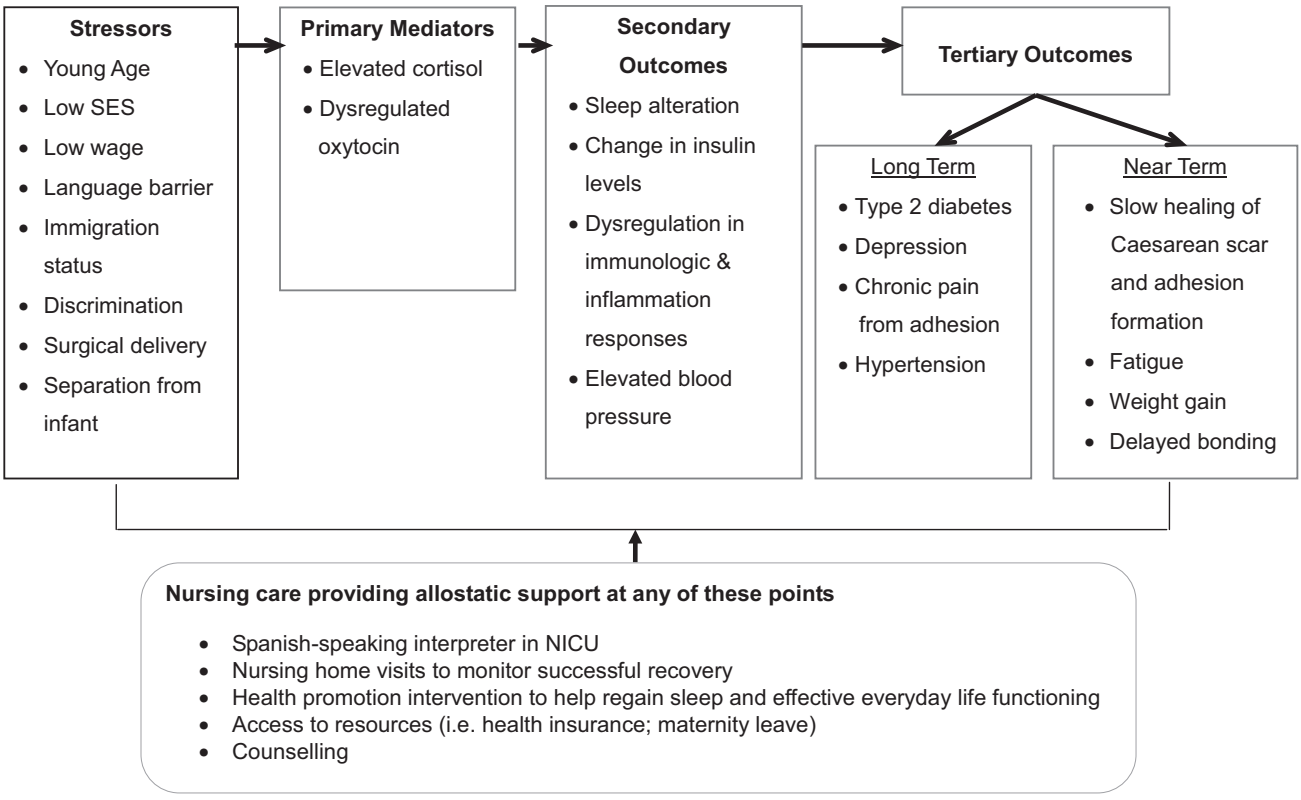

Figure 1 Model Case Illustrating Read and Grundy's (2012) Allostasis–Adaptation Process.

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and secondary outcomes are combined in a clinometric index – an AL index score. When AL was first proposed, an AL index of 10 biomarkers was used to measure the concept. The 10 original AL measures included systolic blood pressure (SBP), diastolic blood pressure (DBP), waist–hip ratio (WHR), high-density lipoprotein (HDL), total HDL/cholesterol ratio, total cholesterol, dehydroepiandrosterone sulphate (DHEA-S), urinary free cortisol, noradrenaline and adrenaline (Seeman *et al.* 1997). However, studies have since used a variety of biomarkers, some using additional biomarkers (Goldman *et al.* 2006, Glei *et al.* 2007, Bellingrath *et al.* 2009) and others using fewer (Gersten 2008, Loucks *et al.* 2008, Evans & Schamberg 2009) based on the outcomes of interest that they are trying to predict or feasibility.

In measuring AL, each of the different physiological systems must be represented. However, there are inconsistencies in the combination of indicators included in AL index across studies (Beckie 2012, Read & Grundy 2012). Given the variation in which indicators are included in the AL index, it is not surprising that there are inconsistencies in study findings.

Scoring is also a source of inconsistency. A summation approach is the most often used method to calculate the index score. Individuals are ranked by the indicator values, ranging between the highest and lowest risks (Seeman *et al.* 1997). Individuals in the highest risk quartile for each indicator are '1' and others are '0'. These are summed so that those with the highest sum score have the highest AL and are considered at risk for poor tertiary outcomes (Read & Grundy 2012). Thus, AL has been operationalised as a count-based multisystemic index representing the sum of biomarkers and anthropometric indicators falling within a high-risk percentile based on the sample's distribution of values (Juster *et al.* 2010). This approach presents some unique challenges in that there is loss of granularity in the data reduction and the amount of risk depends on the nature of the sample itself. Alternative scoring approaches have been considered (Karlamangla *et al.* 2002, Seplaki *et al.* 2005, Gruenewald *et al.* 2006) and more consensus may emerge in the near future.

Extending the analysis of AL concept from clinical case to research examples with two vulnerable populations

The model case scenario above was a clinical example at how the concept of AL could function within a single individual. In the near term, it is more likely that AL's usefulness in nursing will be as a concept deployed in research. So we will extend the illustration of AL as a concept linking stress and adverse health outcomes by exploring studies reported about two stress-vulnerable populations, workers and women of childbearing age.

The workplace represents a major source of stress and thus can impact AL leading to poor health outcomes. First, work relates to SES, and lower SES has shown to be strongly correlated with high AL (Szanton *et al.* 2005). Second, work where employees experience high demand and low control (a phenomenon known as job strain) results in high stress (Karasek & Theorell 1992). Some workers are therefore at risk for high stress and poor health outcomes, making it important to explore AL among workers.

Trauma exposure and sequelae are strongly related to gender, and pregnancy is another stress exposure unique to females, making women another key group to study in relation to AL. McEwen and Seeman (1999) pointed out that early traumatic events combined with ongoing life stress could contribute to AL. In a study with a random sample of 1442 subjects from the USA, 32·3% of women reported childhood sexual abuse (CSA), which was twice as much as in men (Briere & Elliott 2003). In a review of population-based studies, 10–69% of women reported intimate partner violence (Krug *et al.* 2002). The peak age of trauma exposure for women is in adolescence, so post-traumatic stress – where re-experiencing the trauma in memory, flashbacks or nightmares is a hallmark of the disorder and an intrapersonal chronic stress – is also prevalent early in the lifespan and during reproduction (Breslau 2002). There is growing evidence suggesting the causal links between adverse childhood events, adult traumatic events, traumatic stress sequelae and physical and reproductive health outcomes (Felitti *et al.* 1998, Campbell 2002, Groer *et al.* 2016). Thus, women of childbearing age who are experiencing traumatic stress are another priority population among which to explore the mediating role of AL on the association of stress with adverse health outcomes.

To find articles with which to explore these research 'cases' to illustrate the AL model, we searched PubMed, Web of Science, CINAHL, PsycInfo and Scopus databases using the keywords: AL and workers and AL and women of childbearing age. Our initial search yielded 207 articles across all the databases. We only included articles that were written in English and for which full texts were provided. We then limited selection to the handful that specifically used the theory of allostasis as their conceptual framework for the study in relation to workers (six papers, Table 1) or women of childbearing age (six papers, Table 2).

AL and workers

Six studies were identified exploring AL among workers. The studies were conducted in industrialised nations, included men and women, and focused primarily on industry employees. The studies took place in across several countries including the USA, Sweden, Germany and China. There were

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Table 1 Allostatic load and workers

Reference (author/year)	Sample (workers vs. women)	Study Purpose	AL Definition	AL Component	Scoring Method	Role of AL (mediator or predictor)	Study Findings	Notes
de Castro *et al.* (2010)	*N* = 30 male Latino day labourers in Seattle Washington, USA	This was a pilot study – cross-sectional design. To evaluate the feasibility of conducting a research project focused on stressors (work related, economic, social) and AL among day labourers	The physiological effects of chronic stress	SBP, DBP, salivary cortisol, WHR, CRP and BMI	The sum of the number of biological measures on which each participant scored in the top quartile of risk for the total sample	Outcome (dependent variable)	Average age was 46 years and the average length of residency in the USA was 12 years. 47% were married and the majority (97%) spoke Spanish and were from Mexico (77%). Workers who reported more stressors (work, economic, social) had higher AL physically and mentally. They found no statistical significance between the groups compared with those with low AL who have been working as day labourers for just under 5 years	Suggested need for studies to explore AL as a mediator between stressors and clinical health outcomes. Used the finger prick and sterile lancet to collect the blood for the CRP. Trust and collaboration between researchers and community partners are very important. They calculated AL score by summing the number of parameters in which levels were in the highest quartile (at or above the 75% quartile) and the parameters in the lowest quartile. AL scores can range from 0–6. The AL scores were then further dichotomised into two categories low and high

Table 1 (continued)

Reference (author/year)	Sample (workers vs. women)	Study Purpose	AL Definition	AL Component	Scoring Method	Role of AL (mediator or predictor)	Study Findings	Notes
von Thiele *et al.* (2006)	*N* = 241 healthy women working in two public healthcare organisations in Stockholm, Sweden	This was a secondary data analysis. To investigate the relationships between self-rated recovery from work stress and biological dysregulation in terms of AL and individual biomarkers, respectively, in healthy women within the public healthcare sector	A multisystems approach describes how daily stress relates to health and disease	SBP, DBP, HR, HDL, LDL, LDL/HDL ratio, TC, TG, serum DHEA-S, glucose, HbA1c, prolactin and WHR.	The sum of the number of biological measures on which each participant scored in the top quartile of risk for the total sample (except for HDL and DHEA-S, where inclusion into the lowest quartile constitutes risk)	Outcome	No significant differences in the demographic characteristics of study participants. The fatigued women had an increased risk for high AL. In contrast, there was no significant difference in individual biomarkers between recovered and nonrecovered women	Insufficient recovery from work stress may result in high AL. Acknowledged that the operationalisation of AL differs between studies depending on the type and number of biomarkers available
Sun *et al.* (2007)	*N* = 1219 healthy Chinese employees including both men (50%) and women (50%) from five industries in China	This was a cross-sectional study design. To determine the relationship between job strain and AL	1. The accumulation of wear and tear on physiological systems from the process of adaptation to chronic stress. 2. A possible biological warning system for health outcomes. 3. The cumulative physiological toll that may be exacted on the body through its attempts to adapt to life's demands	FIB, CRP, cortisol, adnephrin, BMI, WHR, SBP, DBP, HbA1c, IGR, TC/HDL, HDL and TG	The sum of the number of biological measures on which each participant scored in the top quartile of risk for the total sample (except for HDL in the lowest quartile)	Outcome	The average age was 38. About 70% had a college level education. High job strain had higher AL compared to low job strain. Positive association between AL and age (r = .203, p < 0·001), and positive relationship between AL and education level (lower education yielded to higher job strain) ($r = -0.122$, $P < 0{\cdot}001$)	Excluded people already diagnosed with conditions such as hypertension and diabetes or taking medication for these conditions; also measured type A behaviour which showed to be associated with higher job strain. They also assessed for behavioural responses associated with stress such as smoking, alcohol intake, diet and exercise

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Table 1 (continued)

Reference (author/year)	Sample (workers vs. women)	Study Purpose	AL Definition	AL Component	Scoring Method	Role of AL (mediator or predictor)	Study Findings	Notes
Schnorpfeil *et al.* (2003)	*N* = 324 employees from an airplane manufacturing plant in Germany	This was a cross-sectional study design. To evaluate the relationship between objective health status and work characteristics in the workers	A biological warning system	BMI, WHR, SBP, DBP, CRP, TNF-α, HDL, cholesterol, DHEA-S, HbA1c, urinary cortisol, adrenaline, noradrenaline and albumin	The sum of the number of biological measures on which each participant scored in the top quartile of risk for the total sample (except for HDL, DHEA-S and cholesterol in the lowest quartile)	Outcome	Older individuals and men had higher AL scores than younger participants and women. Job demand related significantly to AL	
Hasson *et al.* (2009)	Female employees from the healthcare sector (*n* = 241) and IT/media sector (*n* = 98), Stockholm, Sweden	To investigate how biological dysregulation, in terms of AL, relates to self-rated health (SRH) in women	A multisystems approach describes how daily stress relates to health and disease.	SBP, DBP, HR, HDL, LDL, LDL/HDL ratio, TC, TG, serum DHEA-S, glucose, HbA1c, prolactin and WHR	The sum of the number of biological measures on which each participant scored in the top quartile of risk for the total sample (except for HDL and DHEA-S in the lowest quartile)	Outcome	A poor self-rated health, along with occupational sector, age and education, were significantly associated with a high AL, particularly for those working within the healthcare sector.	
Li *et al.* (2007)	N-504 industrial employees, China	To evaluate the relationship between job stress and glycolipid metabolic change in healthy industrial employees in China	The price of allostasis	BMI, WHR, HbA1c, B-cell function, TC, TG, HDL, LDL, adiponectin and visfatin	The sum of the number of biological measures on which each participant scored in the top quartile of risk for the total sample (except for HDL, adiponectin and B-cell function in the lowest quartile)	Outcome	50% were male. Most were married (78%). About 70% had a college level education. High job stress was extremely correlated with increased glycolipid AL score. Low job control showed to be the main stressor impacting health outcomes in the participants	

AL, allostatic load; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; DHEA-S, dehydroepiandrosterone sulphate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride; FIB, fibrinogen; IGR, insulin–glucose ratio; HbA1c, glycosylated haemoglobin; HR, heart rate; WHR, waist–hip ratio; CRP, C-reactive protein; TNF-α, tumour necrosis factor alpha.

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Table 2 Allostatic load and women

Reference (author/year)	Sample (workers vs. women)	Study Purpose	AL Definition	AL Component	Scoring Method	Role of AL (mediator or predictor)	Study Findings	Notes
Lindfors *et al.* (2006)	*N* = 200 women with no previously diagnosed pathology in Sweden	To investigate how physiological dysregulation, in terms of AL and clinical risk, respectively, relates to sense of coherence (SOC) in women with no previously diagnosed pathology	The dysregulation in multiple bodily systems in response to stress challenges over the life course	Resting SBP and DBP, HDL, TC, HbA1c, WHR and PEF	The sum of the number of biological measures on which each participant scored in the top quartile of risk for the total sample (except for HDL and PEF in the lowest quartile)	Predictor	All women were 43 years old. 77·5% were married or living with a partner. 94·5% had children. 51·5% had a lower education. AL was found to predict future SOC, whereas clinical risk did not	
Gustafsson *et al.* (2012)	*N* = 394 women in Sweden	To examine whether social and material adversity over the life course is related to AL in mid-adulthood	The cumulative dysregulations which eventually develop across multiple interconnected physiological systems as a result of frequently repeated or chronic activation over the life course	SBP, DBP, BMI, waist circumference, fasting glucose, TC, HDL, TG, apolipoprotein A1 and B, CRP and diurnal salivary cortisol AUC	The sum of the number of biological measures which was divided into tertiles (coded 0, 1, 2), except for cortisol (coded symmetrically with sextile: 1 and 6 = 2, 2 and 5 = 1, 3 and 4 = 0) and HDL (coded inversely: 2, 1, 0)	Outcome	All women were 43 years of age. Social adversity accumulated over the life course was related to AL, independently of cumulative socio-economic disadvantage. Moreover, social adversity in adolescence was related to AL, independently of cumulative socio-economic disadvantage and also of later adversity exposure during adulthood	

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Table 2 (continued)

Reference (author/year)	Sample (workers vs. women)	Study Purpose	AL Definition	AL Component	Scoring Method	Role of AL (mediator or predictor)	Study Findings	Notes
Morrison *et al.* (2013)	*N* = 6131 pregnant women (*n* = 1138) and nonpregnant (*n* = 4993) women in the USA	To determine whether AL can be measured in a meaningful way during pregnancy	The cumulative wear and tear on the body resulting from exposure to chronic stress	SBP, DBP, 60-second pulse rate, homocysteine, CRP, serum albumin, HbA1c, HDL, TC and creatinine	The sum of the number of biological measures on which each participant scored in the top quartile of risk for the total sample (except for HDL and serum albumin in the lowest quartile)	Outcome	Women were aged 15–44 years. Among pregnant women, 56·4% were non-Hispanic White, 14·2% were non-Hispanic Black, 16·1% were Mexican American, and 13·2% were other races; Among nonpregnant women, 66·1% were non-Hispanic White, 12·6% were non-Hispanic Black, 9·4% were Mexican American, and 11·9% were other races. The distribution of each AL-related biomarker differed significantly between pregnant and nonpregnant women. Among nonpregnant women, higher AL was found in women who are Black, are older and who have lower incomes). However, these associations were not seen in pregnant women	

Table 2 (continued)

Reference (author/year)	Sample (workers vs. women)	Study Purpose	AL Definition	AL Component	Scoring Method	Role of AL (mediator or predictor)	Study Findings	Notes
Wallace *et al.* (2013)	*N* = 886 women from the Bogalusa Heart Study in the USA	To examine more closely the relationships between AL, race and adverse birth outcomes within the context of neighbourhood-level poverty	The dysregulation across the body's multiple physiological systems responsible for maintaining equilibrium when faced with physical or social challenges	SBP, DBP, TC, HDL, LDL, TG, glucose, insulin and waist circumference	The sum of the number of biological measures on which each participant scored in the top quartile of risk for the total sample (except for HDL in the lowest quartile)	Predictor	Women were aged 13–41 years. 59·4% of women are White, and 40·6% of women are African American. African American women resided in more impoverished neighbourhoods and had higher AL scores compared with Whites; however, AL was not associated with preterm birth or low birthweight.	
Wallace and Harville (2013)	*N* = 123 women at 26-28 weeks gestation in the USA	To identify associations between AL and birth outcomes and to assess differences in AL and its relation to birth outcomes between White and Black women	The wear and tear on the body that arises from chronic, prolonged or persistent activation of allostatic effectors and a breakdown of the regulatory feedback mechanisms	Cholesterol, cortisol, DHEA-S, HbA1c and SBP	The sum of *z*-scores for all five biological measures	Predictor	Women were aged 20–35 years. All are White or African American. Black women had a lower AL index than White women. Gestational age was associated with AL. A significant interaction with age indicated that the effect wasn't as strong at higher maternal ages. There was no racial difference in the effect of AL on birth outcomes	

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Table 2 (continued)

Reference (author/year)	Sample (workers vs. women)	Study Purpose	AL Definition	AL Component	Scoring Method	Role of AL (mediator or predictor)	Study Findings	Notes
Hux *et al.* (2014)	N = 877 women in the USA	To determine whether past history of having had a pregnancy with low birthweight outcome is associated with higher AL	The cumulative burden of chronic physiological and psychological stress	SBP, DBP, BMI, CRP, serum albumin, HbA1c, HDL, TC and creatinine	The sum of the number of biological measures on which each participant scored in the top quartile of risk for the total sample (except for HDL and serum albumin in the lowest quartile)	Predictor	Women were aged 17–35 years. 62·4% are White, 20·1% are Latino/Hispanic, 14·9% are Black, and 2·6% are other races. Women with history of small for gestational age or preterm birth had higher AL than did those with normal birthweight outcomes	As the study was poorly designed, it is difficult to determine whether differences in AL occur prior to or after pregnancy as a result of the adverse outcomes

AL, allostatic load; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; DHEA-S, dehydroepiandrosterone sulphate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride; FIB, fibrinogen; HbA1c, glycosylated haemoglobin; WHR, waist–hip ratio; CRP, C-reactive protein; AUC, area under the curve; PEF, peak expiratory flow.

significant variations in the operationalisation of AL across the studies. The number of indicators used in the AL index ranged from 6–14 (Table 3). All the studies included primary and secondary indicators in the AL index, and all the studies reviewed used the high-risk scoring approach (e.g. highest quartile for BMI or glucose, lowest quartile for HDL cholesterol or DHEA-S). In all of the studies, AL was used as a dependent variable (an outcome). None of the studies used AL as a mediator or an independent variable (a predictor). All of the studies found a positive relationship between the stressors (i.e. job strain, recovery from work stress) and AL index score. None of the studies explored tertiary outcomes such as chronic diseases, quality of life or mortality.

AL and women of childbearing age

Two of the articles focused on pregnant women to examine the relationships between AL and adverse birth outcomes. All six studies included women of childbearing age, with the age ranging from 13–44 years. Four studies used primary and secondary outcome indicators in the AL index (Table 3). All of the studies except one used the upper and lower quartile scoring approach to AL. Wallace and Harville (2013) used the sum of the *z*-scores for the biomarkers. Again these six studies modelled either the contributing factors of AL (as a dependent variable) or adverse outcomes of AL (AL as a predictor). The predictors of AL included PTSD, age, race, ethnicity, chronic work, financial and caregiving stress, lifestyle factors (e.g. exercise, alcohol consumption and smoking), social adversity (e.g. parental illness or loss, residential instability, exposure to threat/violence) and occupational social class. Adverse outcomes of AL included sense of coherence (Lindfors *et al.* 2006) and adverse birth outcomes [e.g. preterm birth, low birthweight (Wallace & Harville 2013)].

Conclusions

We aimed to extend analysis of the concept of AL to advance its use in nursing research as it is a concept well suited to the nursing meta-paradigm and to health promotion and risk reduction intervention science. Important papers have recently reviewed and clearly delineated the theory (Read & Grundy 2012) and systematically reviewed AL research (Beckie 2012), and these reviews highlighted areas for further methodological work. It is apparent that we need more consistent operationalisation in terms of indicators to include and scoring methods to apply. From examining these two sets of study reports on different populations to serve as research cases to illustrate the concept in use, we see mostly affirmation for the proposition that stress leads to higher AL and for the proposition that higher AL leads to adverse

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Table 3 Measures of AL across each studies

Reference (Author/year)	Measures of AL
de Castro *et al.* (2010)	SBP, DBP, salivary cortisol, WHR, CRP and BMI
von Thiele *et al.* (2006)	SBP, DBP, HR, HDL, LDL, LDL/HDL ratio, TC, TG, serum DHEA-S, glucose, HbA1c, prolactin and WHR
Sun *et al.* (2007)	FIB, CRP, cortisol, adnephrin, BMI, WHR, SBP, DBP, HbA1c, IGR, TC/HDL, HDL and TG
Schnorpfeil *et al.* (2003)	BMI, WHR, SBP, DBP, CRP, TNF-α, HDL, cholesterol, DHEA-S, HbA1c, urinary cortisol, adrenaline, noradrenaline and albumin
Hasson *et al.* (2009)	SBP, DBP, HR, HDL, LDL, LDL/HDL ratio, TC, TG, serum DHEA-S, glucose, HbA1c, prolactin and WHR
Li *et al.* (2007)	BMI, WHR, HbA1c, B-cell function, TC, TG, HDL, LDL, adiponectin and visfatin.
Lindfors *et al.* (2006)	Resting SBP and DBP, HDL, TC, HbA1c, WHR and PEF
Gustafsson *et al.* (2012)	SBP, DBP, BMI, waist circumference, fasting glucose, TC, HDL, TG, apolipoprotein A1 and B, CRP and diurnal salivary cortisol AUC
Morrison *et al.* (2013)	SBP, DBP, 60-second pulse rate, homocysteine, CRP, serum albumin, HbA1c, HDL, TC and creatinine
Wallace *et al.* (2013)	SBP, DBP, TC, HDL, LDL, TG, glucose, insulin and waist circumference
Wallace and Harville (2013)	Cholesterol, cortisol, DHEA-S, HbA1c and SBP
Hux *et al.* (2014)	SBP, DBP, BMI, CRP, serum albumin, HbA1c, HDL, TC and creatinine

AL, allostatic load; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; DHEA-S, dehydroepiandrosterone sulphate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride; FIB, fibrinogen; IGR, insulin–glucose ratio; HbA1c, glycosylated haemoglobin; HR, heart rate; WHR, waist–hip ratio; CRP, C-reactive protein; TNF-α, tumour necrosis factor alpha; AUC, area under the curve.

outcomes. Further research is needed to test the entire model, with AL as the mediator between stress and adverse outcomes – ideally with prospective designs. If such theory-testing research validates AL as a mediator, that will serve as a more solid test of concept for AL to be used as a proximal endpoint for clinical research.

Relevance to clinical practice

Nurse researchers and clinicians working with stress-vulnerable populations need clear points of intervention and ability to determine impact of the interventions in the short term. Health promotion and risk reduction research is usually behavioural and often depends on self-reported, near-term outcomes such as self-efficacy, intention or observation of behaviour. This is because it is notoriously difficult to demonstrate prevention of disease in the long term. Practical considerations also foster adopting simple designs (i.e. one primary outcome) that cannot represent complexity that we know is operating, and often the outcome has to be a proximal endpoint (e.g. change in mean blood pressure) because follow-up to the manifestation of disease (e.g. prevention of hypertension diagnosis) is not feasible. Clinical practice has constraints that are similar. Intervening early and seeing progress during the sometimes extended period of care needed to achieve the intervention goal are sustaining and reinforcing for both the nurse and the client. Being able to explain the concept of AL to clients, being able to run a panel of tests that yield an interpretable 'AL index' result, and being able to adjust interventions in response would be useful.

The theory of allostasis is useful at broader levels as well, including population health and policy. Further developing measurement of multiple levels of stress could take what we know about structural inequalities, as well as toxic and traumatic stress, into account as predictors in all studies. Tailoring with additional measures for specific populations will also be needed (e.g. measures of job strain and work–life balance for studies of workers, and measures of pregnancy-specific stress for perinatal studies). We could advocate for policies that decrease stress and AL as a way to build a culture of health and decrease burden, morbidity and costs of stress-related disease.

Finally, the concept of AL has been paired with the concept of allostatic support (Friedman & McEwen 2004), but this twin concept has not been synthesised formally. Given the state of the science on AL, there may be higher priority tasks. However, the goal of the theory is to depict not only the scenario where dysregulation from overload leads to disease but also the scenario where allostasis leads to adaptation for optimal health under the circumstances. In the future, nursing is well positioned to place the concept of allostatic support within the theoretical framework and operationalise it – in research and in practice.

Contributions

MAR, YL, JS contributed to the conceptualization and development of the manuscript. MAR and YL conducted the literature reviews.

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