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The effect of 90 day administration of a high dose vitamin B-complex on work stress

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Objective Occupational stress is increasing in Western societies and the impact is significant at a personal, organisational and community level. The present study examined for the first time the efficacy of 3 months administration of two forms of high dose vitamin B complex on mood and psychological strain associated with chronic work stress.
Method Sixty participants completed the 3-month, double-blind, randomised, placebo-controlled trial in which personality, work demands, mood, anxiety and strain were assessed.
Results After individual differences in personality and work demands were statistically controlled, the vitamin B complex treatment groups reported significantly lower personal strain and a reduction in confusion and depressed/dejected mood after 12 weeks. There were no treatment-related changes in other measures of mood and anxiety.
Discussion The results of the study are consistent with two previous studies examining multivitamin supplementation and personal (non-work) feelings of strain and suggestive of significant decreases in the experience of workplace stress after 90 day supplementation of a B multivitamin.
Conclusion Given the direct and indirect costs of workplace stress, these findings point to the utility of a cost-effective treatment for the mood and psychological strain effects of occupational stress. These findings may have important personal health, organisational and societal outcomes given the rising cost and incidence of workplace stress.

KEY WORDS—stress; occupational stress; vitamin B; mood; RCT

INTRODUCTION

In the USA, it has been estimated that costs associated with stress-related work claims are approximately 50% higher than for other work claims (Goetzel *et al*., 1998). Hurrell and Aristeguieta (2005) report that in California alone, claims for stress-related illnesses increased by 560% over a 6-year period. In the same period, Australian stress-related claims increased by 37% from1996–1997 to 2002–2003 (National Occupational Health and Safety Commission [NOHSC], 2003). Direct costs associated with compensation claims exceed more than $A200m every year (Quick *et al*., 1986) and stress-related absenteeism costs the Australian economy $A5.12bn per year (Medibank, 2008). Although the cost of stress-related claims is enormous, there are more important consequences associated with high levels of stress in the workplace that surpass the financial considerations (Quick *et al*., 1986). A Scandinavian meta-analysis estimated that work stress increases the risk of heart disease by 50% (Kivimaki *et al*., 2006). In the Whitehall II study of 10 308 British civil servants (Bosma *et al*., 1997), there was a clear relationship between self-reported stress and increased coronary events for the early middle-aged workers (37–49 years); a relationship believed to be mediated directly through stress-activated neuroendocrine pathways and indirectly through unhealthy coping behaviours (Chandola *et al*., 2008). Stress-related drinking behaviour has been directly related to intensity of perceived stress, the level of control over the stress and available coping resources (Virtanen *et al*., 2009). The Dunedin study, a 32-year longitudinal cohort study found that work stress 'appears to precipitate diagnosable depression and anxiety in previously healthy young workers' (Melchior *et al*., 2007). High levels of occupational stress have been associated with higher levels of personal

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psychological distress (e.g. depression, anxiety and burnout), personal physiological functioning (e.g. hypertension and cardiovascular problems) and lower scores on workplace variables such as lower morale and productivity and higher workplace disengagement (Quick *et al*., 1986; Gillespie *et al*., 2001; Winefield *et al*., 2003). The latter variables can be clustered under the umbrella of 'presenteeism' in which high levels of stress lead to lowered productivity of staff prior to absenteeism (e.g. Pauly *et al*., 2008).

Work stress is a response an individual may experience when the pressures and demands expected of them do not match their resources and skills (Leka *et al*., 2004). Interventions in work stress in Australia generally focus on teaching individuals stress management techniques, such as relaxation. These studies have been of limited success, probably due to the reactive nature of the programmes (Caulfield *et al*., 2004). Another approach is to conduct interventions focusing on *preventable* aspects of stress such as the provision of appropriate evidence-based dietary advice.

Adequate levels of vitamins and minerals are essential for the optimal performance of a host of physiological processes that have both direct (e.g. neurotransmitter synthesis, receptor binding, membrane ion pump function) and indirect (e.g. energy metabolism, cerebral blood supply) effects on brain function (Haller, 2005). It is perhaps unsurprising that a relationship exists between dietary consumption of vitamins and cognitive performance. This issue has been investigated in cross-sectional and prospective studies of the elderly. These have revealed positive relationships between cognitive performance and B vitamin intake (Durga *et al*., 2006) coupled with a negative relationship between cognitive performance and levels of plasma homocysteine (high in B vitamin deficiency; Durga *et al*., 2006). Additionally, B vitamins have been shown to be associated with reduced risk of dementia (Del Parigi *et al*., 2006).

Several B vitamins are integral to the synthesis of neurotransmitters critical to psychological well-being. Folate (vitamin B9) and vitamin B12 are required for single-carbon metabolism involved in the synthesis and metabolism of serotonin, other monoamine neurotransmitters and the catecholamines (Bottiglieri, 1996). Vitamin B6 is a cofactor for aromatic L-amino acid decarboxylase (AADC), an enzyme that catalyses the decarboxylation of a variety of aromatic L-amino acids; it converts L-DOPA to dopamine and hydroxytryptamine (5-HTP) to serotonin (Boadle-Biber, 1993). It has also been shown to regulate the levels of 5-HTP (Calderón-Guzmán *et al*., 2004).

B vitamins and homocysteine

Folate, vitamin B12 and vitamin B6 are implicated in the metabolism of homocysteine, which is produced as a by-product of methionine metabolism. Normally, homocysteine is converted back to methionine or used to create cysteine and other substances in the body. Blocking of the conversion process (e.g. by deficiencies of folate or vitamins B12 and B6) leads to elevated levels of homocysteine. Elevated plasma homocysteine has been prospectively associated with an increase in total and cardiovascular mortality, incidence of stroke, incidence of dementia including Alzheimer's disease, incidence of bone fracture and prevalence of chronic heart failure (Selhub, 2008). It is not completely understood whether blood homocysteine is simply a marker for another factor such as folate or vitamin B12/B6 deficiency, or whether it also plays a direct role in disease pathogenesis (Selhub, 2008).

A clear association exists between stress and homocysteine levels. Kang and colleagues demonstrated a significant relationship in a cohort of 152 workers between perceived job-related stress, cardiovascular risk factors and plasma homocysteine levels (Kang *et al*., 2005). Similarly, Stoney demonstrated (in 34 women) that acute psychological stress, in terms of both mental arithmetic (serial subtractions) and speech stressors, induces rapid concomitant elevations in plasma homocysteine concentrations, blood pressure and heart rate (Stoney, 1999). Stoney hypothesised both that the mechanism driving the homocysteine elevations may be the induction of a rapid decline in vitamin B6 levels by acute stressors and that elevated homocysteine may be one mechanism whereby psychological stress may contribute to the initiation and progression of vascular disease. This certainly sits well with interpretations of data that suggest that chronic stress results in depletion of vitamin B6 (Baldewicz *et al*., 1998) and that vitamin B6 supplementation may in itself be an effective anti-stress strategy (McCarty, 2000).

B vitamins and perceived stress

Several double-blind, placebo-controlled studies have assessed the effects of a multivitamin/mineral product, with a predominance of B vitamins (B1, B2, B3, B5, B6 and B12) plus vitamin C, calcium, magnesium and zinc (Berocca, Bayer AG, Leverkusen, Germany) on self-ratings of stress or psychological well-being. The first was a small pilot trial comparing 28 days administration of Berocca with placebo in 24 male participants to determine its effects on cardiovascular parameters and psychological well-being (General Health Questionnaire-12 (GHQ-12); Willemsen *et al*.,

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1997). Although the results on the GHQ-12 were non-significant, possibly due to the small sample size, they were encouraging enough to stimulate a larger trial in 80 healthy men who received either Berocca or placebo for 28 days. Efficacy was assessed with the GHQ-28, the Hospital Anxiety and Depression Scale, the Perceived Stress Scale, plus a number of simple visual analogue scales. There was a significant benefit for Berocca in terms of anxiety/stress ratings across all psychometric instruments (Carroll *et al*., 2000). Another trial compared the efficacy of 30 days administration of Berocca or placebo in 333 participants selected from 1000 screened volunteers on the basis of high levels of stress (Schlebusch *et al*., 2000). Results from the 300 participants that completed the study showed significant advantages for Berocca across a range of measures including the Hamilton Anxiety Rating Scale and the Psychological General Well-being Schedule (a stress index).

Two more recent laboratory studies have focused on the effects of vitamin supplementation on cognitive performance and stress (Haskell *et al*., 2010; Kennedy *et al*., 2010). The first found that 33-day Berroca supplementation to healthy men ($N = 215$) led to improvements in several measures including general psychological health as assessed using the GHQ-12 and the Perceived Stress Scale (Kennedy *et al*., 2010). The second found that 9-week supplementation with a commercial multivitamin (Supradyn®, Bayer AG) to women aged 25–50 years resulted in better performance on a standardised multi-tasking stressor task (The Multi-tasking Framework; Wetherell and Sidgraves, 2005), coupled with reduced fatigue and improved mood responses to multi-tasking and lower levels of homocysteine (Haskell *et al*., 2010). The results of these two more recent studies suggest that multivitamin supplementation reduces fatigue and stress.

Although valuable, these studies did not specifically address whether multivitamin administration decreases *work* stress. We examined whether a popular multivitamin supplement available in Australia ('Blackmores' Executive B Stress Formula') which contains a complex of mostly B group vitamins improved stress specifically associated with work. Secondary measures also included a range of mood variables. We significantly increased the duration of administration of the multivitamin to 90 days (with a 4-week testing point) relative to the 30 days of the three most closely aligned previous studies (e.g. Carroll *et al*., 2000; Kennedy *et al*., 2010; Schlebusch *et al*., 2000), to exceed the 9-week administration of the Haskell and colleagues study (Haskell *et al*., 2010) and to identify if any greater benefit from multivitamin supplementation would be observed over a longer administration period. As stress has also been shown to be related to a range of personality variables (e.g. Chamorro-Premuzic *et al*., 2008), we used personality as a covariate in all of our analyses. This was also undertaken because some authors have suggested that low levels of micronutrients may be related to differences in mood prior to supplementation (e.g. Benton and Cook 1991; Kaplan *et al*., 1997). We hypothesised that after the influence of personality on self-report measures of occupational strain have been taken into account, participants on the active treatment will show a reduction in workplace strain relative to the placebo after 90 days of administration. A secondary aim of the present study was to examine whether two different delivery mechanisms for the active ingredient (slow release versus normal release) would show differential effects of occupational stress relative to placebo.

METHOD

Participants

Sixty participants (19 men and 41 women ($M = 42.2$ years, $SD = 10.1$ years) completed the 12-week trial (80 participants were enrolled into the trial). The three groups had similar sample sizes (Executive B Active ($n = 20$), Executive B Active sustained release ($n = 22$) and placebo ($n = 18$)). Of the sample, 75.0% were employed full-time ($M = 46.2$ h/week, $SD = 7.2$ h/week), and 25% were employed as part-time or casual ($M = 26.8$ h/week, $SD = 6.76$ h/week).

Materials and procedure

Participants completed the following questionnaires: NEO-PI-R (NEO Personality Inventory-Revised; Costa and McCrae, 1985), the Speilberger State-Trait Anxiety Inventory (Speilberger, 1983) and the Profile of Mood Scale (POMS; McNair *et al*., 1992). The 40-item Personal Strain Questionnaire (PSQ) of the Occupational Stress Inventory-Revised (OSI-R; Osipow, 1998) scale measures three aspects of occupational functioning: occupation stress, psychological strain and coping resources through the assessment of relevant environmental and physical characteristics. Occupational stress is measured by role overload, role insufficiency, role ambiguity, role boundary, responsibility and physical environment. Psychological strain is assessed by the sub-scales vocational strain, psychological strain, interpersonal strain and physical strain.

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Study design

The study was a randomised, triple-blind placebo-controlled study in which 80 participants were randomly allocated into three groups (Executive B Active, Executive B Active sustained release and placebo). Each participant was instructed to take two tablets per day. All measures were assessed at baseline, 30 and 90 days post-treatment.

Executive B

The Executive B Active and the Executive B Active sustained release contained identical ingredients and doses. The only difference was that the Executive B Active sustained release allowed the ingredients to be absorbed at a slower rate over a longer period. The exact ingredients and dose of each ingredient is listed in Table 1.

RESULTS

There were pre-treatment group differences in the number of hours worked ($F_{2,57} = 3.82$, $p = 0.03$) and the number of staff supervised ($F_{2,57} = 4.65$, $p = 0.01$), therefore these variables were treated as covariates. All compliance rates were above 70%, and no significant differences in compliance rates were found between the groups ($F_{2,57} = 0.93$, $p = 0.40$). Also, some participants did not provide complete self-ratings of the all outcome variables, these missing data were distributed randomly and equally across the treatment and placebo groups, with the change in group size being detailed in Table 2. The analyses reported in the succeeding section also controlled for the effects of personality on self-reported measures of strain and mood by entering the five personality variables of the NEO-PI-R as covariates: neuroticism, extraversion, openness to experience, agreeableness and conscientiousness.

Table 1. Ingredients and dose for the Executive B formulations

Vitamin B1 (thiamine hydrochloride)	75 mg
Vitamin B2 (riboflavin)	10 mg
Nicotinamide	100 mg
Vitamin B5 (pantothenic acid from calcium pantothenate 75 mg)	68.7 mg
Vitamin B6 (pyridoxine hydrochloride)	25 mg
Vitamin B12 (cyanocobalamin)	30 μg
Vitamin H (biotin)	20 μg
Calcium ascorbate	145 mg
Ascorbic acid (total vitamin C 250 mg)	130 mg
Vitamin E (D-alpha-tocopheryl acid succinate 41.3 mg)	50 IU
Magnesium phosphate	140 mg
Calcium phosphate	100 mg
Potassium phosphate monobasic	117.3 mg
Folic acid	150 μg
Avena sativa (oats) extract equivalent to dry seed	250 mg
Passiflora incarnata (passion flower) extract equivalent to dry herb	100 mg
Lecithin	50 mg
Choline bitartrate	25 mg
Inositol	25 mg

Analysis of two active arms

An analysis of variance (ANOVA) revealed that the two vitamin B treatment groups' mood and strain measures were not significantly different across any of the three testing times (baseline, week 4 and week 12). However, examination of the mood and strain measures scores indicated that both treatment groups improved across the treatment period, suggesting the treatments were equally effective. To ascertain whether the treatments improved ratings of work stress and personal strain in comparison with placebo, the two active treatment arms were combined and treated as a single treatment (Executive B Active). The means and standard deviations for the outcome measures are presented in Table 2 for the three assessment time-points. As such, the analyses of the primary and secondary outcomes for the combined Executive B groups and placebo would be via two-way analysis of covariance (ANCOVA), controlling for personality, hours worked and staff supervised on each work stress and strain variable with time (baseline, 4 weeks and 12 weeks) and treatment (placebo, active) as factors.

Primary outcome (work stress or personal strain)

Repeated measures ANCOVA were conducted on the three OSI-R factors, with the time × treatment interaction trending towards significance for the Personal Strain sub-scale ($F_{2,88} = 2.67$, $p = 0.075$). Further analysis revealed that the combined vitamin B group reported a significant reduction in *Personal Strain* ($F_{1,25} = 6.00$, $p = 0.02$, $\eta^2 = 0.194$), from week 4 ($M = 92.10$, $SE = 2.44$) to week 12 ($M = 85.54$, $SE = 2.27$). This result indicates that there was a 19% improvement in the *Personal Strain* levels of the combined vitamin B groups. In regard to any between group differences at each time-point, no significant differences between the groups were evident at week 4 or week 12. There was no significant difference in self-ratings of both the Organisational Stress sub-scale ($F_{2,92} = 0.97$, $p = 0.499$) or Personal Coping Resources sub-scale ($F_{2,88} = 1.07$, $p = 0.345$) as expected between the treatment groups.

Secondary outcome (anxiety and mood)

A repeated measures ANCOVA revealed that there was no significant effect of vitamin B administration on the state anxiety scores of the vitamin B treatment

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Table 2. Mean (±SD) scores for the mood and strain measures for both treatment conditions across the three testing time-points

	Vitamin B baseline	Placebo baseline	Vitamin B 4 weeks	Placebo 4 weeks	Vitamin B 12 weeks	Placebo 12 weeks
POMS: tension-anxiety	12.20 ± 1.10	12.78 ± 1.49	12.21 ± 0.95	12.75 ± 1.87	10.00 ± 1.10	12.94 ± 1.77
POMS: depression-dejection	11.41 ± 1.62	8.67 ± 1.56	10.58 ± 1.53	12.00 ± 2.60	8.85 ± 1.38	10.50 ± 2.43
POMS: anger-hostility	12.71 ± 1.27	8.28 ± 1.51	10.55 ± 1.53	9.00 ± 2.08	9.05 ± 1.33	9.39 ± 2.12
POMS: vigour-activity	16.34 ± 0.93	14.56 ± 0.98	14.29 ± 1.06	13.12 ± 1.31	14.83 ± 1.03	12.78 ± 1.19
POMS: fatigue-inertia	11.98 ± 1.26	11.50 ± 1.45	12.58 ± 1.26	11.35 ± 1.70	10.20 ± 0.97	13.44 ± 1.43
POMS: confusion-bewilderment	8.24 ± 0.83	7.44 ± 1.01	7.92 ± 0.76	7.65 ± 1.31	7.23 ± 0.77	9.00 ± 1.22
OSI-R: occupational roles	142.78 ± 4.23	136.06 ± 5.66	142.18 ± 4.42	139.00 ± 7.08	142.36 ± 3.88	137.56 ± 7.41
OSI-R: psychological strain	95.18 ± 3.70	88.39 ± 5.13	93.79 ± 3.38	86.20 ± 5.76	85.93 ± 2.90	86.61 ± 4.81
OSI-R: personal resources	120.98 ± 3.09	129.67 ± 5.23	119.89 ± 3.23	124.47 ± 5.46	123.07 ± 2.76	125.83 ± 5.05
Range—*N*	38–42	15–18	38–42	15–18	40–42	18

POMS, Profile of Mood Scale; OSI-R, Occupational Stress Inventory-Revised.

group or the placebo group between baseline and week 4 or week 12 ($F_{2,96} = 1.08$, $p = 0.343$). For investigation of the impact of vitamin B administration on mood, the scores from the POMS were investigated in relation to any changes that occurred over the treatment period. The time × treatment interactions for tension-anxiety ($F_{2,90} = 1.90$, $p = 0.156$), depression-dejection ($F_{2,92} = 3.37$, $p = 0.039$), anger-hostility ($F_{2,92} = 2.28$, $p = 0.109$), fatigue ($F_{2,92} = 3.93$, $p = 0.051$) and confusion ($F_{2,92} = 3.25$, $p = 0.043$) subscales showed improvement across the treatment period for the vitamin B group, whereas the vigour ($F_{2,92} = 0.05$, $p = 0.953$) sub-scale was largely unaffected by the treatments. Further analysis revealed that the combined vitamin B group reported a reduction in depression-dejection ($F_{1,38} = 4.48$, $p = 0.041$) and confusion ($F_{1,38} = 4.06$, $p = 0.051$) between baseline and week 12. The trend interaction for fatigue was driven by an increase in fatigue ratings within the placebo group ($F_{1,38} = 2.21$, $p = 0.155$) and reduction in fatigue ratings in the vitamin B group ($F_{1,38} = 2.51$, $p = 0.122$) between baseline and week 12, although both these comparisons failed to reach significance.

DISCUSSION

Sixty participants, recruited from the community, completed the 3-month, triple-blind, randomised, placebo-controlled trial in which personality, work demands, mood, anxiety and strain were assessed. After individual differences in personality and work demands were statistically controlled, the two vitamin B treatment groups combined (immediate release and slow release) reported significantly lower personal strain measured using the PSQ and a reduction in confusion and depressed/dejected mood after 12 weeks supplementation compared with the placebo group. The other measures of mood, and anxiety were unchanged by the vitamin B complex supplementation.

There were pre-treatment group differences in the number of hours worked and the number of staff supervised, therefore these variables were treated as covariates. The analysis controlled for the effects of personality on self-reported measures of strain and mood by entering the five personality variables of the NEO-PI-R as covariates: neuroticism, extraversion, openness to experience, agreeableness and conscientiousness. The primary analysis revealed that the combined vitamin B group reported significant reduction in *Personal Strain* from week 4 to week 12, whereas the placebo group remained constant. This represents a 19% improvement in the *Personal Strain* measure in the combined vitamin B groups compared with placebo. The slope of the PSQ scores suggests that the effect may have increased past the 90-day period. These results are the first specifically to examine mainly high dose B vitamin supplementation and workplace stress. Consistent with the improvements in workplace *Personal Strain*, both vitamin B treatment groups showed decreases in depression-dejection and anger-hostility, providing a degree of internal consistency within our results. The improvements in mood are supported by previous research, which has shown a decrease in depressed mood with vitamin B administration (Kaplan *et al*., 2007). The results are also consistent with previous attempts at examining the effects of multivitamin supplementation on mood and stress. Kennedy and colleagues (Kennedy *et al*., 2010) reported improvements in perceived stress, GHQ-12 and vigour from the POMS after 33 days of a high dose multi B vitamin. These results and methodology are closest to the design of the current study except that in the current study our treatment duration was 90 days and we assessed workplace stress. Certainly improvements in GHQ-12 are likely to be similar to personal strain associated with workplace stress. In the second study conducted in the same laboratory, multivitamin supplementation for 9 weeks also

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improved fatigue in women after a multi-tasking designed to elicit task-related anxiety. Although the duration of treatment was similar to the present study, the generation of stress/anxiety due to the task was significantly different to the design of both the present study and the study of Kennedy and colleagues (Kennedy *et al*., 2010) making direct comparison more difficult.

In addition to the B-complex vitamins contained in the Blackmores Executive B, the formula contains both *Avena sativa* (oats) and *Passiflora incarnata* (passion flower). Oats are normally consumed as whole-grain cereal and contain small amounts of free phenolic acids, vanillic acids, flavonoids and avenanthramides (AVs), which are hydroxycinnamoylanthranilate alkaloids unique to oats (Chen *et al*., 2007). AVs are bioavailable and thought to be antiatherogenic due to their antioxidant, antiproliferative and anti-inflammatory activities, as such, they could be acting in synergy with other antioxidants in the Executive B formulation, although chronic consumption of AV in addition to normal diet has yet to be examined. Similarly, passion flower has been used extensively as an anxiolytic and sedative, with its central nervous system depressant effects being attributed to harmala alkaloids and flavonoid content (particularly chrysin), although its mode of action is not yet clear (Zanoli *et al*., 2000). Passion flower's anxiolytic effect may have contributed to the reduction in negative mood states for the treatment group, in isolation or in synergism with the predominant constituents of Blackmore's Executive B stress formula.

It is important to note that the statistical effects observed in the present study were only of moderate size. Further research should expand the present study to investigate the effects of multivitamin and B-complex supplementation over longer periods (2–3 yrs) and recruiting a greater numbers of subjects to provide adequate statistical power to detect small, but important changes in levels of workplace stress and mood states. Further to this, the secondary aim of this study was to examine the effect of 'sustained' release B vitamins in comparison with both 'normal' B vitamins and placebo. The small number of participants in the active treatment groups did not allow for sufficiently powered comparisons between the two possible treatment groups to assess any differences between the 'sustained' release and normal vitamin B treatments. Inspection of the outcome measures for the treatment groups identified a similar pattern of improvement for each of the vitamin B treatment groups; as such the groups were combined for analysis of the time by treatment effects in comparison with placebo.

Currently there are few cost-effective interventions available at the individual level for work stress. The results of this study are suggestive of significant decreases in the experience of workplace stress after 90-day supplementation of a B complex vitamin. Improvements in occupational stress may have important personal health, organisational and societal outcomes. These may include increased workplace productivity as a result of reduced stress, with beneficiaries of reduced stress being able to possibly work more effectively when not experiencing symptoms of workplace stress. Further to this, longer-term reduction in the experience of work stress may reduce the number or possibility of stress claims due to workplace pressures. Given the cost of workplace stress claims, the loss of productivity from both presenteeism and absenteeism and the personal cost, an analysis of the economic impact of vitamin B supplementation in the workplace should be assessed. Future research should also replicate these results in significantly larger samples and assess changes in workplace variables such as absenteeism, workplace engagement and productivity.

CONFLICT OF INTEREST

No conflict of interest declared.

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