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SHORT RESEARCH AND DISCUSSION ARTICLE

Arsenic, heavy metals, phthalates, pesticides, hydrocarbons and polyfluorinated compounds but not parabens or phenols are associated with adult remembering condition: US NHANES, 2011–2012

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Abstract Links between environmental chemicals and human health have emerged, but the effects on cognition were less studied. Therefore, it was aimed to study the relationships of different sets of environmental chemicals and the remembering condition in a national and population-based study in recent years. Data was retrieved from the US National Health and Nutrition Examination Surveys, 2011–2012, including demographics, blood pressure readings, serum measurements, lifestyle factors, self-reported remembering condition and urinary environmental chemical concentrations. Analyses included Chi-square test, *t* test and survey-weighted logistic and multinominal regression models. Among the elderly aged 60–80 (n=1791), 320 (17.9 %) had difficulties in thinking or remembering. People who had difficulties in thinking or remembering had higher levels of urinary heavy metals, phthalates, pesticides and hydrocarbon concentrations but lower levels of urinary arsenic and polyfluorinated compound concentrations. During the recent past week, 146 people (8.2 %) had trouble remembering for more than three times while 619 people (35.2 %) had that for one to three times. These people had higher levels of urinary heavy metals, phthalates, pesticides and hydrocarbon concentrations but lower levels of urinary polyfluorinated compound concentrations. There were no associations with urinary bisphenols, parabens, perchlorate, nitrate or thiocyanate concentrations. This is the first time observing statistically significant risk associations of urinary heavy metals, phthalates, pesticides and hydrocarbon concentrations and the remembering condition specifically in the elderly, although the causality cannot be established. Elimination of such environmental chemicals in humans might need to be considered in future health policy and intervention programs.

Keywords Chemicals · Environmental health · Risk factor · Cognition · Population attributable risk · Memory

Introduction

Links between environmental chemicals and human health, including hypertension, cardiovascular diseases, food allergy, lung diseases, cancer and vision, hearing and balancing impairments have emerged (Shiue 2013a, b, c, 2014a, b), but the effects on other domains of cognitive function were less studied. In this context, therefore, it was aimed to examine the relationships of different sets of urinary environmental chemical concentrations and the remembering condition in a national and population-based setting.

Methods

Study sample

As described elsewhere (Centres for Disease Control and Prevention 2012), US National Health and Nutrition Examination Surveys (NHANES) has been a national, population-based, multi-year, cross-sectional study. Study sample are representative sample of the civilian, non-institutionalized US population. Information on demographics, blood pressure readings,

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Table 1 Associations between urinary environmental chemical concentrations and difficulties in thinking or remembering (n=1791, 60–80 years)

	No difficulties (n=1469, 82.1 %) Mean (SD)	Difficulties (n=320, 17.9 %) Mean (SD)	OR (95 % CI)[a]	P value
Arsenic (μg/L)				
Total arsenic	22.7 (65.7)	18.6 (45.9)	0.68 (0.57–0.81)	<0.001
Arsenous	0.6 (2.9)	0.4 (0.2)	0.42 (0.13–1.36)	0.139
Arsenic acid	0.7 (1.8)	0.6 (0.04)	0.12 (0.004–3.58)	0.204
Arsenobetaine	13.0 (54.7)	11.0 (41.7)	0.74 (0.62–0.89)	0.003
Arsenocholine	0.3 (0.5)	0.2 (0.4)	0.28 (0.08–1.03)	0.054
Dimethylarsonic	7.0 (11.4)	5.8 (6.6)	0.78 (0.54–1.11)	0.155
Monomethylarsonic	1.0 (3.2)	0.9 (0.6)	1.41 (0.74–2.70)	0.276
Trimethylarsine	0.2 (0.4)	0.2 (0.1)	0.68 (0.23–2.01)	0.461
Heavy metals (μg/L)				
Barium	1.8 (4.9)	1.3 (1.4)	0.91 (0.65–1.27)	0.553
Cadmium	0.5 (0.5)	0.6 (0.6)	1.04 (0.71–1.54)	0.817
Cobalt	0.5 (1.6)	0.4 (0.5)	1.03 (0.68–1.55)	0.894
Cesium	5.0 (3.3)	4.5 (2.8)	0.71 (0.43–1.17)	0.167
Manganese	0.2 (0.2)	0.2 (0.2)	0.92 (0.71–1.19)	0.512
Molybdenum	51.4 (44.3)	51.2 (37.8)	1.02 (0.71–1.45)	0.912
Lead	0.8 (1.2)	0.7 (0.8)	1.02 (0.75–1.40)	0.887
Antimony	0.07 (0.15)	0.08 (0.17)	1.47 (1.05–2.05)	0.027
Strontium	110.6 (171.3)	96.1 (63.4)	0.92 (0.57–1.49)	0.718
Thallium	0.2 (0.1)	0.1 (0.1)	0.77 (0.48–1.24)	0.264
Tin	2.0 (4.7)	1.4 (1.7)	0.88 (0.69–1.11)	0.261
Tungsten	0.1 (0.1)	0.1 (0.2)	1.00 (0.72–1.38)	0.984
Uranium	0.01 (0.02)	0.02 (0.08)	0.94 (0.75–1.19)	0.606
Phthalates (ng/mL)				
Mono(carboxyoctyl)	40.9 (94.0)	31.6 (57.8)	1.11 (0.86–1.43)	0.396
Mono(carboxynonyl)	3.5 (4.8)	9.3 (61.2)	1.38 (0.97–1.97)	0.068
Mono-2-ethyl-5-carboxypentyl	24.5 (63.5)	19.5 (20.1)	1.17 (0.90–1.52)	0.219
Mono-n-butyl	25.2 (126.7)	43.4 (239.7)	1.21 (1.01–1.46)	0.039
Mono-(3-carboxypropyl)	15.4 (130.5)	7.8 (18.3)	1.05 (0.87–1.28)	0.583
Mono-ethyl	236.1 (722.4)	119.2 (223.9)	0.90 (0.68–1.20)	0.443
Mono-(2-ethyl-5-hydroxyhexyl)	17.7 (65.2)	13.8 (21.6)	1.18 (0.91–1.52)	0.206
Mono-(2-ethyl)-hexyl	2.5 (7.9)	2.5 (5.6)	1.11 (0.93–1.33)	0.225
Mono-isobutyl	10.3 (15.0)	12.0 (17.0)	1.16 (0.86–1.55)	0.310
Mono-n-methyl	2.8 (7.0)	2.4 (3.8)	0.96 (0.71–1.30)	0.787
Mono-isononyl	2.2 (5.9)	3.0 (10.7)	1.24 (0.99–1.56)	0.063
Mono-(2-ethyl-5-oxohexyl)	10.7 (31.0)	8.8 (12.8)	1.14 (0.84–1.54)	0.389
Mono-benzyl	9.1 (20.8)	8.2 (11.6)	1.13 (0.81–1.59)	0.447
Cyclohexane-1,2-dicarboxylic acid monohydroxy isononyl ester	0.4 (0.7)	0.4 (0.5)	0.78 (0.30–2.05)	0.597
Pesticides (ng/L)				
Urinary 2,5-dichlorophenol	252.7 (1534.0)	307.7 (2113.2)	1.15 (0.98–1.35)	0.082
Urinary 2,4-dichlorophenol	7.8 (50.5)	8.5 (50.6)	1.24 (1.09–1.41)	0.003
Perchlorate (ng/mL)	4.6 (6.5)	4.6 (6.5)	0.89 (0.59–1.35)	0.577
Nitrate (ng/mL)	49,015.4 (49,611.5)	40,912.3 (27,593.8)	0.99 (0.60–1.63)	0.967
Thiocyanate (ng/mL)	1347.4 (1645.6)	1377.7 (2238.4)	0.83 (0.57–1.20)	0.298
Polyaromatic hydrocarbons (ng/L)				
2-Hydroxyfluorene	445.7 (834.7)	604.2 (1798.7)	0.83 (0.59–1.15)	0.239
3-Hydroxyfluorene	200.4 (470.0)	220.1 (604.4)	0.83 (0.60–1.14)	0.223
9-Hydroxyfluorene	465.3 (748.7)	414.0 (607.8)	0.92 (0.65–1.31)	0.614
1-Hydroxyphenanthrene	174.2 (201.4)	230.9 (764.6)	0.96 (0.73–1.26)	0.750
2-Hydroxyphenanthrene	93.0 (116.3)	108.9 (335.9)	0.77 (0.59–1.00)	0.047

Table 1 (continued)

	No difficulties (n=1469, 82.1 %) Mean (SD)	Difficulties (n=320, 17.9 %) Mean (SD)	OR (95 % CI)[a]	P value
3-Hydroxyphenanthrene	98.9 (136.8)	145.6 (680.3)	0.83 (0.67–1.04)	0.099
1-Hydroxypyrene	147.0 (243.7)	167.1 (562.4)	0.86 (0.68–1.08)	0.178
1-Hydroxynapthalene (1-naphthol)	19,244.6 (242,474.8)	202,636.1 (1,706,814.0)	1.05 (0.83–1.32)	0.696
2-Hydroxynapthalene (2-naphthol)	7388.2 (13,845.0)	6129.5 (9052.8)	0.87 (0.60–1.27)	0.447
4-Hydroxyphenanthrene	29.5 (56.2)	26.1 (35.0)	0.85 (0.64–1.14)	0.257
Polyfluorinated compounds (ng/mL)				
Perfluorooctanoic acid	3.1 (2.2)	2.7 (1.6)	0.80 (0.52–1.24)	0.300
Perfluorooctane sulfonic acid	13.8 (16.7)	14.7 (12.5)	1.42 (0.93–2.15)	0.095
Perfluorohexane sulfonic acid	2.3 (3.4)	2.2 (2.4)	0.95 (0.70–1.29)	0.728
2-(N-Ethyl-perfluorooctane sulfonamido) acetic acid	0.08 (0.05)	0.08 (0.04)	1.34 (0.40–4.51)	0.623
2-(N-Methyl-perfluorooctane sulfonamido) acetic acid	0.3 (0.5)	0.3 (0.5)	1.09 (0.77–1.55)	0.614
Pefluorodecanoic acid	0.4 (1.0)	0.4 (0.4)	1.11 (0.67–1.83)	0.675
Perfluorobutane sulfonic acid	0.07 (0.04)	0.07 (0.04)	1.16 (0.35–3.84)	0.793
Perfluoroheptanoic acid	0.11 (0.09)	0.09 (0.05)	0.30 (0.15–0.63)	0.003
Perfluorononanoic acid	1.6 (4.2)	1.3 (0.8)	1.09 (0.65–1.81)	0.471
Perfluorooctane sulphonamide	0.07 (0.01)	0.08 (0.07)	151.29 (0.02–1,344,824.0)	0.260
Perfluoroundecanoic acid	0.3 (0.5)	0.3 (0.5)	1.17 (0.66–2.05)	0.567
Perflurododecanoic acid	0.09 (0.08)	0.08 (0.05)	0.63 (0.21–1.85)	0.375

[a] Adjusted for age, sex, body mass index, education level, ratio of family income to poverty, serum cotinine (smoking status), alcohol status, physical activity level, urinary creatintine and survey design

serum measurements, lifestyle factors, self-reported remembering condition and urinary environmental chemical concentrations was obtained by household interview. In the current analysis, the 2011–2012 cohorts as the most recent study cohort with available information mentioned above was selected for statistical analysis. Informed consents were obtained from participating subjects by the NHANES researchers. BP was measured on all examinees 8 years and older at the household interview and for three times (details via: http://www.cdc.gov/nchs/nhanes/nhanes2009-2010/BPX_F.htm). The standard measuring protocol can be found here: http://www.cdc.gov/nchs/nhanes/nhanes20092010/BPX_F.htm#Protocol_and_Procedure. Participants with any of the following on both arms were excluded from the exam according to the standard protocol: rashes, gauze dressings, casts, edema, paralysis, tubes, open sores or wounds, withered arms, a-v shunts and radical mastectomy or if BP cuff does not fit on the arm. The measurements took three times, and in the present study, we took the second time BP measurement in the analysis. People with ≥140 mmHg systolic BP and ≥90 mmHg diastolic BP were classified as high BP.

Biomonitoring

Urines were only collected in a subsample, being one third of the whole cohort (still representative), to measure environmental chemical concentrations in urines among people aged 6 and above. Urine specimens were processed, stored under appropriate frozen (−20 °C) conditions and shipped to the Division of Environmental Health Laboratory Sciences, National Centre for Environmental Health, Centres for Disease Control and Prevention for analysis. According to the NHANES Website (details via: http://wwwn.cdc.gov/nchs/nhanes/2011-2012/PERNT_G.htm), ion chromatography coupled with electrospray tandem mass spectrometry was used to detect and measure the amount. Chromatographic separation is achieved using an IonPac AS16 column with sodium hydroxide as the eluent. The eluent from the column is ionized using an electrospray interface to generate and transmit negative ions into the mass spectrometer. Comparison of relative response factors (ratio of native analyte to stable isotope labelled internal standard) with known standard concentrations yields individual analyte concentrations. For statistical analysis purpose in the present study, urinary environmental chemical concentrations were all log transformed since they were highly skewed to one side.

Statistical analysis

Older adults aged 60–80 were included in the current statistical analysis since the remembering condition was only asked in this age group. Associations of urinary environmental chemical concentrations and risk of the remembering condition were examined by t test and survey-weighted logistic and

Table 2 Associations between urinary environmental chemical concentrations and troubles in remembering in the last 7 days (n=1791, 60–80 years)

	Never (n=1012, 56.6 %) RRR (95 % CI)[a]	1–3 times (n=629, 35.2 %) RRR (95 % CI)[a]	>3 times (n=146, 8.2 %) RRR (95 % CI)[a]
Arsenic (μg/L)			
Total arsenic	1.00	1.10 (0.83-1.46)	1.08 (0.77–1.51)
Arsenous	1.00	0.99 (0.42–2.32)	0.64 (0.17–2.40)
Arsenic acid	1.00	n/a	n/a
Arsenobetaine	1.00	1.11 (0.92–1.34)	1.08 (0.78–1.49)
Arsenocholine	1.00	0.59 (0.23–1.52)	0.31 (0.06–1.58)
Dimethylarsonic	1.00	1.04 (0.70–1.55)	1.14 (0.75–1.73)
Monomethylarsonic	1.00	0.94 (0.42–2.08)	1.72 (0.77–3.82)
Trimethylarsine	1.00	0.31 (0.06–1.53)	0.82 (0.27–2.45)
Heavy metals (μg/L)			
Barium	1.00	1.10 (0.79–1.53)	1.52 (0.90–2.57)
Cadmium	1.00	1.15 (0.82–1.61)	1.18 (0.65–2.14)
Cobalt	1.00	1.52 (1.01–2.30)	1.36 (0.89–2.08)
Cesium	1.00	0.88 (0.51–1.52)	0.99 (0.47–2.07)
Manganese	1.00	1.17 (0.74–1.85)	1.50 (0.77–2.92)
Molybdenum	1.00	0.95 (0.66–1.37)	1.85 (1.14–2.98)
Lead	1.00	1.05 (0.72–1.53)	1.67 (0.94–3.00)
Antimony	1.00	1.27 (0.79–2.05)	2.54 (1.57–4.10)
Strontium	1.00	1.41 (1.00–1.98)	1.28 (0.56–2.93)
Thallium	1.00	0.91 (0.54–1.54)	1.41 (0.78–2.53)
Tin	1.00	1.32 (0.93–1.87)	1.32 (0.84–2.07)
Tungsten	1.00	1.07 (0.70–1.63)	1.86 (1.03–3.38)
Uranium	1.00	0.74 (0.57–0.96)	0.86 (0.64–1.17)
Phthalates (ng/mL)			
Mono(carboxyoctyl)	1.00	1.09 (0.79–1.51)	1.10 (0.67–1.79)
Mono(carboxynonyl)	1.00	1.16 (0.80–1.70)	1.31 (0.87–1.96)
Mono-2-ethyl-5-carboxypentyl	1.00	1.06 (0.73–1.54)	1.22 (0.85–1.75)
Mono-*n*-butyl	1.00	1.09 (0.89–1.33)	1.20 (0.88–1.64)
Mono-(3-carboxypropyl)	1.00	1.18 (0.86–1.61)	1.09 (0.77–1.53)
Mono-ethyl	1.00	0.93 (0.77–1.13)	1.08 (0.81–1.44)
Mono-(2-ethyl-5-hydroxyhexyl)	1.00	0.96 (0.69–1.32)	1.18 (0.83–1.68)
Mono-(2-ethyl)-hexyl	1.00	1.11 (0.81–1.52)	0.94 (0.64–1.38)
Mono-isobutyl	1.00	1.08 (0.78–1.50)	1.27 (0.79–2.04)
Mono-n-methyl	1.00	0.93 (0.76–1.14)	1.38 (0.87–2.17)
Mono-isononyl	1.00	1.28 (0.93–1.76)	1.28 (0.88–1.86)
Mono-(2-ethyl-5-oxohexyl)	1.00	1.04 (0.71–1.50)	1.26 (0.87–1.81)
Mono-benzyl	1.00	1.11 (0.90–1.37)	1.38 (1.03–1.85)
Cyclohexane-1,2-dicarboxylic acid monohydroxy isononyl ester	1.00	3.49 (1.34–9.11)	1.47 (0.26–8.27)
Pesticides (ng/mL)			
Urinary 2,5-dichlorophenol	1.00	1.00 (0.87–1.16)	1.28 (0.99–1.64)
Urinary 2,4-dichlorophenol	1.00	1.03 (0.89-1.19)	1.05 (0.83-1.31)
Perchlorate (ng/mL)	1.00	0.83 (0.52-1.34)	0.90 (0.47-1.73)
Nitrate (ng/mL)	1.00	1.03 (0.74–1.44)	1.13 (0.68–1.85)
Thiocyanate (ng/mL)	1.00	0.97 (0.64–1.46)	0.97 (0.59–1.58)
Polyaromatic hydrocarbons (ng/L)			
2-Hydroxyfluorene	1.00	1.03 (0.76–1.39)	1.41 (0.69–2.88)
3-Hydroxyfluorene	1.00	1.01 (0.70–1.47)	1.47 (0.68–3.17)

Table 2 (continued)

	Never (n=1012, 56.6 %) RRR (95 % CI)[a]	1–3 times (n=629, 35.2 %) RRR (95 % CI)[a]	>3 times (n=146, 8.2 %) RRR (95 % CI)[a]
9-Hydroxyfluorene	1.00	0.93 (0.65–1.34)	1.20 (0.66–2.19)
1-Hydroxyphenanthrene	1.00	1.05 (0.67–1.62)	1.59 (0.92–2.74)
2-Hydroxyphenanthrene	1.00	0.94 (0.61–1.46)	1.33 (0.77–2.31)
3-Hydroxyphenanthrene	1.00	1.07 (0.76–1.53)	1.39 (0.74–2.64)
1-Hydroxypyrene	1.00	1.10 (0.78–1.56)	1.69 (1.02–2.81)
1-Hydroxynapthalene (1-naphthol)	1.00	1.00 (0.79–1.26)	1.23 (0.79–1.92)
2-Hydroxynapthalene (2-naphthol)	1.00	0.97 (0.70–1.34)	1.25 (0.78–2.01)
4-Hydroxyphenanthrene	1.00	1.01 (0.73–1.40)	1.34 (0.64–2.81)
Polyfluorinated compounds (ng/mL)			
Perfluorooctanoic acid	1.00	0.65 (0.42–1.03)	0.56 (0.32–.0.98)
Perfluorooctane sulfonic acid	1.00	0.86 (0.59–1.26)	0.75 (0.44–1.26)
Perfluorohexane sulfonic acid	1.00	0.56 (0.41–0.79)	0.45 (0.25–0.81)
2-(*N*-Ethyl-perfluorooctane sulfonamido) acetic acid	1.00	0.68 (0.28–1.64)	0.43 (0.10–1.95)
2-(*N*-Methyl-perfluorooctane sulfonamido) acetic acid	1.00	1.25 (0.98–1.60)	1.31 (0.68–2.51)
Pefluorodecanoic acid	1.00	0.78 (0.45–1.36)	1.01 (0.54–1.90)
Perfluorobutane sulfonic acid	1.00	3.14 (0.61–16.09)	1.65 (0.15–17.51)
Perfluoroheptanoic acid	1.00	0.45 (0.19–1.06)	0.28 (0.08–0.98)
Perfluorononanoic acid	1.00	0.83 (0.54–1.26)	0.94 (0.45–1.99)
Perfluorooctane sulphonamide	1.00	0.83 (0.17–3.95)	0.48 (0.08–2.73)
Perfluoroundecanoic acid	1.00	1.00 (0.71–1.42)	0.93 (0.54–1.57)
Perflurododecanoic acid	1.00	2.25 (0.79–6.38)	3.80 (0.91–15.97)

[a] Adjusted for age, sex, body mass index, education level, ratio of family income to poverty, serum cotinine (smoking status), alcohol status, physical activity level, urinary creatintine and survey design

multi-nominal regression models, with $P<0.05$ considered statistically significant. Covariates including urinary creatinine, age, sex, ratio of family income to poverty (proxy of socioeconomic status), body mass index (BMI), serum cotinine (biomarker of smoking status), alcohol habit, physical activity level and education level were adjusted. Statistical software STATA version 13.0 (STATA, College Station, Texas, USA) was used to perform all the analyses. Since the present study is only a secondary data analysis, no further ethics approval was required.

Results

Among the elderly aged 60–80 (n=1791), 320 (17.9 %) had difficulties in thinking or remembering. People who had difficulties in thinking or remembering had higher levels of urinary heavy metals, phthalates, pesticides and hydrocarbon concentrations but lower levels of urinary arsenic and polyfluorinated compound concentrations (see Table 1). During the recent past week, 146 people (8.2 %) had trouble remembering for more than three times while 619 people (35.2 %) had that for one to three times. These people had higher levels of urinary heavy metals, phthalates, pesticides and hydrocarbon concentrations but lower levels of urinary polyfluorinated compound concentrations (see Table 2). There were no associations with urinary bisphenols, parabens, perchlorate, nitrate or thiocyanate concentrations.

Discussion

Previous research

As mentioned earlier, literature on the relationships of environmental chemicals and the remembering condition specifically is limited. This is in particular in heavy metals, phthalates, arsenic and polyfluorinated compounds. How arsenic and polyfluorinated compounds could have potential protective effects on the remembering condition among the elderly is unknown. The complex relationships between hydrocarbons and cognitive function could be due to the disruption of T4 regulation in the hypothalamus–pituitary–thyroid axis, blood, brain, neurons, liver and pre- and postnatal development (Builee and Hatherill 2004). Research in this area has been into children and even birth outcomes but not the elderly.

The link between pesticides and neurocognitive development could have been better observed and established than others. Not long ago, it was observed that pesticides were related to trouble remembering and other neurological symptoms in farmers and their spouses in an eight-county area in north-eastern Colorado, USA (Stallones and Beseler 2002). Pesticides were also associated with verbal memory in manufacturing workers (Berent et al. 2014), although only at baseline but not longitudinally. There might be a concern on the methodological bias in that study. Memory/learning domain of children aged 4–9 could have been affected by exposure to pesticides (Suarez-Lopez et al. 2013) as well. In addition, pesticide exposure was found to induce spatial learning and memory deficits in rats with a simultaneous decrease of *N*-methyl-D-aspartate receptor 1, synaptophysin and synapsin I, all of which are memory-related synaptic proteins (Chen et al. 2012).

Strengths and limitations

The present study has a number of strengths. First, this study was conducted in a large and nationally representative human sample with mixed ethnicities and socioeconomic status. Second, this is the first time examining the risk associations of urinary heavy metals, phthalates, pesticides and hydrocarbon concentrations and the remembering condition in the elderly. However, there are still some limitations that cannot be ignored. First, there could be still other emerging chemicals from the living environments that we might not yet know and would need future research to further identify and examine. Second, it was not possible to examine the memory function by other tests due to the limitation of the current dataset. Third, the causality cannot be established in the present study due to the cross-sectional study design in nature. Therefore, future studies with a longitudinal study design to confirm or refute the current findings and, if at all, to understand the persisting risk effects along the life course from those above-mentioned environmental chemicals would be suggested.

Conclusion

In sum, people who had difficulties in thinking or remembering had higher levels of urinary heavy metals, phthalates, pesticides and hydrocarbon concentrations but lower levels of urinary arsenic and polyfluorinated compound concentrations. There were no associations with urinary bisphenols, parabens, perchlorate, nitrate or thiocyanate concentrations. Elimination of such environmental chemicals in humans might need to be considered in future health policy and intervention programs.

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Conflict of interest None.

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