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Title: Associations of change in television viewing time with biomarkers of postmenopausal breast cancer risk: The Australian Diabetes, Obesity and Lifestyle Study

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ABSTRACT

Purpose: Sedentary behavior has been previously shown, in a cross-sectional study, to have deleterious associations with biomarkers of postmenopausal breast cancer risk. We examined the associations of change in sedentary behavior (daily television [TV] viewing time, h/day) over a five-year period with putative markers of postmenopausal breast cancer risk. **Methods:** The analytic cohort consisted of 1,001 postmenopausal women from the Australian Diabetes, Obesity and Lifestyle (AusDiab) study (1999-2005). Multivariate linear regression models were used to examine associations of change in TV viewing time with biomarkers of the following risk mechanisms: adiposity (body mass index [BMI], waist circumference); metabolic dysfunction (fasting plasma glucose, 2-h plasma glucose, fasting insulin, insulin resistance (homeostasis model assessment of insulin resistance [HOMA-IR]); and, inflammation (high-sensitivity C-reactive protein [hs-CRP]). All analyses were adjusted for age, baseline TV viewing, and potential confounders. **Results:** Hourly increments of change in TV viewing time were positively associated with BMI (β = 0.50, 95%CI: 0.20, 0.81; $p = 0.001$), waist circumference (β = 1.18, 95%CI: 0.49, 1.87; $p = 0.001$), fasting insulin (β = 38.13%, 95%CI: 37.08, 39.20; $p = 0.01$) and HOMA-IR (β = 37.93%, 95%CI: 36.92, 38.98; $p = 0.03$) in fully adjusted models. Significant associations with BMI, waist circumference, fasting insulin and HOMA-IR were also present in analyses using categories of change in TV viewing time (reduced, same, increased). **Conclusions:** The findings suggest that increasing habitual sedentary behavior over time could increase breast cancer risk amongst postmenopausal women. Further investigation into the role of sedentary behavior in breast cancer etiology is warranted.

INTRODUCTION

Sedentary behavior (any waking behavior of low energy expenditure 1.0 – 1.5 metabolic equivalents (METs) performed whilst in a seated or reclined posture) has become increasingly prevalent within contemporary society [1]. Data from the American Heritage Time Use Study (AHTUS) indicates that, over a 45 year period, women have increased their screen-based sedentary behaviors – predominantly television [TV] viewing – from 8.3 h/week to 16.5 h/week [2]. A cross-sectional study from the Princeton Affect and Time Survey (PATS) observed greater TV viewing time with age, and a linear relationship between the frequency of TV viewing episodes and proportion of hours spend watching TV after the age of 35 years [3].

Sedentary behaviors, including TV viewing time, have been associated with all-cause and cardiovascular mortality [4-6], diabetes [7,8] and deterioration in a broad range of markers of cardiometabolic health [9-11]. These associations have been shown to be independent of leisure-time moderate- to vigorous-intensity physical activity [1]. It has also been suggested that sedentary behavior may increase postmenopausal breast cancer risk via its influence on central adiposity, metabolic dysfunction, and inflammation, all of which have been associated with the carcinogenic process [12].

To date, only one study has specifically considered the associations between sedentary behavior and biomarkers of breast cancer risk in postmenopausal women [13]. A cross-sectional study of 1,556 postmenopausal women from the U.S National Health and Nutrition Examination Survey (NHANES) cohort found significant associations between

accelerometer-assessed sedentary time and body mass index [BMI], waist circumference, C-reactive protein, insulin and homeostatic insulin resistance [HOMA-IR] [13]. Whether an increase in TV viewing time over time in postmenopausal women is similarly associated with body weight and breast cancer-related markers of metabolic dysfunction is unknown.

Our aim was to investigate in a representative sample of Australian postmenopausal women the associations between change in TV viewing time (h/day) over five years and biomarkers of postmenopausal breast cancer risk at follow-up, including adiposity (BMI, waist circumference), metabolic dysfunction (fasting plasma glucose, 2-h plasma glucose, fasting insulin, HOMA-IR) and inflammation (high-sensitivity C-reactive protein [hs-CRP]).

METHODS

The Australian Diabetes, Obesity and Lifestyle (AusDiab) study was a population-based investigation of 11,247 Australian participants aged ≥ 25 years initiated in 1999/2000 to determine the prevalence of diabetes and other selected non-communicable diseases and their associated risk factors. All living, non-institutionalized participants from the baseline study were invited to participate in the follow-up study during 2004/05. Follow-up blood, urine and anthropometric measurements were taken for 6,537 participants (61% response rate). The methods and sample recruitment of the baseline AusDiab study have been previously reported [14]. Ethical approval for collection of the original study data at baseline and follow-up was granted by the International Diabetes Institute Ethics

Committee, with written informed consent obtained from all participants. Ethical approval for the current study was granted by the Alfred Health Human Ethics Committee and Deakin University Human Research Ethics Committee.

Study population

The principal inclusion criterion for this study was menopausal status at baseline. Women were classified as postmenopausal if they reported having gone through menopause, or were aged 55 years or older (n = 2,250) [13]. Women who met these criteria yet reported being currently pregnant or using oral contraceptives were excluded from the sample (n = 683).

We also excluded participants who were missing TV viewing time data at baseline (n = 1,292) or follow-up (n = 1,621) and who had reported previous breast cancer diagnosis (n = 87). Women who had diabetes at baseline (n = 176) or follow-up (n = 141) were also excluded, due to the influence that this condition and its treatment may have on metabolic parameters. Exclusion criteria were not mutually exclusive, thus participants could be excluded based upon one or more criterion. The final analytic cohort comprised 1,001 postmenopausal women. We also conducted a sensitivity analysis where we further excluded women with a previous diagnosis of any invasive cancer (n = 21; analytic sample for sensitivity analysis, n = 980).

Assessment of television viewing time

At baseline and follow-up, TV viewing time was measured using an interviewer-administered questionnaire. Participants were asked to report the amount of time spent watching TV or videos over the past week, separately for weekdays and weekends while it was their main activity. Change in TV viewing time was assessed using both continuous *(h/day)* and categorical *(decrease; no change (+/- half hour per day); increase)* measures.

Assessment of markers of breast cancer risk at follow-up

Adiposity was assessed using BMI and waist circumference. Height was measured to the closest 0.5 cm, without shoes using a stadiometer on a flat surface. Weight was recorded to the nearest 0.1 kg using a mechanical beam balance scale without shoes and excess clothing. BMI was then calculated as weight (kg)/height (m^2). Waist circumference was measured twice to the nearest 0.5 cm, using a tape measure over the participant's light clothing, halfway between the lower border of the ribs and the iliac crest on a horizontal plane. If measurements between the two readings varied by more than 2 cm a third measurement was taken, and the mean of the two nearest measurements were recorded.

Metabolic dysfunction was assessed through fasting plasma glucose, 2-h plasma glucose, fasting insulin, and HOMA-IR. Overnight fasting (≥9 hours) blood samples were collected by venepuncture prior to an oral glucose tolerance test. Blood samples were collected in fluoride/oxalate tubes and centrifuged on-site to separate serum and plasma. Samples were transported daily to a central laboratory, or stored immediately on-site in a

freezer at -20°C if daily transportation was not possible. Fasting plasma glucose levels were measured using a spectrophotometric-hexakinase method utilizing a Roche Modular (Roche Diagnostics, Indianapolis, IN). Fasting serum levels were determined using a human insulin specific radioimmunoassay kit (Linco Research, St. Charles, MO). HOMA-IR was calculated based on estimates using the HOMA2-calculator, version 2.2 (University of Oxford, Headington, Oxford) [15]. Extreme values of fasting plasma glucose (<3 or >25 mmol/l) and insulin (<20 or >300 pmol/l) were excluded, as these are the acceptable valid ranges for the HOMA2-calculator functions.

Hs-CRP levels were measured using chemiluminescent enzyme immunoassays (Immulite DPC 2000, CA) [16].

Assessment of covariates

Information relating to covariates was collected by an interviewer-administered questionnaire. Socio-demographic covariates included: age *(years)*, educational attainment *(did not complete high school; completed high school; completed degree or higher)*; employment status *(working (full-time; part-time); retired (not working); home duties (not working; not retired; not unable to work); other (students; unable to work)*, age at first birth *(years)*, and age at menopause *(years)*. Health-related covariates included duration of oral contraceptive pill use *(<6-months; 6-months to 2-years; 2- to 5-years; 5- to 10-years; >10-years)*, parity *(number of births)*, prescription of estrogen or hormone replacement therapy *(yes; no; unsure)* and smoking status *(current smoker; ex-smoker; non-smoker)*. Alcohol consumption *(g/day)* was estimated using the 121-item

self-administered validated [17] Anti-Cancer Council of Victoria (Australia) food frequency questionnaire (FFQ). Dietary energy intake *(kJ/day)* was assessed using the aforementioned FFQ; participants reported their usual eating habits over the past 12 months [18]. Diet quality *(Dietary Quality Index (DQI) score)* was assessed with the Diet Quality Index-Revised dietary assessment tool modified for Australian dietary recommendations [19], with diet quality reported on an overall index of diet quality using a scale of 1-100 (100 indicative of a high quality diet) [20]. Total leisure-time moderate- to vigorous-intensity physical activity *(minutes)* was reported for the previous week using the Active Australia questionnaire, which has been shown to have reasonable validity and reliability [21,22].

Statistical analysis

All statistical analyses were performed using STATA SE12 (College Station, TX, Stata Corporation). Significance was set at $p < 0.05$.

Multiple linear regression models were used to estimate the beta-coefficients (β) and 95% confidence intervals (CI) of the associations between continuous and categorical change in TV viewing time with markers of adiposity *(BMI (kg/m^2); waist circumference (cm))*, metabolic dysfunction *(fasting plasma glucose (mmol/l); 2-h plasma glucose (mmol/l); fasting insulin (pmol/l); HOMA-IR)*, and inflammation *(hs-CRP (mg/l))*, adjusting for potentially confounding variables.

Model 1 was adjusted for age. Model 2 was additionally adjusted for a broad range of potential confounders; a backward-stepwise procedure was applied, using $p < 0.20$ for variable retention, to determine covariates to retain in the fully adjusted model. To determine if associations were independent of leisure-time physical activity, Model 3 was adjusted for the covariates included at Model 2, plus leisure-time moderate- to vigorous-intensity physical activity *(min/week)*. Model 3 was considered the fully adjusted model for markers of adiposity. Model 4 included additional adjustment for waist circumference; this model was considered the fully adjusted model for metabolic dysfunction and inflammation. All models included baseline TV viewing time in order to model change in this exposure appropriately [23].

Participants with missing covariate data (BMI [n = 1], HOMA-IR [n = 17] and hs-CRP [n = 301]) were excluded from the fully adjusted models.

RESULTS

In comparison to the postmenopausal women who completed the baseline examination but were not included in this study, the final analytic cohort of 1,001 postmenopausal women were younger (56.9 ± 8.4 years vs. 63.7 ± 11.0 years, $p < 0.001$), had less children (2.7 ± 1.2 vs. 3.0 ± 1.6, $p < 0.001$) with a younger mean age at first birth (24.5 ± 4.7 years vs. 24.0 ± 4.9 years, $p = 0.005$), had lower mean TV viewing time at baseline (1.8 ± 1.3 h/day vs. 2.0 ± 1.5 h/day, $p = 0.0001$) and follow-up (1.9 ± 1.3 h/day vs. 2.4 ± 1.5 h/day, $p < 0.001$), and lower mean BMI (27.1 ± 5.0 kg/m^2 vs. 28.9 ± 6.0 kg/m^2), waist circumference 86.9 ± 12.0 cm vs. 92.2 ± 14.0 cm), mean fasting (5.3 ± 0.6 mmol/l vs. 5.8

± 1.3 mmol/l) and 2-h plasma glucose (5.9 ± 1.8 mmol/l vs. 6.9 ± 2.8 mmol/l), median fasting insulin (47.3% vs. 58.5%), HOMA-IR (0.9 vs. 1.1) and hs-CRP (2.5 mg/l vs. 2.9 mg/l) levels.

--- Insert Table 1 about here ---

Adiposity

Hourly increments of change in TV viewing time were positively associated with both BMI (β = 0.58, 95%CI: 0.30, 0.86; $p < 0.001$) and waist circumference (β = 1.25, 95%CI: 0.59, 1.91; $p < 0.0001$) in the age adjusted model (Model 1) (Table 2). We did not observe any meaningful change in multivariate model results (Model 2) when moderate- to vigorous-intensity physical activity was added (Model 3). Change in TV viewing time remained positively associated with both BMI and waist circumference in this fully adjusted model, with each hourly increment of change in TV viewing time associated with a 0.5 kg/m^2 higher BMI, and 1.18 cm greater waist circumference (Table 2).

Significant associations were also present when categories of change in TV viewing time were considered. Relative to women who had a reduction in TV viewing time from baseline to follow-up, BMI and waist circumference at follow-up were 1.50 kg/m^2 (p_{trend} = 0.002) and 3.28 cm (p_{trend} = 0.004) higher respectively in those women who had an increase in their TV viewing time in fully adjusted models (Figure 1).

--- Insert Figure 1 about here ---

Metabolic Dysfunction

In age-adjusted models, each hourly increment of change in TV viewing time was positively associated with all markers of metabolic dysfunction at follow-up – fasting plasma glucose (β = 0.05, 95%CI: 0.02, 0.08; $p = 0.003$), 2-h plasma glucose (β = 0.11, 95%CI: 0.02, 0.21; $p = 0.02$), fasting insulin (β = 39.75%, 95%CI: 38.49, 41.06; $p < 0.001$), and HOMA-IR (β = 39.26%, 95%CI: 38.05, 40.51; $p < 0.001$) (Table 2). 2-h fasting glucose was no longer significant after the addition of covariates (Model 2) and additional adjustment for physical activity (Model 3). In fully adjusted models (Model 4), associations between hourly increments of change in TV viewing time with fasting insulin (β = 38.13, 95%CI: 37.08, 39.20; $p = 0.01$) and HOMA-IR (β = 37.93, 95%CI: 36.92, 38.98; $p = 0.03$) were attenuated but remained statistically significant. Associations of hourly increments of change in TV viewing time with fasting plasma glucose or 2-h plasma glucose were attenuated and no longer significant in the fully adjusted models (Table 2).

When considering categories of change in TV viewing time, women who increased their TV viewing time had higher fasting insulin values at follow-up compared to women who reduced their TV viewing time (β = 41.48%, 95%CI: 37.91, 45.84; $p_{trend} = 0.006$) (Figure 2). Likewise, women with an increase in their TV viewing time had greater HOMA-IR values at follow-up compared to women who reduced their TV viewing time (β = 41.07%, 95%CI: 37.53, 45.38; $p_{trend} = 0.01$) in the fully adjusted model (Figure 2).

Inflammation marker

Hourly increments of change in TV viewing time were associated with 40% higher hs-CRP levels at follow-up (95%CI: 37.81, 43.37; $p = 0.006$) in age-adjusted models (Table 2). The association was attenuated in Model 2 (β = 39.45%, 95%CI: 36.66, 42.44; $p = 0.06$) and Model 3 (β = 39.40%, 95%CI: 36.63, 42.38; $p = 0.07$) (Table 2). The strength of the association was further reduced following additional adjustment for waist circumference (β = 38.36%, 95%CI: 35.87, 41.02; $p = 0.22$) (Table 2).

No associations were observed between categories of change in TV viewing time and hs-CRP levels (Figure 2).

--- Insert Table 2 and Figure 2 about here ---

After additionally excluding 21 women who had previously been diagnosed with other forms of invasive cancer there were no significant changes to the results.

DISCUSSION

In this cohort of postmenopausal women from the AusDiab study, change in TV viewing time from baseline (1999/2000) to follow-up (2004/05), was positively associated with markers of adiposity and metabolic dysfunction at follow-up in fully adjusted models. No associations were observed for change in TV viewing time and inflammation (hs-CRP) at follow-up.

Previous longitudinal studies, among women from a broader age spectrum, have considered the relationship between self-reported baseline sedentary behavior and subsequent change in waist circumference, and observed a positive association [24,9]. An association between sedentary behavior and obesity has also been observed in cross-sectional studies among both postmenopausal women [13] and women of broader age groups [25,26].

The observed association between change in TV viewing time and both BMI and waist circumference may have implications for breast cancer risk. Higher levels of adiposity (particularly increases in central adiposity, such as indicated by waist circumference) are common in women following menopause [27,28]. The reasons underlying this however, are unclear [29]. One hypothesis is that a reduction in estrogen levels, which has been associated with increased adipocyte fatty acid storage factors and decreased fatty acid oxidation, may potentially lead to higher body fat storage in postmenopausal women [29,28]. From a breast cancer perspective, this additional weight gain after menopause is of concern, since adipose tissue becomes the primary source of endogenous estrogen [27] and has been associated with estrogen-receptor positive carcinogenic tumors [30].

Greater levels of fasting insulin and HOMA-IR at follow-up were observed in women who increased their TV viewing time, compared to women who reduced their TV viewing time in the current study. Positive associations between TV viewing time (h/day) and insulin levels ($\beta = 0.02$, 95%CI: 0.001, 0.03; $p \leq 0.05$) were observed by Thorp *et al.* in a cross-sectional analysis of the full AusDiab follow-up sample [26]. Similarly, Lynch

et al. demonstrated that objectively-assessed sedentary time was positively associated with fasting insulin levels and HOMA-IR in postmenopausal women in NHANES [13]. It is hypothesized that higher levels of insulin secretion may influence breast cancer risk due to insulin growth factor-1 and its cell proliferative and anti-apoptotic properties [31]. Our study suggests that increasing the volume of TV viewing time may influence this pathway and potentially have a detrimental role in postmenopausal breast cancer risk.

Change in TV viewing time was not associated with hs-CRP (a marker of inflammation) at follow-up in this study. The absence of an association is in contrast to the findings of previous research in which positive associations between cross-sectional TV viewing time and hs-CRP levels have been reported [13,32]. This may be due to a lower mean waist circumference (86.9 cm) observed in our study compared to previous research (96.1 cm) [13]. Previous literature has found elevated hs-CRP levels and waist circumference to be positively correlated [33,34], which suggests that adiposity may be a strong mediating factor in the association between sedentary behavior and inflammation. This view is supported by the associations observed between hourly increments of change in TV viewing time and hs-CRP at follow-up being close to significance (models 2 and 3), but after further adjustment for waist circumference, the association was strongly attenuated.

Although little research has been conducted in this area, factors potentially related to increased TV viewing over time include increased leisure-time availability and additional barriers to leisure-time activities [3]. A reduction in the demands related to caring for

children and an increase in discretionary leisure-time due to retirement or semi-retirement are both circumstances that can free up time for TV viewing. In addition, age-related barriers to leisure-time activities and exercise (i.e. mobility and health co-morbidities) [3,35] may both be associated with greater sedentary time and hence increased TV viewing with age.

This large, prospective study of change in self-reported TV viewing time and biomarkers of postmenopausal breast cancer risk has a number of strengths. The population-based nature of the study is an important strength, even though non-response and loss to follow-up may mean that the cohort is not entirely representative of Australian postmenopausal women. A wide variety of potentially confounding factors such as parity and age at first birth were also collected as part of the AusDiab study. This study is one of the few studies to have investigated the associations of sedentary behavior with biomarkers of breast cancer risk specifically in postmenopausal women. Importantly, it is the first study to have investigated a change in a sedentary behavior over time (5-years) allowing for a measurement of change in habitual sedentary behavior (TV viewing time) in the breast cancer biomarker context, confirming the associations observed in a previous cross-sectional study [13].

Despite the number strengths in the current study, limitations do exist. Observational data do not allow inference of causality [36]; hence it is not certain that the associations noted in this study are due to the change in sedentary behavior assessed. That is, it is possible that declining health (reflected in increasing fasting insulin levels, for example) led to an

increase in TV viewing time over time. Also, the self-reported nature of both the sedentary behavior measure and important covariates, such as diet and physical activity, are susceptible to reporting error and biases [37]. This could potentially reduce the association between exposure and outcome variables due to regression dilution bias [9]. Additionally, only a single sedentary behavior (TV viewing time) was assessed, thus not providing complete description of participants' sedentary behavior. However, self-reported TV viewing time has been demonstrated to be valid and reliable [38], and has been positively associated with accelerometer-derived sedentary time [39]. Even though the study included multiple potentially confounding variables, it is possible there may be additional confounding variables that could potentially influence outcomes not included in the models. Despite the fact that biomarkers can indicate an increase in the risk of developing cancer, the current study did not assess the risk of breast cancer itself, which may differ with a change in TV viewing time. A further limitation of the current study is the number of statistically significant different results of demographic and socioeconomic characteristics between the analytic cohort and those excluded women. This limitation implies that the results may not be generalizable to other populations. This issue can be largely attributed to the attrition rate between baseline and follow-up.

Future research investigating sedentary behavior and biomarkers of postmenopausal breast cancer risk should consider objective measurement of sedentary behavior, ideally using inclinometers such as the activPAL, to allow for more precise measurements of sedentary time. Furthermore, intervention studies investigating the impact of limiting or reducing sedentary behavior upon biomarkers of postmenopausal breast cancer risk

should also be considered to further establish the relationship between sedentary behavior and postmenopausal breast cancer risk.

Our findings suggest that change in sedentary behavior may have a significant impact on markers of postmenopausal breast cancer risk such as adiposity and metabolic dysfunction. Adopting strategies to reduce sedentary behaviors such as TV viewing may therefore potentially have beneficial effects on breast cancer risk in postmenopausal women. The current study is one of the few to have investigated the impact of sedentary behavior on multiple putative biomarkers of breast cancer risk in postmenopausal women, and the first to utilize change in TV viewing time as an exposure variable. With few studies in the area, future research investigating the impact of sedentary behavior on postmenopausal breast cancer risk remains of high importance.

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Ethical standards

All Australian legal and ethical standards and protocols were adhered to during the implementation of this study.

Conflict of interest

The authors declare that they have no conflict of interest.

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Table 1: Demographic, socioeconomic, physical activity and biological characteristics of the analytical cohort from the current study stratified by categorical change in TV viewing time

Participant Characteristics (n = 1,001)	Analytic cohort	Reduced TV viewing time	Maintained TV viewing time (+/- 0.5 h/day)	Increased TV viewing time	*p*-value
Age (years)	56.9 (8.4)	57.6 (8.9)	57.0 (8.8)	56.2 (7.6)	0.12
Education					0.01
Did not complete high school	543 (54.3%)	137 (13.7%)	209 (20.9%)	197 (19.7%)	
Completed high school	323 (32.3%)	72 (7.2%)	142 (14.2%)	109 (10.9%)	
University degree or higher	134 (13.4%)	26 (2.6%)	74 (7.4%)	34 (3.4%)	
Employment					0.05
Employed	546 (54.5%)	113 (11.3%)	232 (23.2%)	201 (20.1%)	
Retired	248 (24.8%)	64 (6.4%)	106 (10.6%)	78 (7.8%)	
Home duties	183 (18.3%)	48 (4.8%)	78 (7.8%)	57 (5.7%)	
Other (students (F/T or P/T), unable to work)	24 (2.4%)	11 (1.1%)	9 (0.9%)	4 (0.4%)	
Duration of oral contraceptive pill use					0.56
Never	229 (23.0%)	56 (5.6%)	95 (9.5%)	78 (7.8%)	
< 6-months	62 (6.2%)	13 (1.3%)	26 (2.6%)	23 (2.3%)	
6-months to 2-years	114 (11.4%)	29 (2.9%)	52 (5.2%)	33 (3.3%)	
2- to 5-years	170 (17.0%)	39 (3.9%)	69 (6.9%)	62 (6.2%)	
5- to 10-years	173 (17.3%)	46 (4.6%)	81 (8.1%)	46 (4.6%)	
> 10-years	250 (25.1%)	53 (5.3%)	101 (10.1%)	96 (9.6%)	
Prescribed HRT or estrogen					0.51
Yes	550 (56.7%)	127 (12.7%)	226 (22.6%)	197 (19.7%)	
No	418 (43.1%)	100 (10.0%)	186 (18.6%)	132 (13.2%)	
Unsure	2 (0.2%)	1 (0.1%)	1 (0.1%)	-	
Age at menopause (years)	46.9 (4.8)	46.9 (5.3)	46.8 (4.8)	47.0 (4.4)	0.84

Parity	2.7 (1.2)	2.7 (1.2)	2.7 (1.3)	2.7 (1.2)	0.99
Age at first birth (years)	24.5 (4.7)	24.0 (4.7)	24.9 (4.9)	24.4 (4.4)	0.30
Alcohol consumption (g/day)	8.4 (12.4)	8.2 (12.2)	8.5 (12.1)	8.5 (12.8)	0.95
Energy intake (kJ/day)	7127.9 (2918.8)	7055.5 (2518.5)	7069.4 (3100.4)	7249.5 (2947.2)	0.66
DQI score	89.0 (13.7)	89.0 (13.3)	89.3 (13.2)	88.6 (14.4)	0.75
Smoking status					0.06
Current smoker	87 (8.8%)	25 (2.5%)	42 (4.2%)	20 (2.0%)	
Ex-smoker	241 (24.4%)	56 (5.6%)	112 (11.2%)	73 (7.3%)	
Non-smoker	600 (59.9%)	151 (15.1%)	266 (26.6%)	243 (24.3%)	
Leisure exercise time (MVPA) (min/day)	34.4 (42.8)	36.4 (45.2)	35.2 (43.4)	32.1 (40.2)	0.13
Change in leisure-time physical activity [baseline to follow-up] (MVPA) (min/day)	5.5 (44.4)	10.1 (50.4)	4.1 (41.0)	4.1 (44.1)	0.20
Fasting plasma glucose (mmol/l)	5.3 (0.6)	5.2 (0.6)	5.3 (0.5)	5.3 (0.6)	0.13
2-h plasma glucose (mmol/l)	5.9 (1.8)	5.9 (1.9)	5.9 (1.7)	6.1 (1.9)	0.87
Fasting Insulin (pmol/l)[a]	47.3 (1.8)	45.1 (2.3)	45.4 (2.5)	51.4 (2.4)	0.005
HOMA-IR[a]	0.9 (1.7)	0.9 (2.2)	0.9 (2.4)	1.0 (2.3)	0.007
hs-CRP (mg/l)[a]	2.5 (2.9)	2.3 (4.1)	2.5 (5.0)	2.6 (4.6)	0.62
BMI (kg/m^2)	27.1 (5.0)	26.8 (4.8)	26.8 (4.8)	27.7 (5.5)	0.02
Height (cm)	161.2 (6.2)	161.4 (6.3)	161.2 (6.3)	161.1 (6.1)	0.88
Weight (kg)	70.5 (13.6)	69.7 (12.8)	69.8 (13.1)	71.9 (14.7)	0.05
Waist-to-hip ratio	0.82 (0.06)	0.83 (0.06)	0.82 (0.06)	0.82 (0.06)	0.59
Waist (cm)	86.9 (12.0)	86.6 (11.8)	86.3 (11.5)	87.9 (12.6)	0.16
Hip (cm)	105.4 (10.4)	104.5 (10.0)	104.7 (9.8)	106.8 (11.2)	0.009
Baseline TV viewing time (h/day)	1.8 (1.3)	2.7 (1.5)	1.6 (1.1)	1.3 (0.9)	<0.001
Follow-up TV viewing time (h/day)	1.9 (1.3)	1.4 (1.2)	1.6 (1.1)	2.6 (1.4)	<0.001

Data presented as mean (SD) and n (%).

[a] Data presented as mean interquartile range for variables not normally distributed.

[b] Differences across categories of TV viewing time assessed by one-way ANOVA (continuous variables) or χ^2 tests (categorical variables).

Outcome variable participant numbers: HOMA-IR (n=984); hs-CRP (n=700); and BMI (n=1,000).

Table 2: Prospective associations of change in continuous TV viewing time (h/day) with biomarkers of postmenopausal breast cancer (BMI, n=1,000; waist circumference, n=1,001; fasting plasma glucose, n = 1,001; 2-h plasma glucose, n = 1,001; fasting insulin, n = 1,001; HOMA-IR, n = 984; hs-CRP, n = 700)

	β-coefficient (95% CI)	*p*-value
BMI (kg/m^2)		
Model 1	0.58 (0.30, 0.86)	<0.001
Model 2	0.51 (0.20, 0.82)	0.001
Model 3[a]	0.50 (0.20, 0.81)	0.001
Waist circumference (cm)		
Model 1	1.25 (0.59, 1.91)	<0.001
Model 2	1.25 (0.55, 1.95)	<0.001
Model 3[b]	1.18 (0.49, 1.87)	0.001
Fasting plasma glucose (mmol/l)		
Model 1	0.05 (0.02, 0.08)	0.003
Model 2	0.04 (0.006, 0.07)	0.02
Model 3	0.04 (0.006, 0.07)	0.02
Model 4[c]	0.03 (-0.003, 0.06)	0.08
2-h plasma glucose (mmol/l)		
Model 1	0.11 (0.02, 0.21)	0.02
Model 2	0.09 (-0.02, 0.20)	0.10
Model 3	0.09 (-0.02, 0.19)	0.11
Model 4[d]	0.06 (-0.04, 0.17)	0.22
Fasting insulin (pmol/l)*		
Model 1	39.75 (38.49, 41.06)	<0.001
Model 2	38.80 (37.53, 40.12)	0.002
Model 3	38.76 (37.50, 40.07)	0.002
Model 4[e]	38.13 (37.08, 39.20)	0.01
HOMA-IR*		
Model 1	39.26 (38.05, 40.51)	<0.001
Model 2	38.50 (37.26, 39.78)	0.006
Model 3	38.47 (37.23, 39.74)	0.007
Model 4[f]	37.93 (36.92, 38.98)	0.03
hs-CRP (mg/l)*		
Model 1	40.49 (37.81, 43.37)	0.006
Model 2	39.45 (36.66, 42.44)	0.06
Model 3	39.40 (36.63, 42.38)	0.07
Model 4[g]	38.36 (35.87, 41.02)	0.22

* Data presented as back-transformed percentage change in values for natural log-transformation outcomes.
[a] Fully adjusted model includes: age, baseline TV viewing time, education, duration of oral contraceptive pill use, prescription of HRT or estrogen therapy, age at menopause, parity, alcohol intake, dietary energy intake, smoking status, and MVPA.
[b] Fully adjusted model includes: baseline TV viewing time, age, duration of oral contraceptive pill use, age at menopause, prescription of HRT or estrogen therapy, parity, smoking status and MVPA.
[c] Fully adjusted model for baseline TV viewing time, age, age at menopause, parity, alcohol intake, baseline DQI score, smoking status, MVPA, and waist circumference.
[d] Fully adjusted model for baseline TV viewing time, age, age at menopause, age at first birth, baseline DQI score,

MVPA and waist circumference.
[e] Fully adjusted model for baseline TV viewing time, age, age at menopause, alcohol intake, dietary energy intake, baseline DQI score, MVPA and waist circumference.
[f] Fully adjusted model for baseline TV viewing time, age, age at menopause, alcohol intake, dietary energy intake, baseline DQI score, smoking status, MVPA and waist circumference.
[g] Fully adjusted model for baseline TV viewing time, age, education, duration of oral contraceptive pill use, parity, alcohol intake, smoking status, MVPA, and waist circumference

Figure Legends

Figure 1: Associations of change in categorical TV viewing time from baseline (1999/00) to follow-up (2004/05) with anthropometric measures of adiposity in AusDiab.

Figure 2: Associations of change in categorical TV viewing time from baseline (1999/00) to follow-up (2004/05) with blood biomarkers of metabolic dysfunction and inflammation in AusDiab.