

## ABSTRACT (UPDATED)

Approximately 25% of older Americans consume  $\geq 4$  dietary supplements/day. Block et al. reported an unusually low prevalence of diabetes in a cohort of long-term ( $\geq 20$  y) users of multiple nutritional supplements. A decade later, we collected medical histories and measured HbA1c in members of the original sample plus an additional sample of the cohort who used multiple supplements for 3-5 years. Long-term multi-supplement users (LTMS, n=206, 22-89 y) were compared to NHANES 07-10 participants (20-80 y), characterized as non-supplement users (n=1409), multivitamin only users defined as  $\geq 10$  vitamins/minerals (n=488), users of only one single component supplement (e.g., fish oil) or one single purpose supplement with fewer than 10 vitamins and minerals (e.g., calcium and vitamin D) (n=300), or users of  $\geq 2$  supplement products (n=1170). As the Block study participants were essentially all non-Hispanic white (98.1%) and all non-smokers, we limited the NHANES sample to NHW, non-smoking participants. However, even after this restriction, the LTMS sample showed demographic differences from the NHANES sample including an older age, a higher percentage of women, higher incomes, more college educated, and lower BMI. The sex & BMI adjusted prevalence of diabetes was lower among members of the LTMS cohort compared to the NHANES sample, with the most striking difference among those aged  $\geq 60$  years (6.2% for LTMS cohort vs 17.7% for the NHANES sample). After adjusting for age, sex, income, education and BMI, we observed that the prevalence of diabetes among non-supplement users was almost 2-fold higher (9.2%, 95% CI: 7.6-10.9%) compared to the LTMS users (5.4%, 95% CI: 2.0-8.8%). Prevalence of diabetes in other supplement user groups was not significantly different from that of the non-supplement users. Analyses yet to be completed will assess nutritional status and additional metabolic risk factors. A limitation of this study is potential for self-selection of healthier individuals into the LTMS group. However, given the importance of addressing the high incidence of type 2 diabetes and the relative safety of fortified food and supplement use, and the previous observation of improved cardiovascular health (1), further investigations in LTMS users are warranted.

## BACKGROUND

A previous study of a cohort of 20+ year users of multiple dietary supplements found, in addition to better nutritional status vs. NHANES controls, improved risk factors and lower prevalence of disease, including diabetes.(1) That study did not include diabetes-related clinical chemistry, or collect information on the use of diabetes medication. We report initial findings with respect to diabetes prevalence from a new study of this cohort, including both participants in the original study and a sample of 3-5 year multiple supplement users.

## METHODS

Long term multiple vitamin users (LTMS), 2+ supplements/week, were recruited from a dietary supplement manufacturer and distributor (Shaklee Corp.). Participants from the 2007-2010 NHANES were used for comparison to the LTMS sample. To match the characteristics of the LTMS sample, NHANES subjects were restricted to non-Hispanic white(NHW) adults, 20 + years of age, who did not currently smoke, were not pregnant and were free of cancer.

LTMS and NHANES data were combined for analysis. To preserve complex sampling design of NHANES, we incorporated the strata & primary sampling unit (PSU) designations for NHANES participants and recalibrated the sample weights as the original sample weight divided by the sum of the sample weights within the supplement category. The LTMS sample was assigned one strata, and each LTMS subject was given a unique PSU and a weight of 1/LTMS sample size. This recalibration allowed for equal weighting for each supplement group and more precise variance estimation but no longer provides estimates that are considered nationally representative. We used SUDAAN statistical software and SAS survey procedures to account for the complex sampling design in the variance estimates.

## RESULTS

Participant Characteristics: Weighted Means and Percents (95% Conf. Intervals)

	No Suppl. Use	Single/Single Purpose Suppl.	Multivitamin	2+ Suppl./day	Long-term Multiple Suppl.
Sample N	1409	300	488	1170	206
Age (years)	44.2 (43.1, 45.4)	52.3 (50.3, 54.4)*	45.1 (43.1, 47.0)	55.3 (54.1, 56.5)*	64.8 (62.8, 66.8)*
Female (%)	44.6 (42.4, 46.8)	53.9 (46.3, 61.4)*	50.1 (45.0, 55.1)	64.1 (60.1, 67.9)*	70.4 (63.8, 76.3)*
Non Hispanic Hispanic (%)	100 0	100 0	100 0	100 0	98.1 (94.9, 99.3)* 1.9 (0.7, 5.1)*
Income (%)					
<\$40,000	31.7 (26.9, 36.9)	29.8 (23.6, 36.8)	23.7 (19.7, 28.3)*	31.6 (28.0, 35.5)	9.7 (6.3, 14.6)*
>\$40,000	63.0 (58.0, 67.7)	66.4 (60.1, 72.2)	70.5 (65.5, 75.0)*	63.6 (60.3, 66.7)	75.2 (68.8, 80.7)*
Education (%)					
< 9 <sup>th</sup> grade	2.8 (1.8, 4.2)	3.2 (1.7, 5.9)	1.6 (0.8, 3.3)*	2.0 (1.1, 3.7)	0 (0, 0)*
9-11 <sup>th</sup> grade	9.5 (7.6, 11.8)	8.0 (4.7, 13.2)	5.0 (3.1, 7.9)*	7.9 (6.2, 10.0)	1.9 (0.7, 5.1)*
HS graduate	23.4 (20.2, 26.9)	27.7 (21.3, 35.1)	19.4 (14.8, 25.1)	22.4 (20.0, 24.9)	10.2 (6.7, 15.2)*
Some college	32.3 (29.3, 35.5)	28.7 (23.3, 34.7)	33.9 (29.0, 39.3)	30.1 (26.9, 33.5)	26.2 (20.6, 32.7)*
College & above	32.0 (28.4, 35.9)	32.5 (25.7, 40.1)	40.0 (33.6, 46.9)*	37.6 (33.9, 41.6)*	62.7 (54.8, 68.1)*
BMI (kg/m <sup>2</sup> ) <sup>1</sup>	29.1 (28.7, 29.5)	28.1 (27.2, 29.0)*	27.9 (27.3, 28.5)*	27.2 (26.8, 27.7)*	25.5 (24.9, 26.1)*
Dietary fiber (g/d) <sup>2</sup>	13.6 (13.0, 14.2)*	15.1 (14.0, 16.2)*	14.6 (13.8, 15.4)*	16.1 (15.5, 16.8)*	20.1 (19.3, 21.2)*
Energy (kcal/d) <sup>1</sup>	1900 (1851, 1952)	1879 (1800, 1962)	1985 (1915, 2058)	1993(1936, 2050)*	1711(1621, 1804)*

<sup>1</sup>Age & sex adjusted geometric means & 95% CIs. <sup>2</sup>Age, sex & energy adjusted geometric means and 95% CIs. <sup>3</sup>Dietary data derived from the Block FFQ (2014, version 3) for LTMS group and 24 hr recall for NHANES participants. \*Estimates are significantly different from the No supplement use category (p<0.05)

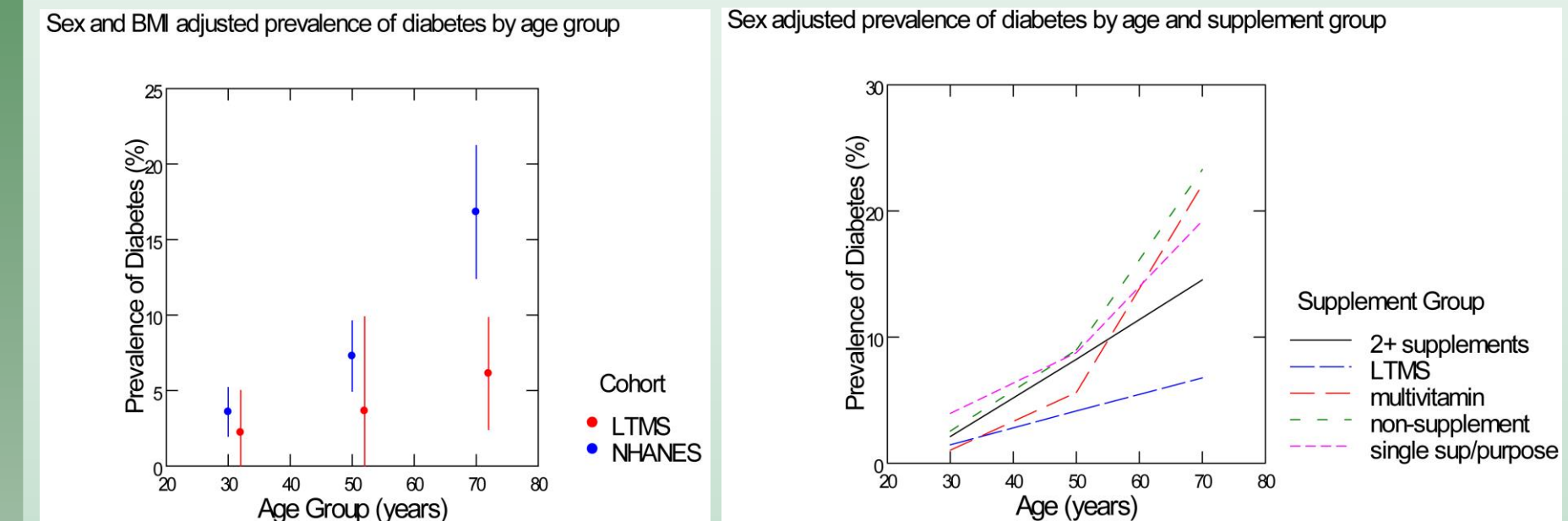
Prevalence of diabetes based on elevated HbA1c, medication use & self report (95% conf. intervals)

	No Suppl. Use (n=1409)	Single/Single Purpose Suppl. (n=300)	Multivitamin (n=488)	2+ Suppl./day (n=1170)	Long-term Multiple Suppl. (n=206)
Model 1 <sup>1</sup> p-value <sup>2</sup>	9.2 (7.6, 10.9)	10.2 (6.7, 13.7) 0.61	8.8 (6.1, 11.6) 0.76	8.9 (6.8, 10.9) 0.77	5.4 (2.0, 8.8) 0.07
Model 1 + dietary fiber (g) + energy (kcal/d) p-value <sup>2</sup>	9.6 (7.9, 11.3)	10.4 (6.7, 14.1) 0.66	8.9 (6.1, 11.8) 0.64	8.6 (6.6, 10.7) 0.47	5.1 (1.6, 8.5) 0.035

<sup>1</sup>Age Model 1 is adjusted for age (years), sex, income (<\$40,000, >\$40,000, undisclosed), education level (<9<sup>th</sup> grade, 9-11<sup>th</sup> grade, high school, some college, College & above), and BMI (kg/m<sup>2</sup>). <sup>2</sup>p-values compared to No Suppl. Use.

**Diabetes Prevalence:** we separated subjects into 3 age groups (20-39, 40-59, 60+ years), and performed an ANCOVA adjusting for sex & BMI. Least square means and 95% CIs by age group stratified by cohort are presented below.

We used the same methods to provide sex adjusted estimates for each age group by supplement group, graphed as line series. Compared with NHANES, the LTMS group exhibited progressively improved diabetes prevalence with age. Within the NHANES data, the use of two or more supplements also trended towards better outcomes with age (significant interaction with age, p<0.01).



## DISCUSSION

There is evidence that improved nutritional status (e.g., calcium & D (2)), choice of a low glycemic index meal plan (3), or low levels of nutritionally modifiable markers of inflammation (4,5) can lower the risk of type 2 diabetes. In a previous study of the LTMS population, the sample showed improved nutritional status, lower risk factors including CRP, and the prevalence of diabetes was only 2.9% at an average age of 63 (1). We have now repeated this diabetes observation and further supported it with measurement of HbA1c and capture of diabetes medication use. Analyses yet to be completed include measures of nutritional status and risk factors. A limitation of this study is non-random nature of the subject selection. However, given the importance of addressing the high incidence of type 2 diabetes and the relative safety of fortified food & supplement use, further investigations in this population are warranted.

## REFERENCES

- Block G et al. 2007. Usage patterns, health, and nutritional status of long-term multiple dietary supplement users: a cross-sectional study. *Nutrition Journal* 2007, 6:30 doi:10.1186/1475-2891-6-30
- Pittas AG et al. 2007. The Role of Vitamin D and Calcium in Type 2 Diabetes. A Systematic Review and Meta-Analysis. *J Clin Endocrinol Metab* (2007) 92 (6): 2017-2029. DOI: <https://doi.org/10.1210/jc.2007-0298>
- Willett W, Manson J, Liu S. 2002. Glycemic index, glycemic load, and risk of type 2 diabetes. *Am J Clin Nutr* 76(1): 274S-280S.
- Hu FB et al. 2004. Inflammatory Markers and Risk of Developing Type 2 Diabetes in Women. *Diabetes* 53(3): 693-700. <https://doi.org/10.2337/diabetes.53.3.693>
- Spranger J et al. 2003. Inflammatory Cytokines and the Risk to Develop Type 2 Diabetes. *Diabetes* 2003 Mar; 52(3): 812-817. <https://doi.org/10.2337/diabetes.52.3.812>