

Preplanned Studies

Impact of Daily Step Count on Diabetes Management and Complications Among Elderly Individuals — Jiangsu Province, China, 2020–2022

Peng Yu^{1,✉}; Xuejian Ni^{2,✉}; Li Xu^{3,✉}; Lei Zhang¹; Ling Cao¹; Qiyu Chen¹; Yixin Hu⁴;
Kun Qian⁴; Xiaoying Li¹; Xiaomu Li^{1,✉}; Jianying Gu^{4,✉}

Summary

What is already known about this topic?

Current literature underscores the significance of appropriate physical activity in managing diabetes, primarily utilizing self-reported data. Yet, the impact of objectively measured physical activity in older diabetic populations remains unclear.

What is added by this report?

Our research on elderly diabetic patients indicated a correlation between an increased number of daily steps and improved metabolic profiles, as well as a decrease in the incidence of cardiovascular complications.

What are the implications for public health practice?

Elevated daily step counts may confer significant benefits to elderly individuals with diabetes. The use of devices to monitor these steps could serve as a potent cardiovascular marker, and hold great potential as a screening or intervention tool in community-oriented settings.

The prevalence of type 2 diabetes mellitus (T2DM) is notably increasing within the population of older adults. Research has noted a compelling link between elevated levels of physical activity (PA) and enriched functional health, diminished risk of falls, and enhanced cognitive health in older adults (1). More specifically, PA quantified in daily step counts emerges as a vital modifiable behavior for diabetes management among the geriatric population. Substantial evidence from various studies substantiates that regular PA can lead to a better prognosis on diabetes. Historically, PA was primarily evaluated through questionnaires, which often yielded higher outputs when compared to device-measured activities (2). The advent of movement sensors, such as pedometers, has facilitated more accurate, tangible measurement of PA, in terms of daily step counts. This metric communicated as steps/day is

highly translatable, memorable, and readily accessible via modern wearables and smartphones that are now ubiquitous (3). The detection and quantification of appropriate PA levels in older adults has become an area of intensified focus as it plays a significant role in estimating and promoting their overall health status (4).

In the course of this study, we assembled a geriatric diabetic cohort and undertook an analysis of baseline data collected between 2020 and 2022. Our primary focus was the correlation between daily steps and diabetic complications. To accurately assess step counts, we distributed electronic smart wristbands in three distinct streets in Xiangcheng District, Suzhou City, Jiangsu Province. These were primarily given to the elderly diabetic population during freely provided annual health check-ups, sponsored by the local government (5). A total of 1,415 individuals, all 65 years or older and diagnosed with diabetes according to the standards set by the American Diabetes Association (6), participated in the study from 2020 to 2022 (305, 964, and 146 cases per year, respectively).

High-sensitivity cardiac troponin T (hs-cTnT), albuminuria, serum creatine, and other laboratory parameters were measured using Roche Cobas 6000. Microalbuminuria (MA) was defined as a urine albumin-creatinine ratio ≥ 30 mg/g, subclinical myocardial injury (SMI) as hs-cTnT ≥ 14 ng/L (7), and chronic kidney disease (CKD) as an estimated glomerular filtration rate (eGFR) < 60 mL/(min·1.73 m²) using the CKD-EPI equation (8). Additional pre-existing conditions such as cancer, chronic obstructive pulmonary disease (COPD), etc. were self-reported by participants through questionnaires, with reference to previous studies (9). This research received approval from the Ethics Committee of Zhongshan Hospital, Fudan University [Approval No. B2020-201(3)], and all participants willingly gave consent to partake in this study.

The study employed *t*-tests and chi-squared tests for the evaluation of means and category distributions, respectively, based on variables calculated according to steps per day categories. A linear regression model was utilized to estimate correlations, with adjustments made for key potential confounding variables, which included age, gender, body mass index (BMI), HbA1c, amongst other factors. Covariates adjusted for in the logistic regression consisted of age (categorized, <75 and ≥ 75), gender, BMI (categorized, <18.5, 18.5–23.9, 24.0–27.9, and ≥ 28.0), HbA1c (categorized, <7% and $\geq 7\%$), and triglycerides (TG) (categorized, <1.7 and ≥ 1.7). Statistical analysis of all data was performed using STATA for Windows (Version 17.0; Stata-Corp, College Station, TX, USA), and two-tailed *P* values less than 0.05 were deemed statistically significant.

The participant pool of 1,415 individuals comprised 664 males and 751 females, each averaging 6,370 steps/day ($\pm 4,431$). A trend emerged wherein those who walked more steps daily were generally younger and demonstrated lower BMIs, diastolic blood pressure, and triglyceride levels. Correspondingly, there was a general decrease in HbA1c levels as daily step counts increased. Interestingly, no significant variances were observed in education level, the proportions of current drinkers or smokers, or residential status in relation to step count. With respect to comorbid conditions, the incidences of cancer, COPD, and MA appeared to decline with increased daily steps, albeit falling short of statistical significance. Importantly, higher daily steps were associated with lower levels of the myocardial injury biomarker hs-cTnT, as well as reduced UACR, an indicator of kidney damage or elevated kidney disease risk. Simultaneously, higher estimated glomerular filtration rates (eGFR) correlated with increased steps/day (Table 1).

The linear correlation analysis results indicated negative correlations between the steps per day, and both hs-cTnT ($\beta = -0.207$, $r = 0.14$, $P < 0.001$) and the log-transformed UACR ($\beta = -0.0268$, $r = 0.087$, $P < 0.001$). A positive correlation surfaced with eGFR ($\beta = 0.709$, $r = 0.16$, $P < 0.001$). The correlations involving hs-cTnT and eGFR remained significant even after adjusting for variables such as age, gender, BMI, HbA1c, TG, LDL-c, UA, smoking status, residential status, educational level, and insulin administration. (Table 2).

The results from multivariable-adjusted logistic regressions suggest that, when compared to the first quartile, the odds ratios [95% confidence interval (CI)]

for self-reported cardiovascular diseases (CVD) (comprising stroke, coronary heart disease, and heart failure) were 0.398 (0.230–0.689), and 0.620 (0.386–0.994) for elevated hs-cTnT — indicating SMI; both showing a statistically significant trend ($P < 0.05$, Table 3). In terms of renal complications, such as MA and decreased eGFR (indicative of CKD), the odds ratios (95% CI) stood at 0.886 (0.617–1.272) and 0.777 (0.374–1.616) respectively. However, these results did not achieve statistical significance (Table 3).

DISCUSSION

In this study, we explored the correlation between daily step counts and various laboratory parameters as well as complications amongst community-dwelling elderly residents diagnosed with diabetes. Our data indicates that senior residents with diabetes on average took 6,370 steps daily. Interestingly, our analysis also revealed that a higher step count was associated with lower metabolic markers, specifically BMI and TG. Furthermore, a significant association was found between daily step counts and incidence of cardiovascular events, alongside cardiovascular and renal damage indicators.

Pedometers enabled us to evaluate the intensity of physical activity. The recommended daily step count for healthy older adults falls between 7,000 and 10,000, while for individuals with chronic illnesses like diabetes, the suggested range is between 6,500 and 8,500. This recommendation is based on limited evidence. It should be noted that increasing physical activity in the elderly, particularly those with diabetes, necessitates a clinical approach as opposed to a public health strategy. A previous meta-analysis has indicated that PA levels are inversely associated with risks of CVD and T2DM incidence, an association which is also influenced by changes in PA, primarily based on self-reported questionnaires (10). However, to the best of our understanding, no prior studies have investigated how physically active levels, objectively measured using devices, impact community-dwelling elderly individuals with diabetes.

Our findings notably suggest that reduced daily step counts could act as potential biomarkers for identifying complications in community-dwelling elderly individuals. These results also offer clinical evidence that a decrease in daily steps among those with diabetes might present new risk factors and biomarkers for the development of cardiovascular disease. To the best of our knowledge, this represents the first study to

TABLE 1. Descriptive characteristics and number of steps walked per day by geriatric diabetes patients.

Variables	Steps/d, n (%)					P value
	<4,000 (n=460, 32.56%)	4,000–7,999 (n=506, 35.73%)	8,000–11,999 (n=293, 20.72%)	≥12,000 (n=156, 10.99%)	Total (n=1,415)	
Steps daily	1,774±1,150	5,915±1,129	9,822±1,139	14,954±2,935	6,370±4,431	
Male, n (%)	222 (48.26)	236 (46.64)	131 (44.71)	75 (48.08)	664 (46.93)	0.800
Age, mean±SD, years	73.38±5.32	72.12±4.80	70.87±4.28	70.86±3.90	72.13±4.89	<0.001
Very elderly (≥75 years), n (%)	159 (34.57)	122 (24.11)	45 (15.36)	26 (16.67)	352 (24.88)	<0.001
Education						0.162
<High school	436 (94.78)	467 (92.29)	270 (92.15)	150 (96.15)	1,323 (93.50)	
≥High school	24 (5.22)	39 (7.71)	23 (7.85)	6 (3.85)	92 (6.50)	
Alcohol						0.874
Never drinker	387 (84.13)	425 (83.99)	238 (81.23)	129 (82.69)	1,179 (83.32)	
Former drinker	17 (3.70)	17 (3.36)	10 (3.41)	4 (2.56)	48 (3.39)	
Current drinker	56 (12.17)	64 (12.65)	45 (15.36)	23 (14.74)	188 (13.29)	
Smoking						0.117
Never smoker	336 (73.04)	362 (71.54)	226 (77.13)	120 (76.92)	1,044 (73.78)	
Former smoker	42 (9.13)	37 (7.31)	27 (9.22)	15 (9.62)	121 (8.55)	
Current smoker	82 (17.83)	107 (21.15)	40 (13.65)	21 (13.46)	250 (17.67)	
Residential status						0.054
Living with family	413 (90.17)	444 (87.92)	275 (93.86)	138 (88.46)	1,270 (89.94)	
Living alone	45 (9.83)	61 (12.08)	18 (6.14)	18 (11.54)	142 (10.06)	
Examination						
BMI, kg/m ²	25.21±3.4	25.16±3.11	24.8±2.95	24.27±2.68	25±3.14	0.006
Waist, cm	86.89±9.37	86.8±9.23	85.5±10.08	84.7±9.55	86.33±9.52	0.027
BMI category						0.010
<18.5 (lean)	6 (1.35)	2 (0.40)	3 (1.03)	1 (0.66)	12 (0.87)	
18.5–23.9 (normal)	158 (35.59)	181 (36.13)	115 (39.52)	76 (50.33)	530 (38.21)	
24–27.9 (overweight)	196 (44.14)	232 (46.31)	139 (47.77)	59 (39.07)	626 (45.13)	
28–42.9 (obesity)	84 (18.92)	86 (17.17)	34 (11.68)	15 (9.93)	219 (15.79)	
SBP, mmHg	146.64±19.66	146.4±17.72	146.23±18.27	146.5±18.31	146.45±18.52	0.993
DBP, mmHg	79.26±10.95	80.22±10.49	78.4±10.09	78.17±10.27	79.3±10.55	0.054
Laboratory						
FBG, mmol/L	8.4±2.65	8.35±2.45	8.45±2.28	8.31±2.31	8.38±2.47	0.928
HbA1C, %	7.47±1.65	7.37±1.53	7.37±1.63	7.13±1.45	7.37±1.58	0.113
TG, mmol/L	1.9±1.26	1.93±1.53	1.77±1.25	1.57±1.10	1.85±1.35	0.020
TC, mmol/L	4.93±1.21	4.99±1.18	4.98±1.17	4.92±1.11	4.96±1.18	0.837
LDL-C, mmol/L	2.83±1.00	2.91±0.96	2.94±0.98	2.87±0.93	2.88±0.97	0.426
HDL-C, mmol/L	1.33±0.30	1.36±0.33	1.39±0.35	1.43±0.33	1.36±0.33	0.002
ALT, U/L	20.66±17.33	21.9±17.32	21.81±14.8	21.15±14.12	21.39±16.52	0.705
AST, U/L	22.92±9.18	23.4±11.86	22.87±10.16	22.16±7.91	23.00±10.29	0.603
UA, μmol/L	336±111.88	323.83±92.26	310.68±87.89	301.92±84.27	322.65±98.05	<0.001
Medication						
Metformin	280 (60.87)	303 (59.88)	170 (58.02)	91 (58.33)	844 (59.65)	0.866
SU	197 (42.83)	231 (45.65)	149 (50.85)	74 (47.44)	651 (46.01)	0.187
Insulin	73 (15.87)	69 (13.64)	27 (9.22)	26 (16.67)	195 (13.78)	0.047

Continued

Variables	Steps/d, n (%)				Total (n=1,415)	P value
	<4,000 (n=460, 32.56%)	4,000–7,999 (n=506, 35.73%)	8,000–11,999 (n=293, 20.72%)	≥12,000 (n=156, 10.99%)		
Comorbidity						
Cancer	14 (3.04)	13 (2.57)	7 (2.39)	3 (1.92)	37 (2.61)	0.876
COPD	11 (2.39)	5 (0.99)	1 (0.34)	1 (0.64)	18 (1.27)	0.059
Stroke	60 (13.04)	42 (8.30)	14 (4.78)	9 (5.77)	125 (8.83)	<0.001
Coronary heart disease	24 (5.22)	8 (1.58)	9 (3.07)	3 (1.92)	44 (3.11)	0.010
hs-cTnT, ng/L	11.51±7.78	9.81±6.01	8.96±4.66	8.73±4.79	10.05±6.36	<0.001
SMI	97 (24.49)	74 (16.41)	34 (13.08)	17 (12.14)	222 (17.80)	<0.001
IgUACR, mg/g	3.42±1.39	3.29±1.36	3.12±1.29	3.02±1.3	3.26±1.35	0.007
MA	151 (42.18)	188 (43.62)	97 (38.34)	42 (31.34)	478 (40.65)	0.063
eGFR, mL/(min·1.73 m ²)	88.87±21.4	92.29±19.47	96.49±16.29	97.40±17.05	92.61±19.52	<0.001
CKD	49 (10.65)	43 (8.51)	12 (4.10)	7 (4.49)	111 (7.85)	0.004

Abbreviation: BMI=body mass index; SBP=systolic blood pressure; DBP=diastolic blood pressure; FBG=fasting blood glucose; HbA1c=glycated hemoglobin; TG=triglycerides; TC=total cholesterol; HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol; RC=remnant cholesterol; ALT=alanine aminotransferase; AST=aspartate aminotransferase; UA=uric acid; eGFR=estimated glomerular filtration rate; SU=sulfonylurea; COPD=chronic obstructive pulmonary disease; SMI=subclinical cardiac injury with hs-cTnT≥14 ng/L; UACR=urinary albumin-to-creatinine ratio; MA=microalbuminuria with UACR≥30 mg/g; eGFR=estimated glomerular filtration rate; CKD=chronic kidney disease, eGFR<60 mL/(min·1.73 m²).

TABLE 2. Linear regression analysis for the association between daily step count and cardiac and renal damage in elder T2DM patients.

Cardiorenal injury marker	Model 1	Model 2	Model 3
hs-cTnT β (t, P)	-0.207*** (-5.11, <0.001)	-0.116** (-3.03, 0.003)	-0.083* (-2.12, 0.034)
IgUACR β (t, P)	-0.027** (-2.99, 0.003)	-0.023* (-2.57, 0.010)	-0.013 (-1.45, 0.146)
eGFR β (t, P)	0.709*** (6.13, <0.001)	0.377*** (3.44, 0.001)	0.224* (2.04, 0.042)

Note: Model 1: crude model. Model 2: adjusted for age and gender. Model 3: adjusted to account for variables such as age, gender, BMI, HbA1c, TG, LDL-c, UA, smoking status, residential status, education level, and insulin usage.

Abbreviation: T2DM=type 2 diabetes mellitus; IgUACR=log-transformed urinary albumin-to-creatinine ratio; eGFR=estimated glomerular filtration rate; BMI=body mass index; HbA1c=glycated hemoglobin; TG=triglycerides; LDL-C=low-density lipoprotein cholesterol; UA=uric acid.

* P<0.05;

** P<0.01;

*** P<0.001.

evaluate the impact of objectively measured step count in community-dwelling elderly individuals with diabetes and to discuss implications on comorbidity status, backed by a moderately-sized sample. Given the obstacles associated with identifying complications or symptoms in a community setting, utilizing decreased daily step counts as indicators could aid in the early identification of elderly individuals with diabetes who are at an increased risk for cardiovascular disease.

Modern smartwatches now incorporate advanced health monitoring capabilities, equipped with sensors for tracking heart rate, sleep, and physical activity. Leveraging on sophisticated algorithms, these devices provide personalized insights, and can integrate seamlessly with existing healthcare systems, positioning them as vital tools for managing health and lifestyle

patterns. Furthermore, these devices engender an ability to accumulate long-term health data, consequently empowering healthcare providers to make more informed decisions. It also fosters seamless communication between families and medical teams, promoting all-inclusive care and support.

This study was subject to some limitations. Due to its cross-sectional design, it is unable to establish a causal connection between daily step counts and the incidence of cardiovascular disease. Furthermore, the pedometers utilized in this research did not gather information concerning the intensity or duration of walking, nor the type of exercise being performed. These omissions may introduce added layers of complexity and expense to the monitoring process, potentially inhibiting access in certain applications.

TABLE 3. Odds ratio (OR) and 95% confidence intervals (CIs) for cardiac and renal damage according to quartiles of daily step count.

Outcomes	1,000 steps/day ORs (95% CIs)				P trend
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	
CVD cases/total	65/354 (18.36)	37/354 (10.45)	36/354 (10.17)	25/353 (7.08)	
Model 1	1 (ref.)	0.519 (0.336–0.801)**	0.503 (0.325–0.779)**	0.339 (0.208–0.552)***	<0.001
Model 2	1 (ref.)	0.522 (0.338–0.806)**	0.525 (0.338–0.816)**	0.363 (0.221–0.594)***	<0.001
Model 3	1 (ref.)	0.606 (0.376–0.978)*	0.544 (0.334–0.887)*	0.398 (0.230–0.689)**	<0.001
SMI	75/304 (24.67)	61/303 (20.13)	48/327 (14.68)	38/313 (12.14)	
Model 1	1 (ref.)	0.770 (0.525–1.129)	0.525 (0.351–0.785)**	0.422 (0.275–0.647)***	<0.001
Model 2	1 (ref.)	0.763 (0.509–1.141)	0.599 (0.392–0.915)*	0.524 (0.334–0.823)**	0.003
Model 3	1 (ref.)	0.786 (0.512–1.206)	0.659 (0.424–1.025)	0.620 (0.386–0.994)*	0.035
MA	112/271 (41.33)	128/289 (44.29)	128/310 (41.29)	110/306 (35.95)	
Model 1	1 (ref.)	1.129 (0.807–1.578)	0.998 (0.717–1.390)	0.797 (0.569–1.115)	0.137
Model 2	1 (ref.)	1.106 (0.786–1.555)	1.036 (0.738–1.454)	0.813 (0.576–1.149)	0.220
Model 3	1 (ref.)	1.076 (0.752–1.539)	1.042 (0.732–1.484)	0.886 (0.617–1.272)	0.499
CKD	37/354 (10.45)	37/353 (10.48)	22/354 (6.21)	15/353 (4.25)	
Model 1	1 (ref.)	1.003 (0.620–1.624)	0.568 (0.328–0.984)*	0.380 (0.205–0.706)**	<0.001
Model 2	1 (ref.)	1.024 (0.628–1.669)	0.661 (0.378–1.156)	0.481 (0.256–0.905)*	0.009
Model 3	1 (ref.)	1.350 (0.756–2.409)	0.818 (0.430–1.556)	0.777 (0.374–1.616)	0.282

Note: Model 1: crude model. Model 2: adjusted for age, gender. Model 3: adjusted for variables including age, gender, BMI, HbA1c, TG, LDL-c, UA, smoking status, residential status, education level, and insulin usage.

Abbreviation: CVD=cardiovascular disease, including stroke, coronary heart disease, and heart failure; SMI=subclinical myocardial injury, high-sensitivity cardiac troponin T (hs-cTnT) ≥ 14 ng/L; MA=microalbuminuria; UACR=urinary albumin-to-creatinine ratio, UACR ≥ 30 mg/g; CKD=chronic kidney disease, eGFR=estimated glomerular filtration rate, eGFR < 60 mL/(min \cdot 1.73 m²); BMI=body mass index; HbA1c=glycated hemoglobin; TG=triglycerides; LDL-C=low-density lipoprotein cholesterol; UA=uric acid.

* $P < 0.05$;

** $P < 0.01$;

*** $P < 0.001$.

In conclusion, our research suggests a significant inverse correlation between daily step count and cardiovascular disease risk in community-dwelling elderly individuals afflicted with diabetes.

Conflicts of interest: No conflicts of interest.

Acknowledgements: All dedicated health workers in the Xiangcheng District health system, and all participants who took part in the construction of this geriatric diabetes cohort.

doi: 10.46234/ccdcw2023.189

Corresponding authors: Xiaomu Li, li.xiaomu@zs-hospital.sh.cn; Jianying Gu, gu.jianying@zs-hospital.sh.cn.

¹ Department of Endocrinology and Metabolism, Zhongshan Hospital, Fudan University, Shanghai, China; ² Taiping Community Healthcare Center, Suzhou City, Jiangsu Province, China; ³ Yuanhe Community Healthcare Center, Suzhou City, Jiangsu Province, China; ⁴ Department of Information and Intelligence Development, Zhongshan Hospital, Fudan University, Shanghai, China.

§ Joint first authors.

Submitted: July 28, 2023; Accepted: September 12, 2023

REFERENCES

- Piercy KL, Troiano RP, Ballard RM, Carlson SA, Fulton JE, Galuska DA, et al. The physical activity guidelines for Americans. *JAMA* 2018;320(19):2020 – 8. <http://dx.doi.org/10.1001/jama.2018.14854>.
- Althoff T, Sosić R, Hicks JL, King AC, Delp SL, Leskovec J. Large-scale physical activity data reveal worldwide activity inequality. *Nature* 2017;547(7663):336 – 9. <http://dx.doi.org/10.1038/nature23018>.
- Garduno AC, Lacroix AZ, Lamonte MJ, Dunstan DW, Evenson KR, Wang GX, et al. Associations of daily steps and step intensity with incident diabetes in a prospective cohort study of older women: the OPACH study. *Diabetes Care* 2022;45(2):339 – 47. <http://dx.doi.org/10.2337/dc21-1202>.
- Jefferis BJ, Iliffe S, Kendrick D, Kerse N, Trost S, Lennon LT, et al. How are falls and fear of falling associated with objectively measured physical activity in a cohort of community-dwelling older men? *BMC Geriatr* 2014;14:114. <http://dx.doi.org/10.1186/1471-2318-14-114>.
- Wei Y, Zhou GQ, Wu XY, Lu XF, Wang XJ, Wang B, et al. Latest incidence and electrocardiographic predictors of atrial fibrillation: a prospective study from China. *Chin Med J (Engl)* 2023;136(3):313 – 21. <http://dx.doi.org/10.1097/CM9.0000000000002340>.
- American Diabetes Association Professional Practice Committee. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes—2022. *Diabetes Care* 2022;45(S1):S17–38. <http://dx.doi.org/10.2337/dc22-S002>.
- Rubin J, Matsushita K, Ballantyne CM, Hoogeveen R, Coresh J, Selvin E. Chronic hyperglycemia and subclinical myocardial injury. *J Am Coll*

- [Cardiol](http://dx.doi.org/10.1016/j.jacc.2011.10.875) 2012;59(5):484 – 9. <http://dx.doi.org/10.1016/j.jacc.2011.10.875>.
8. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF, Feldman HI, et al. A new equation to estimate glomerular filtration rate. [Ann Intern Med](http://dx.doi.org/10.7326/0003-4819-150-9-200905050-00006) 2009;150(9):604 – 12. <http://dx.doi.org/10.7326/0003-4819-150-9-200905050-00006>.
9. Zhao Y, Hu Y, Smith JP, Strauss J, Yang G. Cohort profile: the China health and retirement longitudinal study (CHARLS). [Int J Epidemiol](http://dx.doi.org/10.1093/ije/dys203) 2014;43(1):61 – 8. <http://dx.doi.org/10.1093/ije/dys203>.
10. Wahid A, Manek N, Nichols M, Kelly P, Foster C, Webster P, et al. Quantifying the association between physical activity and cardiovascular disease and diabetes: a systematic review and meta-analysis. [J Am Heart Assoc](http://dx.doi.org/10.1161/JAHA.115.002495) 2016;5(9):e002495. <http://dx.doi.org/10.1161/JAHA.115.002495>.