

The proportions of death from heart diseases tended to be higher in males with Q-QS abnormality, atrio-ventricular conduction defect, and ventricular codes than in females. Although the number of cases was limited, it was true of the deaths from ischemic heart disease.

But the percentage proportions of death from heart diseases tended to be higher in females with the other ECG code groups, especially left high R, ST depression, T abnormality, ectopic beats, atrial fibrillation or flutter, low voltage, or even counter clock or clock-wise rotation codes. The death proportion of deaths from cerebral infarction tended to be high in females with atrial fibrillation or flutter, but not so high in males (25.9% vs 12.5 %).

## **Discussion**

One of major contributions of this study comes from the extensive national samples residing in exactly 300 stratified randomly sampled areas which were sub-samples defined by the Statistical Information Bureau, Ministry of Health and Welfare (Ministry of Health, Labor, and Welfare after reorganization in 2001) for several national surveys in 1962, 1972, 1980, 1990, and 2000. The over-all response rate was over 79% in the relevant National Survey on Circulatory Disorders in 1980 <sup>(1)</sup>, but the response rates in municipal area were lower than those in rural areas.

The high hazard ratio of the subjects with abnormal Q-QS findings showing the possible past history of myocardial infarction was observed even considering for sex, age, systolic blood pressure, blood glucose, and smoking habits. In the subjects with Q-S finding, proportion of death from heart disease were two third of all deaths and that was almost double to those in the reference subjects (Table 5). This result corresponds to the fact that a subject with history of myocardial infarction has the higher risk of recurrence.

Although prevalence of the extreme axis deviation (code 2-4, n=5) or indeterminate axis

(code 2-5, n=6) were relatively rare, the observed high hazard ratios of early death might come from any disposition of the heart or abnormal propagation of the excitation due to any serious heart disease. The genesis of indeterminate axis was suggested as a posterior, rightward and superior orientation of terminal QRS forces, which might result from number of causes, by a quantitative vectorcardiographic analysis by Goldberger AL <sup>(21)</sup>

The high Cox hazard ratios of subjects with left high R (code 3-1 or code 3-3), due to hypertension, cardiomyopathy, valvular disease, or sports heart as well as merely thin chest, shows the significance of myocardial hypertrophy for prevention of early deaths. The Cox hazard ratio of subjects with right high R (code 3-2) was the higher than those of code 3-1 and code 3-3, though significance was lower maybe due to fewer cases with 3-2 code. The highest but not significant hazard ratio was observed for subjects with bi-ventricular high R (code 3-4) which was added in the revised Minnesota Codes 1982 <sup>(3)</sup>.

The hazard ratio of subjects with ST depression was higher than that of those with T abnormality. Since ST depression code should be with T abnormality by definition in Minnesota codes<sup>2)</sup>, the hazard ratio of subjects with ST depression may show a combination effect of ST and T abnormalities. Besides coronary atherosclerosis, ST depression with T abnormality might be developed in hypertension. ST depression might be assumed as a sign of arterio-sclerosis and/or hypertensive stress leading to the relevant complication such as not only heart disease but also cerebrovascular disease, finally to death, as shown in Table 5.

One of striking facts was that the T abnormality was always more frequent in females than males in almost all of Japanese communities. However, the hazard ratios of subjects with T abnormality (code 5-1 to code 5-3) were high in males and in females. The hazard ratio of subjects with T abnormality code 5-4 was high but not significant in this analysis. The code 5-5, minimally low T, was added according to Japanese scientists to Minnesota codes <sup>(18)</sup>. However, this study could not support the significance at the moment.

The hazard ratio of subjects with complete left bundle branch block was higher than that of complete right bundle branch block in males. However, the ratio of complete right bundle branch block in female was significantly high and larger than that of complete left bundle branch block.

It was reasonable that the hazard ratio of subjects with frequent ectopic beats was higher than that of less frequent ectopic beats (code 8-9-1). The frequent ectopic beats might lead to atrial fibrillation in case of supraventricular beats, and ventricular fibrillation in case of ventricular beats. The hazard ratio of atrial fibrillation was comparable with major high-risk codes as Q-QS, ST depression, T abnormality, and so on.

Resting heart rate was an independent predictor of 16.5-year death in this same Japanese cohort reported by Okamura T et al <sup>(10)</sup>. The significant relation was observed only in males in this study, as shown in Table 4. The association of heart rate with coronary heart disease was reported in males and females, particularly striking in black women according Gillum RF et al without any specific explanation <sup>(15)</sup>.

The Cox hazard ratio of subjects with ST elevation code 9-2 was significantly high in males and in the sex combined, but not in females as shown in Table 4. Recently Brugada syndrome which included a type of ST elevation has been presented as a new insight <sup>(22)</sup>, and so further analysis of subjects with code 9-2 should be done for their prognoses in detail.

It is noteworthy that the hazard ratio of subjects with clockwise rotation code 9-4-2 was significantly high and close to that of low voltage, atrial conduction defects, or high T wave. The observed significantly high hazard ratio for code 9-4-2 was a surprise, for the authors did not expect any prognostic significance in this code beforehand. The mechanism or the reason should be clarified by a further analysis as far as possible.

According to the definition of Cox proportional hazard model <sup>(20)</sup>, the calculated hazard ratios would go up or down by those confounding factors, such as sex, age, systolic blood pressure, blood glucose, smoking habits, and the other factors. Naturally the hazard ratio to

early deaths should be evaluated by considering all of those risk factors included in this analysis. The one practical way to apply these results was to evaluate over-all death risk done directly by a computer and one of the other ways would be with using multidimensional table including typical levels of these risk factors, which will appear in a later paper.

Naturally the sex difference of the results comes from the biological difference as well as their social life difference, such as social stress, eating habits, education and so on.

The effect of the removal of deaths within 5 year after the examination on the hazard ratios was examined. Though the other confounding factors, such as age, systolic blood pressure, blood glucose, and smoking habits, showed a trivial or no significant effect, any of major ECG findings might contribute more in some cases of deaths in the early phase of observed period.

The cause of deaths among the subjects with any ECG code might be interesting and was demonstrated as the percentage proportion in Table 5. The highest death hazard ratios of heart diseases were observed in the subjects with Q-QS findings, and then with T abnormality and also with ST depression. It was impressive that the hazard ratios of subjects with ST elevation were comparable with those of ST depression code 4-4, considering recent reports of Burgada syndrome <sup>(22)</sup>. It was worth note that the death proportions from the other cause of deaths among the subjects with low voltage were relatively higher, though the hazard ratios were significant only in the sexes combined. The authors are going to analyze and to discuss the relationship in details and will publish the results before long.

This study demonstrated a series of striking results using national samples to give clear data the relationship of ECG findings objectively diagnosed to deaths from all causes. These data would be the base to prevent early deaths by intervening as a national project, such as the Health Japan 21 or Healthy people 2010 in the USA. Although the authors could not discuss much about the subjects group of small size, there would be a starting point for further studies.

The morbidity hazard ratio of specific disease, such as cerebral stroke or myocardial infarction, would be much more interesting along with mortality, however, it was very hard to get such morbidity data of the subjects throughout country at the moment.

In this analysis, each specific ECG finding evaluated by Cox proportional hazard for deaths of all cause, and any combination of ECG findings would show a much higher significant hazard. Some of the further analysis on combination of ECG findings will come in our later papers.

## **Acknowledgement**

This study conducted under the auspices of the Japanese Association for Cerebro-Cardiovascular Disease Control with a research grant from the Ministry of Health and Welfare (Recently Ministry of Health, Labor, and Welfare), Japan. In order to get an official permission to use the national database of deaths from the Japanese Government, Masumi Minowa, M.D. (National Institute of Public Health) worked hard and deserved the author's special appreciation. The authors would like to express many thanks to the contribution by many listed and unlisted collaborators with the principal investigators and associates listed in Appendix II and I.

**Appendix I** NIPPON DATA80 Research Group. In alphabetical order by the family name of principal investigators, but not by the associates)

NIPPON DATA80: Abbreviation of "National Integrate Projects for Prospective Observation of Non-communicable Diseases And its Trend in the Aged, based on the data of the National Survey in 1980"

1. **Chairperson:** Hirotsugu Ueshima (Department of Health Science, Shiga University of Medical Science, Otsu, Shiga)
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**Appendix II** (List of principal collaborators and his associates in the Working Group for ECG coding in the National Survey on Circulatory Disorders, 1980 in alphabetical order by the family name of principal collaborators with their institution in 1980)

1. **Moderator:** Hiroshi Horibe (National Cardiovascular Center in 1980)

2. *Principal Collaborators:* Mitunori Doi (Tosa-Yamada Health Center, Kochi), Syuichi Hatano (National Institute of Public Health), Masamitsu Konishi (National Cardiovascular Center), Yasushi Morisawa (Dokkyo University School of Medicine), Chiaki Sasade (Takikawa Health Center, Hokkaido), Koryo Sawai (Japanese Association for Cerebro-Cardiovascular Disease Control), Shigeo Shibata (Kagawa Nutrition University), Takashi Shimamoto (University of Tsukuba School of Medicine), Hironori Toshima (Kurume University School of Medicine), Hiroshi Yanagawa (Jichi Medical University), Tsutomu Hashimoto (Jichi Medical School)

3. *Associate Collaborators:* Takashi Kato (Aichi Medical University), Takahiro Usami (Dokkyo University School of Medicine), Kazuaki Shimamoto (Sapporo Medical University), Kazuo Suzuki (Akita Institute of Cerebrovascular Disease), Yoshihiko Watanabe (Fujita Health University School of Medicine), Takashi Watanabe (National Ohta Hospital, Shimane)

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Table 1. Number of subjects and deaths (in parenthesis) among them with electrocardiographic findings by Minnesota code, 19-year follow up, 1980-1999, NIPPON DATA 80 (the death percentages in *boldface italic type*)

ECG code	ECG sub-code										Total
	-1	-2	-3	-4	-5	-6	-7	-8	-9		
1 Q-QS code	16 (11) <b>68.8</b>	36(19) <b>52.8</b>	136 (51) <b>37.5</b>								188 (81) <b>43.1</b>
2 Axis	160 (71) <b>44.4</b>	8 (1) <b>12.5</b>	141 (25) <b>17.7</b>	5 (4) <b>80.0</b>	6 (3) <b>50.0</b>						351 (104) <b>29.6</b>
3 R wave	903 (293) <b>32.4</b>	26 (8) <b>30.8</b>	598 (142) <b>23.7</b>	2 (1) <b>50.0</b>							1518 (444) <b>29.2</b>
4 ST depression	61 (49) <b>80.3</b>	120 (70) <b>58.3</b>	72 (37) <b>51.4</b>	278 (87) <b>31.3</b>							528 (243) <b>46.0</b>
5 T abnormality	25 (22) <b>88.0</b>	240 (116) <b>48.3</b>	226 (103) <b>45.6</b>	99(38) <b>38.4</b>	276 (78) <b>28.3</b>						849 (357) <b>42.0</b>
6 A-V conduction	3 (2) <b>66.7</b>	3 (2) <b>66.7</b>	187 (63) <b>33.7</b>	12 (2) <b>16.7</b>	34 (7) <b>20.6</b>						237 (76) <b>32.1</b>
7 Ventricular conduction	20 (13) <b>65.0</b>	120 (63) <b>52.5</b>	188 (66) <b>35.1</b>	5 (2) <b>40.0</b>	228 (46) <b>20.2</b>	0 <b>0</b>					558 (190) <b>34.1</b>
8 Arrhythmia	120 (33) <b>27.5</b>	2 (2) <b>100.0</b>	62 (43) <b>69.4</b>	2 (0) <b>0</b>	0 <b>0</b>	7 (5) <b>71.4</b>	133 (28) <b>21.1</b>	162 (43) <b>26.5</b>	496(148) <b>29.8</b>		984 (302) <b>30.7</b>
9 Miscellaneous	97 (41) <b>42.3</b>	343 (74) <b>21.6</b>	9 (5) <b>55.6</b>	4647 (927) <b>19.9</b>	505 (117) <b>23.2</b>						5601(1164) <b>20.8</b>

8-9-1 Premature beats <10%: 239(104) **43.5 %** See text for code 5-5

9-4-1 Counter clockwise rotation: 3954(709) **17.9 %**, 9-4-2 Clockwise rotation: 693(218) **31.2 %**

The control group without major ECG codes: 5,535 (836) **15.1%**

Table 2 Cox hazard ratios of major risk factors to all cause mortality among the subjects in the 19 years of follow-up period, 1980 to 1999, NIPPON DATA 80.

Risk factors included	Males and Females	Males	Females
Sex (Males vs Females)	0.65 (0.52-0.74) ***	-	-
Years of age	1.12 (1.11-1.12) ***	1.11 (1.11-1.12) ***	1.12 (1.12-1.13) ***
Systolic BP (mmHg)	1.004 (1.002-1.006) ***	1.004 (1.001-1.007) **	1.004 (1.001-1.007) *
Blood glucose (mg/dl)	1.003 (1.002-1.004) ***	1.003 (1.002-1.004) ***	1.003 (1.002-1.005) ***
Smoking habits (0-3)+	1.22 (1.14-1.318) ***	1.18 (1.10-1.28) ***	1.29 (1.08-1.54) **
Abnormal ECG (0,1) ++	1.28 (1.17-1.408) ***	1.34 (1.18-1.52) ***	1.19 (1.04-1.36) *

\*\*\* p < 0.001 \*\* p < 0.01 \* p < 0.05

+ See text This was a multivariate analysis by Cox proportional hazard model, done by sexes.

++ Number (deaths) in Abnormal ECG group with any major ECG code: 4,103 (1,174): 28.6% died.

95 % confidence intervals of the ratio in parenthesis

Table 3 Cox hazard ratio of major risk factors to all cause mortality before and after exclusion of the deaths within 3 and 5 years just after the examination in 1980, NIPPON DATA 80.

	1980 to 1999	1983 to 1999	1985 to 1999
Sex (Males vs Females)	0.645 (0.582-0.714) ***	0.648 (0.583-0.721) ***	0.631 (0.564-0.706) ***
Years of age	1.117 (1.112-1.122) ***	1.117 (1.112-1.122) ***	1.117 (1.111-1.122) ***
Systolic BP (mmHg)	1.004 (1.002-1.006) ***	1.004 (1.002-1.007) ***	1.004 (1.002-1.007) ***
Blood glucose (mg/dl)	1.003 (1.002-1.004) ***	1.003 (1.002-1.004) ***	1.003 (1.002-1.004) ***
Smoking habits (0-3)+	1.219 (1.136-1.308) ***	1.216 (1.129-1.309) ***	1.217 (1.127-1.315) **
Abnormal ECG (0,1)++	1.276 (1.165-1.398) ***	1.245 (1.113-1.368) ***	1.210 (1.096-1.335) *

\*\*\* p < 0.001 \*\* p < 0.01 \* p < 0.05

+ See text

++ Abnormal ECG: Any major electrocardiographic finding by Minnesota Code: 0=no, 1=yes

Table 4 Cox hazard ratios of the subjects with major electrocardiographic findings for all cause mortality in 1980 to 1999, NIPPON DATA80.

Minnesota code	Males and Females	Males	Females
Q-QS 1-1	3.71 (1.78-7.71) ***	3.71 (1.78-7.71) ***	4.46 (1.41-14.05) *
Q-QS 1-2	1.75 (1.10-2.78) *	2.22 (1.27-3.86) **	1.24 (0.51-2.99)
Q-QS 1-3	1.57 (1.18-2.09) **	1.59 (1.08-2.34) *	1.54 (1.01-2.35) *
Axis 2-1	1.37 (1.07-1.76) *	1.19 (0.86-1.66)	1.81 (1.57-2.65) **
Axis 2-2	0.69 (0.10-4.92)	1.22 (0.17-8.68)	-
Axis 2-3	1.80 (1.21-2.69) **	1.83 (1.12-2.98) *	1.71 (0.84-3.47)
Axis 2-4	2.85 (1.06-7.67) *	3.36 (1.24-9.09) *	-
Axis 2-5	4.16 (1.325-13.05) *	4.56 (1.45-14.4) **	-
High R 3-1	1.34 (1.16-1.54) ***	1.33 (1.08-1.56) **	1.40 (1.11-1.75) **
High R 3-2	1.91 (0.95-3.84)	3.39 (1.08-10.6) *	1.45 (0.60-3.50)
High R 3-3	1.35 (1.12-1.62) **	1.30 (1.03-1.55) *	1.45 (1.08-1.94) *
High R 3-4	3.56 (0.50-25.38)	6.31 (0.87-45.68) +	-
ST 4-1	2.59 (1.91-3.52) ***	2.79 (1.85-4.22) ***	2.46 (1.56-3.86) ***
ST 4-2	2.00 (1.55-2.57) ***	2.38 (1.56-3.61) ***	1.91 (1.39-2.64) ***
ST 4-3	1.63 (1.16-2.29) **	1.55 (0.90-2.65)	1.72 (1.10-2.67) *
ST 4-4	1.15 (0.92-1.44)	1.35 (0.97-1.87) +	1.00 (0.73-1.37)
T 5-1	2.33 (1.51-3.61) ***	2.27 (1.24-4.16) **	2.53 (1.34-4.78) **
T 5-2	1.82 (1.49-2.22) ***	2.52 (1.86-3.42) ***	1.43 (1.09-1.87) **
T 5-3	1.54 (1.24-1.91) ***	1.62 (1.14-2.31) **	1.56 (1.18-2.05) **
T 5-4	1.35 (0.96-1.88) +	1.45 (0.90-2.32)	1.26 (0.78-2.03)
T 5-5	1.06 (0.84-1.34)	1.02 (0.68-1.52)	1.05 (0.79-1.41)
AV 6-1	2.01 (0.50-8.10)	4.16 (0.58-29.93)	1.22 (0.17-8.70)
AV 6-2	7.82 (1.95-31.39) **	14.29 (1.97-104.0) **	5.37 (0.75-38.25) +
AV 6-3	1.23 (0.95-1.60)	1.38 (1.02-1.87) *	0.98 (0.58-1.64)
AV 6-4	1.16 (0.29-4.65)	1.33 (0.33-5.36)	-
AV 6-5	2.21 (1.05-4.66) *	3.71 (1.38-9.97) **	1.41 (0.45-4.41)
V 7-1	2.11 (1.22-3.67) **	3.06 (1.50-6.24) **	1.47 (0.61-3.57)
V 7-2	1.44 (1.11-1.88) **	1.21 (0.87-1.68)	1.85 (1.19-2.89) **
V 7-3	1.20 (0.93-1.55)	1.37 (0.97-1.92) +	1.02 (0.70-1.50)
V 7-4	2.20 (0.55-8.87)	3.23 (0.80-13.13)	-
V 7-5	1.03 (0.76-1.38)	1.16 (0.78-1.71)	0.80 (0.50-1.27)
AR 8-1	1.92 (1.45-2.54) ***	2.41 (1.67-2.49) ***	1.44 (0.92-2.23)
AR 8-2	2.14 (0.53-8.64)	2.41 (0.59-9.80)	-
AR 8-3	2.42 (1.77-3.31) ***	1.94 (1.16-3.22) *	2.76 (1.85-4.11) ***
AR 8-6	1.31 (0.54-3.16)	0.92 (0.13-6.57)	1.36 (0.50-3.67)
AR 8-7	1.34 (0.97-1.97)	2.73 (1.51-4.93) ***	0.99 (0.60-1.64)
AR 8-8	1.29 (0.94-1.75)	1.48 (1.06-2.07) *	0.63 (0.26-1.53)
AR 8-9-1	1.45 (1.18-1.79) ***	2.07 (1.58-2.72) ***	0.91 (0.64-1.28)
M 9-1	1.47 (1.07-2.03) *	1.70 (0.93-3.11) +	1.28 (0.87-1.87)
M 9-2	1.33 (1.04-1.71) *	1.32 (1.02-1.71) *	0.98 (0.37-2.64)
M 9-3-1	1.76 (0.73-4.27)	1.89 (0.78-4.59)	-
M 9-3-2	1.45 (0.90-2.36)	1.36 (0.77-2.42)	2.07 (0.86-5.01)
M 9-4-1	1.08 (0.96-1.22)	1.18 (1.01-1.39) *	0.97 (0.82-1.14)
M 9-4-2	1.47 (1.26-1.71) ***	1.55 (1.26-1.90) ***	1.36 (1.07-1.72) *
M 9-5	1.28 (1.05-1.56) *	1.29 (1.04-1.60) *	1.11 (0.62-1.99)

\*\*\* p < 0.001 \*\* p < 0.01 \* p < 0.05 + p < 0.1

AV: Atrioventricular V: Ventricular AR: Arrhythmia; M: Miscellaneous codes

Adjusted for age, systolic pressure, blood glucose, smoking habits, and sex if applicable.

95 % confidence interval of the ratio in parenthesis

Table 5. Death proportions among subjects with selected ECG codes by selected disease categories, 1980-1999, NIPPON DATA80.

Males	N of deaths	Cereb D	(C Inf)	Heart D	(I.H.D.)	Cancer	Others
Control group	405	17.8	10.1	13.8	6.7	35.3	33.1
Abnormal ECG group	686	16.9	10.2	17.2	6.3	31.0	34.8
Q-QS abnormality (mc1-1 to 1-3)	50	12.0	6.0	34.0	12.0	20.0	34.0
Axis deviation (mc2-1 to 2-5)	41	17.1	14.6	17.1	4.9	22.0	43.9
L High R (mc3-1,3-3)	287	19.9	12.9	15.0	6.6	30.3	34.8
ST depression (mc4-1 to 4-4)	115	19.1	12.2	21.7	7.8	23.5	35.7
T abnormality (mc5-1 to 5-5)	150	17.3	10.7	25.3	7.3	22.7	34.7
Atrioventricular codes (mc6-1 to 6-5)	56	14.3	7.1	23.2	12.5	37.5	25.0
Ventricular codes (mc7-1 to 7-5)	116	17.2	7.8	19.0	7.8	31.0	32.8
Ectopic beats (mc8-1,8-9-1)	99	15.2	8.1	21.2	6.1	29.3	34.3
Atrial fibrillation (mc8-3)	16	12.5	12.5	18.8	0	31.3	37.5
Low voltage (mc9-1)	11	18.2	9.1	9.1	0	27.3	45.5
ST elevation (mc9-2)	70	14.3	8.6	21.4	8.6	30.0	34.3
Counter clock rotation (mc9-4-1)	348	15.5	9.5	12.1	4.9	36.8	35.6
Clock rotation (mc9-4-2)	132	16.7	7.6	22.0	6.8	31.8	29.5
High T (mc9-5)	107	16.8	11.2	10.3	4.7	38.3	34.6
Females	N of deaths	Cereb D	(C Inf)	Heart D	(I.H.D.)	Cancer	Others
Control group	431	15.8	7.7	16.7	7.2	30.9	36.7
Abnormal ECG group	488	19.3	10.7	21.9	8.2	21.1	37.7
Q-QS abnormality (mc1-1 to 1-3)	31	19.4	3.2	29.0	12.9	12.9	38.7
Axis deviation (mc2-1 to 2-5)	30	26.7	10.0	16.7	3.3	20.0	36.7
L High R (mc3-1,3-3)	148	23.0	11.5	26.4	10.1	16.2	34.5
ST depression (mc4-1 to 4-4)	128	22.7	13.3	29.7	14.1	17.2	30.5
T abnormality (mc5-1 to 5-5)	207	19.8	11.1	28.0	12.1	16.9	35.3
Atrioventricular codes (mc6-1 to 6-5)	20	25.0	5.0	10.0	0	20.0	45.0
Ventricular codes (mc7-1 to 7-5)	74	18.9	10.8	10.8	4.1	21.6	48.6
Ectopic beats (mc8-1,8-9-1)	58	17.2	12.1	32.8	12.1	17.2	32.8
Atrial fibrillation (mc8-3)	27	33.3	25.9	33.3	3.7	11.1	22.2
Low voltage (mc9-1)	30	10.0	0	23.3	3.3	13.3	53.3
ST elevation (mc9-2)	4	0	0	25.0	25.0	25.0	50.0
Counter clock rotation (mc9-4-1)	361	15.2	7.2	20.5	9.4	26.0	38.2
Clock rotation (mc9-4-2)	86	17.4	9.3	30.2	9.3	16.3	36.0
High T (mc9-5)	10	20.0	20.0	30.0	10.0	50.0	0

Minnesota codes (mc) in parentheses

Cereb D: Cerebrovascular diseases; C Inf: Cerebral infarction is a part of cereb D;

Heart D: Cardiovascular diseases; I.H.D.: Ischemic heart diseases is a part of Heart disease

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厚生労働科学研究費補助金  
長寿科学総合研究事業

健康寿命およびADL、QOL低下に影響を与える要因の分析と  
健康寿命危険度評価テーブル作成に関する研究  
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総合研究報告書

平成17年3月31日発行

発行者 「健康寿命およびADL、QOL低下に影響を与える要因の分析と  
健康寿命危険度評価テーブル作成に関する研究  
:NIPPON DATA80・90の19年、10年の追跡調査より」研究班  
発行所 滋賀医科大学福祉保健医学講座 教授 上島弘嗣

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