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Increase in lifestyle-related diseases following the evacuation after the Fukushima Daiichi Nuclear Power Plant accident: a retrospective study of Kawauchi village with long-term follow-up.

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Abstract

Objectives Kawauchi Village lies 20 km west of the Fukushima Daiichi Nuclear Power Plant. On March 16th 2011, evacuation was ordered due to the threat of radiological exposure until April 2012. In this study, we aimed to evaluate the pre- vs. post-disaster health status of the Kawauchi Villagers, measured by routine yearly physical exams in long-term.

Methods We analyzed annual health check-up data of Kawauchi Villagers by the Law of the health and Medical service for the elderly from 2008 to 2013. Data from 2011 was not available due to the disaster. As the health data included the same subjects repeatedly, the sample was non-independent, and generalized estimated equation modeling was used. A pre-disaster time period (2008-2010) was categorized for comparison with post-disaster 2012 and 2013. The outcome examined was the presence or absence of lifestyle and metabolic disease, and adjusted for confounding factors.

Results Data for 777, 797, 779, 674, and 576 residents were available in 2008, 2009, 2010, 2012, and 2013, respectively. In 2013, the prevalence of metabolic syndrome (from 17.0% to 25.2%, $p<0.001$), diabetes (from 11.3% to 17.0%, $p<0.001$), dyslipidemia (from 43.2% to 56.7%, $p<0.0001$), hyperuricemia (from 5.2% to 8.4%, $p=0.006$), and chronic kidney disease (from 16.1% to 26.7%, $p<0.001$) were all found to be elevated significantly compared to pre-disaster years.

Conclusions The present follow-up study for Kawauchi Villagers revealed that a universal increase in the lifestyle-related diseases has been triggered by the evacuation and this trend still continues in two years following the disaster.

(249 words：maximum of 250 words)

Strengths and limitations of this study

Kawauchi Village consists of the first residents returning to their homes following evacuation in the 2011 northeastern Japan disaster.

This study revealed that risk of various lifestyle-related diseases increased due to the evacuation and this trend have still continued even two years past the disaster.

The data consists of all residents of the village that attended their yearly health consultation, in accordance with the Japanese National Healthcare System, which may cause a selection bias.

INTRODUCTION

On March 11th, 2011, an historic magnitude 9.0 earthquake struck the northeastern coast of Japan. Located in the mountains, Kawauchi Village, in Fukushima Prefecture escaped major damage from either the earthquake or subsequent tsunami. However, the village lies 20 km west of the Fukushima Daiichi Nuclear Power Plant, and was bisected by the March 16th mandatory evacuation, as the situation at the nuclear power plant deteriorated. The entire village moved to nearby evacuation centers, such as Koriyama City. The government authorized return to the village a year later, in April 2012. By April 2013, 1,299 of the original 2816 villagers had returned (46.1%), with more than 70% of returnees being above the age of 50. The fallout surrounding the evacuation, including potential radiological exposure, increases in unemployment, loss of living area, and disintegration of families, has constituted innumerable challenges to the returning population. [1]

Numerous studies, both within and outside of Japan, have demonstrated the health impact of disasters and their subsequent personal, environmental, and societal responses. After the Great Hanshin Earthquake struck Kobe City in 1995, mean blood pressure increased significantly for both those patients who were living in disaster area, as well as those in the surrounding area. In the former, the elevation in blood pressure peaked in the first week and lasted for 4 weeks, but then returned to the baseline within 6 weeks of the disaster [2]. Similar temporary hypertension was reported after Hurricane Katrina, with HbA1c levels also increasing throughout the observational period (6-16 months post-disaster) [3]. A recent study on the Fukushima region demonstrated the short-term impact of the disaster on metabolic measures within evacuated populations, including differences delineated among those evacuating due to radiological threat and those whose evacuation was due to the destruction of their homes by tsunami. Significantly higher body weight, body mass index, waist circumference, and HbA1c, as well as lower high-density lipoprotein

(HDL) cholesterol levels were found 5 months following the earthquake [4]. An evaluation of diabetes prevalence examined all 27,486 people who were residents of the 12 municipalities surrounding the Fukushima Daiichi power plant, of which Kawauchi Village is a part. Comparing data from before and after the disaster, the evacuated population was found to have a higher incidence of diabetes than those who remained unevacuated. [5]

However, the majority of studies available report only short-term observations, with follow-up typically running less than a year. With the exception of temporary hypertension, only a few previous researches have evaluated whether metabolic measures return to baseline over time [6].

The triple-threat of regional earthquake, tsunami, and radiological damage from the Tohoku quake is unprecedented. However, studies have demonstrated that the risk of radiological exposure and consequential increase in cancer rate in the Tohoku region around the nuclear power plant has been reported as low [7-10]. As the majority of international attention has been focused on radiological threat to the Tohoku population, it is possible if not likely that changes in metabolic health measures may be overlooked in the region.

In this study, we aimed to evaluate the pre- vs. post-disaster health status of the Kawauchi Village medical checkup examinee under national health insurance system, over a multi-year followup period. Kawauchi Village consists of the first residents returning to their homes following evacuation in the northeastern Japan disaster, and this is the first study to evaluate the long-term impact of the disaster, evacuation, and return, on their health status.

METHODS

Population Data

This retrospective study was approved by the ethical review board of the Graduate School of Medicine at Kyoto University (approval number E1809, 23 July 2013). Japanese ethical guidelines provide for waiver of informed consent for research use of existing medical records after anonymization. A descriptive and analytical epidemiological study was conducted using medical examination data. The yearly national health screening obtains a wealth of information about individual residents, and is used for health prevention as dictated by the Japanese Ministry of Health, Labor, and Welfare. Japanese National Healthcare System medical examination data, taken by physicians in Kawauchi Village and surrounding evacuation centers from 2008 through 2010, and 2012 through 2013, were obtained. Data from 2011 was excluded due to low participation rate immediately following the disaster and evacuation. Access to Japanese National Healthcare System data for Kawauchi Village was obtained with permission from the Mayor of Kawauchi Village. Villagers were offered the opportunity to individually withhold their medical data from the study.

Healthcare records included birthdate, age, gender, height, weight, body mass index (BMI), systolic and diastolic blood pressure, waist circumference, blood glucose, hemoglobin A1c (HbA1c), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglyceride (TG), aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ-glutamyl transpeptidase (γ-GTP), and from 2010 estimated glomerular filtration rate (eGFR) and serum creatinine. Additionally, self-reported lifestyle-related factors were available, such as sleep patterns, diet changes, smoking and drinking habits and approximate amount consumed, exercise habits, and medications for blood pressure, diabetes, hypercholesterolemia, and other diseases.

Due to a change in the measurement of HbA1c from the Japan Diabetes Society (JDS) standard to the National Glycohemoglobin Standardization Program (NGSP) reference value from 2008 to 2012, the HbA1c values were shifted accordingly to ensure data comparability

[11]. The equivalent value was calculated using the following equation: NGSP(%)=1.02×JDS(%)-0.245%. Here, we present data using the NGSP.

Lifestyle-related disease definitions

Subjects with missing data or missing information regarding the use of drugs were excluded from this study.

Metabolic syndrome was defined as the presence of any three abnormal findings of five risk factors [12]: (1) a waist circumference ≥ 90 cm in males or ≥ 80 cm in females, (2) a TG ≥ 150 mg/dL (1.7 mmol/L), (3) a HDL-C < 40mg/dL (1.0 mmol/L) in males, < 50mg/dL (1.3 mmol/L) in females, (4) a systolic blood pressure ≥ 130 and/or diastolic blood pressure ≥ 85 mmHg (with antihypertensive pharmaceutical usage in a subject treated as an alternate indicator), (5) a fasting glucose ≥100mg/dL (with pharmaceutical treatment for elevated glucose as an alternate indicator).

Obesity was defined as a body mass index (BMI) ≥ 25 kg/m^2 [13].

Hypertension was defined as a systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg, or if patients were undergoing pharmaceutical treatment for hypertension. [14]

Diabetes was defined as a fasting plasma glucose level ≥ 126 mg/dL (7.0 mmol/L) and/or an HbA1c level ≥ 6.5% (NGSP), or if the patient was undergoing treatment for elevated glucose. [15]

Dyslipidemia was defined as a HDL-C < 40 and/or LDL-C ≥ 140 and/or TG ≥ 150, or when treatment for lipidemia was noted. [16]

Hyperuricemia was defined as a uric acid measurement > 7.0 mg/dL. [17]

Chronic Kidney Disease (CKD) was defined as an eGFR < 60 mL/min/1.73m^2. [18]

Statistical methodology

Continuous variables were evaluated using ANOVA and Tukey's HSD test to identify differences due to aging. Significance was defined as a p-value less than 0.05. Statistica 12 software (StatSoft, Tulsa, USA) was used.

As the health data from 2008 to 2013 included the same subjects repeatedly, the sample was non-independent, and generalized estimating equation modeling was used. [19] A pre-disaster time period (2008-2010) was categorized for comparison with post-disaster 2012 and 2013. The outcome examined was the presence or absence of lifestyle and metabolic disease. In repeated measure logistic regression analysis with generalized estimating equations, the presence or absence of lifestyle-related disease was set as the dependent variable, with medical examination consultation year, age at time of visit (continuous variable), and gender set at independent variables, and adjusted for both age and gender. An unstructured correlation structure was chosen for correction. The least-squares means and odds ratio, adjusted for confounding factors (age and gender), was used for repeated measure logistic regression analysis based on generalized estimating equations. Significance was set to a level of 0.05. SAS 9.3 (SAS Institute Inc., Cary, USA) was used for analysis.

RESULTS

Demographics

From 2008 to 2013 (excluding 2011), medical examinees numbered 777, 797, 779, 674, and 576 people, respectively (Table 1). The proportion of residents who returned to the village ("returnees") was 64% in 2012 and 83% in 2013. The average age was significantly different only between 2008 and 2012. No significant differences in gender ratio were seen.

Table 1 Number of participants in Kawauchi Village Health Checkup under national health insurance system

Examination year	2008	2009	2010	2011	2012	2013
Villagers	777	797	779	Disaster	674	576
In Kawauchi	777	797	779	-	431	477
Evacuated (Koriyama City)	-	-	-	-	184	99
Evacuated (Fukushima Prefecture)	-	-	-	-	26	-
Evacuated (Elsewhere)	-	-	-	-	33	-
Age (Mean±SD)	68.6 ±11.0	68.3 ±11.3	68.0 ±11.2	-	66.7 ±11.7	68.3 ±10.9
ANOVA p=0.016	A#	AB#	AB#	-	B#	AB#
Gender (Male/Female) Chi-square test p=0.704	42%/58%	43%/57%	41%/59%	- -	44%/56%	43%/57%

#: Means that do not share a letter are significantly different.

Interview Questionnaire Analysis

The results of the health exam interview questions are summarized in Table 2. No significant differences were seen in self-reported rates of physical activity, alcohol consumption, or tobacco consumption. However, a significant decline was noted in reported sleep quality.

Table 2 Results of self-reported lifestyle-related factors assessment by using medical questionnaire

Examined year		2008	2009	2010	2012	2013	Chi-square test
Test items	Question (Answer choices)	percentage (%) (n)					p-value
Physical activity	Do you do exercise that makes you sweat for at least 30 minutes twice a week, and have you been doing this for at least 1 year? (Yes/No)	35/65 (n=720)	40/60 (n=557)	38/62 (n=552)	41/59 (n=511)	42/59 (n=411)	0.170
Alcohol consumption	How often do you drink alcohol? (Everyday/Occasionall	21/18/18/44 (n=739)	20/21/21/39 (n=779)	20/20/21/39 (n=760)	23/20/17/41 (n=649)	19/20/20/40 (n=572	0.146

	y/Rarely/Never)					)		
Tobacco consumption	At present, do you have a smoking habit? (Yes/No)	13/87 (n=745)	14/86 (n=787)	12/88 (n=765)	12/88 (n=649)	14/86 (n=574)	0.660	
Sleep patterns	Do you feel you get sound sleep and get enough rest? (Yes/No)	81/19 (n=720)	77/23 (n=565)	74/26 (n=555)	69/31 (n=518)	67/33 (n=437)	0.0001	*

Changes in laboratory value averages

The trend of the average value of each examined item is listed in Table 3. During the study period, a significant change was seen in all values except for AST and creatinine. Abdominal circumference also showed an increasing trend. On comparing medical results from 2012 to any of the pre-earthquake years available, body weight, BMI, fasting blood glucose, TG, ALT, and γ-GTP were significantly increased, while systolic blood pressure and eGFR decreased significantly. On comparing 2013 to all pre-earthquake years, body weight, fasting blood glucose, HbA1c, and TG had all substantially increased, while diastolic blood pressure, systolic blood pressure, and eGFR were significantly decreased. These differences were tested in relation to patient self-reported physical activity and antihypertensive pharmaceutical usage, but there were no significant differences noted.

Table 3 Demographics of the total Kawauchi Population

Examined year	2008		2009		2010		2012		2013		ANOVA	
Test items			Mean±SD (n)		Tukey's HSD test						p-value	
Height	152.2±9.8 (684)	A	152.7±9.6 (666)	A	153.1±9.4 (650)	AB	154.6±9.7 (572)	B	154.6±9.6 (488)	B	<0.0001	*
Weight	55.6±10.4 (684)	A	55.8±10.5 (666)	A	55.8±10.5 (650)	A	58.7±11.1 (572)	B	58.1±11.3 (488)	B	<0.0001	*
BMI	23.9±3.4 (684)	A	23.9±3.5 (666)	A	23.7±3.5 (650)	A	24.5±3.7 (572)	B	24.2±3.6 (488)	AB	<0.0001	*
Waist circumferen	84.3±9.8 (381)	A	84.5±9.5 (382)	A B	85.7±9.1 (391)	ABC	86.3±9.7 (390)	BC	87.4±9.4 (296)	C	<0.0001	*

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Systolic blood pressure	135.6±14.7 (684)	A	133.0±17.5 (666)	B	134.6±17.1 (650)	AB	126.6±14.3 (572)	C	126.2±14.8 (488)	C	<0.0001	*
Diastolic Blood Pressure	76.3±9.2 (684)	A	75.2±9.7 (666)	AB	75.9±10.8 (650)	AB	74.5±9.2 (572)	B	71.4±9.9 (488)	C	<0.0001	*
eGFR	–	–	–	–	72.1±13.4 (391)	A	68.8±13.9 (615)	B	66.0±12.8 (534)	C	<0.0001	*
Blood Glucose	97.4±16.5 (596)	A	96.8±18.3 (544)	A	96.5±16.0 (556)	A	101.0±21.4 (508)	B	103.3±20.2 (425)	B	<0.0001	*
HbA1c	5.5±0.6 (676)	A	5.5±0.7 (659)	A	5.5±0.6 (643)	A	5.6±0.7 (572)	A	5.8±0.8 (488)	B	<0.0001	*
HDL-C	60.1±14.7 (676)	A	59.7±14.5 (659)	A	58.2±14.1 (643)	AB	56.3±14.4 (572)	B	56.7±13.5 (488)	B	<0.0001	*
LDL-C	114.9±26.7 (676)	AB	113.6±26.2 (659)	A	114.9±27.0 (643)	AB	116.8±31.3 (572)	AB	118.6±29.8 (488)	B	0.033	*
TG	97.0±52.7 (676)	A	92.9±60.0 (659)	A	95.8±55.4 (643)	A	109.3±81.0 (572)	B	109.9±69.7 (488)	B	<0.0001	*
AST	25.8±8.3 (676)	–	27.0±59.3 (659)	–	24.1±7.6 (643)	–	27.3±11.9 (572)	–	25.5±9.4 (488)	–	0.29	
ALT	19.8±9.5 (676)	AB	19.6±17.9 (659)	AB	18.9±9.4 (643)	A	23.3±17.2 (572)	C	21.5±13.9 (488)	BC	<0.0001	*
γ-GTP	31.0±34.6 (676)	AB	29.9±34.3 (659)	A	27.9±27.5 (643)	A	37.4±53.2 (572)	C	36.8±52.0 (488)	BC	<0.0001	*
Blood Creatinine	–	–	–	–	0.75±0.23 (391)	–	0.77±0.18 (615)	–	0.78 ±0.18 (534)	–	0.06	
Uric Acid	5.08±1.33 (380)	AB	5.00±1.29 (382)	A	5.00±1.33 (391)	A	5.29±1.41 (615)	B	5.26±1.39 (534)	B	<0.0001	*

#: Means that do not share a letter are significantly different.

Lifestyle-related diseases

Table 4 shows the trends in prevalence of lifestyle-related factors determined by least squares mean, adjusted for confounding factors (age and sex), using repeated measure logistic regression analysis with generalized estimating equations. A significant increase was seen in metabolic syndrome, diabetes, dyslipidemia, hyperuricemia, and chronic kidney disease in the two years following the disaster. Table 5 shows that the odds ratio for 2012, in comparison with pre-earthquake health values, indicates significantly elevated metabolic syndrome, obesity, diabetes, dyslipidemia, hyperuricemia, as well as increased prevalence of chronic kidney disease. Meanwhile, hypertension significantly decreased. For 2013, the odds ratio indicated significantly increases in metabolic syndrome, diabetes, dyslipidemia, hyperuricemia, and the prevalence of CKD was elevated, in comparison with the pre-disaster period. However, significant differences in obesity and hypertension were not seen.

Table 4 Trends in prevalence of lifestyle-related diseases

Examined year	pre-earthquake	2012	2013	Trend test	
Test items	prevalence of lifestyle-related diseases (95% CI)			p-value	
Metabolic syndrome	17.0% (15.0-19.2)	24.2% (21.0-27.7)	25.2% (21.9-29.0)	<0.0001	*
Obesity	35.3% (32.4-38.3)	39.7% (36.3-43.3)	36.9% (33.4-40.5)	0.344	
Hypertension	65.7% (62.7-68.5)	61.8% (58.2-65.2)	63.7% (59.9-67.4)	0.246	
Diabetes	11.3% (9.6-13.4)	14.7% (12.4-17.3)	17.0% (14.4-20.0)	<0.0001	*
Dyslipidemia	43.2% (40.3-46.1)	53.9% (50.2-57.6)	56.7% (52.8-60.6)	<0.0001	*
Hyperuricemia	5.2% (3.9-6.9)	10.0% (7.8-12.7)	8.4% (6.3-11.3)	0.006	*
Chronic kidney disease	16.1% (12.7-20.1)	21.7% (18.5-25.3)	26.7% (23.0-30.8)	<0.0001	*

*: p<0.05

Table 5 Odds ratio and 95% confidence intervals (CI) of lifestyle-related diseases after the Great East Japan Earthquake

Examined year	2012 vs pre-earthquake	2013 vs pre-earthquake	2013 vs 2012
Test items	odds ratio (95% CI)		
Metabolic syndrome	1.55* (1.29-1.88)	1.64* (1.35-2.01)	1.06 (0.87-1.28)
Obesity	1.21* (1.06-1.38)	1.07 (0.93-1.24)	0.89* (0.79-0.99)
Hypertension	0.85* (0.75-0.96)	0.92 (0.80-1.06)	1.09 (0.94-1.25)
Diabetes	1.35* (1.13-1.61)	1.6* (1.32-1.95)	1.19* (1.02-1.39)
Dyslipidemia	1.54* (1.33-1.78)	1.72* (1.47-2.02)	1.12 (0.95-1.32)
Hyperuricemia	2.03* (1.50-2.75)	1.69* (1.16-2.45)	0.83 (0.59-1.17)
Chronic kidney disease	1.45* (1.09-1.92)	1.91* (1.43-2.54)	1.32* (1.10-1.57)

*: p<0.05

When 2013 was compared to 2012, metabolic syndrome, diabetes, and chronic kidney disease were significantly increased, but obesity had significantly reduced.

DISCUSSION

On review of the available Kawauchi Village medical records, a significant increase in the prevalence of lifestyle-related diseases was found. Increases were noted in metabolic syndrome, diabetes, dyslipidemia, hyperuricemia, and chronic kidney disease following the disaster period. On the other hand, obesity only increased significantly in 2012, and hypertension was significantly reduced. Previous studies of the region had found an increase in diabetes due to evacuation [5], and our evaluation of Kawauchi Village, which was fully evacuated, reinforces this result. Further, the increase in diabetes continued over the long term, into 2013. This may indicate that it was not the combined stresses of the disaster and evacuation alone, but additional stress relating to trouble following return, including a perceived threat from the nearby Fukushima nuclear power plant.

The nuclear accident impacted Kawauchi Village in a multitude of ways. The changes in population demographics, ongoing evacuation areas, and shuttering of businesses chain resulted in a diminishment of communal resources. Significant portions of the village, including commercial and welfare institutions, health care facilities, schools, and others, was dependent on the adjacent nuclear power plant in the neighboring Tomioka Town area, and as they closed with the changing makeup of the region, there were few if any replacements. Consequently, younger members of the village are not returning, and this has lead to a demographic collapse. As of April 2013, only 26% of former residents below the age of 50 had returned to the village, and 58% of those villagers who have returned are 50 years or older. In particular, working-aged parents and their children have not returned. This has lead to both a rapid aging in the village, as well as causing separation of families and subsequent diminishment in communal support. Furthermore residents were unable to farm the land in 2012, potentially leading to a diminishment in physical activity among returnees; thankfully, residents were able to resume rice planting in 2013. Taken together, social and mental stress in concert with decreased physical activity triggered and continued a universal increase in the lifestyle-diseases herein in the years following the disaster.

Curiously, systolic blood pressure (in 2012 and 2013) and diastolic blood pressure (in 2013) underwent significant decreases, despite no reported change in usage of antihypertension medications, or, as reported by physicians in the village itself, any noticed change in the type of medications generally being provided. Previous reports have shown that blood pressure tends to increase immediately following a disaster, but stabilize in the weeks and months thereafter [2-3]. As our report looked primarily as long-term outcomes over a year after the disaster period, it would not be possible to detect these short-term changes in blood pressure. Moreover, why systolic and diastolic blood pressure appeared to improve in the population following evacuation remains undetermined, and will require more study.

The rate of diabetes increasing in a population, though expected, is concerning. Focused attention on those residents with diabetic prevention, or exhibiting symptoms of poor sleep and mental stress, may allow health officials to prevent development or worsening of diabetes within the population [20-21]. Though these methods are present in Kawauchi, systemic resources, and thus the ability to offer population-wide support, remain limited. However, the conditions the residents were living did not worsen from 2012 to 2013, and may, in fact, have improved; however, the rate of lifestyle disease continued to increase. Ongoing health improvement efforts in Kawauchi and the surrounding regions may thus need to focus on improving the lifestyle of residents on an individual level, in addition to efforts to support rebuilding of the community, regenerate industry and livelihoods, and bring back younger members of the population.

There were limitations to this study. The data consists of all residents of the village that attended their yearly health consultation, in accordance with the Japanese National

Healthcare System. Thus, there may be a selection bias in the population. It is conceivable that, if the healthiest individuals in the village were the ones to undergo health screening, then the actual health status in the village may be substantially worse than seen here. [22] Also, even adjusting for age and gender, it is possible that the significant increase seen in lifestyle disease is due to this bias. Further, measurements of patient physical activity, alcohol consumption, tobacco consumption, and medication usage, among others, were obtained by self-report or interview, and were not explicitly measured; no differences between these were seen pre- and post-disaster. There remains a possibility for individual overestimation of physical activity and underestimation of tobacco/alcohol consumption. [23] Further, as specific questionnaires were used individualized follow-up was unavailable, and so it is possible that other unidentified causes may be involved in the increase in lifestyle disease. It must be noted that in order to properly diagnose chronic kidney disease using eGFR, a decrease must be observed over more than 3 months. [18] However, in our study, only single data points at yearly intervals were available, and so the diagnosis is imperfect. In addition, eGFR was not included in the National Healthcare System data prior to 2010. As such, changes seen over the earthquake time period may have been background changes already occurring prior to the disaster. Because a social epidemiological approach was not taken here, future study taking into account specifically the loss of industry and individual livelihood, and subsequent changes in habits and lifestyle should be taken, to better grasp the full picture of what changes are occurring in the disaster environment.

Conclusions

On examination of Kawauchi Village, it appears that regardless of patient return, evacuee health has continued to deteriorate. Kawauchi Village and its residents are undergoing difficulties associated with regional regeneration following the disaster and subsequent evacuation. It is not enough to focus on individual lifestyle diseases, but comprehensive preventative measures must be established to combat lifestyle disease development.

Contributors

AK designed the study, performed the statistical analysis and drafted the manuscript. MO, DE, KI and KHH performed the statistical analysis and helped to draft the manuscript. All the authors read and approved the final manuscript.

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Competing interests None declared.

Ethical approval This study protocol was approved by the ethical review board of the Graduate School of Medicine at Kyoto University (approval number E1809, 23 July 2013). Japanese ethical guidelines provide for waiver of informed consent for research use of existing medical records after anonymization. Access to Japanese National Healthcare System data for Kawauchi Village was obtained with permission from the Mayor of Kawauchi Village.

Data sharing statement No additional data are available.

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract written in line 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found written in lines 27-47
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported written in lines 68-95
Objectives	3	State specific objectives, including any prespecified hypotheses written in lines 96-98
Methods		
Study design	4	Present key elements of study design early in the paper written in lines 108-109
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection written in lines 111-115
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up written in lines 111-115 *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable written in lines 118-131, 135-154
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group written in lines 111-113
Bias	9	Describe any efforts to address potential sources of bias written in lines 113-115, 161-162
Study size	10	Explain how the study size was arrived at written in lines 111-113
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why written in lines 158-160
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding written in lines 161-172
		(*b*) Describe any methods used to examine subgroups and interactions We considered it was not readily possible in this study due to the reduced statistical power.
		(*c*) Explain how missing data were addressed written in lines 135-136

		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed not applicable *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses It was not used in this study.

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed written in lines 176-179
		(b) Give reasons for non-participation at each stage written in lines 111-115
		(c) Consider use of a flow diagram shown in Table 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders shown in Table 1
		(b) Indicate number of participants with missing data for each variable of interest shown in Table 1,2,3
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) shown in Table 1
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time shown in Table 2,3
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included shown in Table 4,5
		(*b*) Report category boundaries when continuous variables were categorized written in lines 162-164; and 137-154
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses It was not used in this study.
Discussion		
Key results	18	Summarise key results with reference to study objectives written in lines 222-226
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias written in lines 268-289
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence written in 226-267
Generalisability	21	Discuss the generalisability (external validity) of the study results written in lines 226-231,
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based written in lines 302-303

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Lifestyle-related diseases following the evacuation after the Fukushima Daiichi Nuclear Power Plant accident: a retrospective study of Kawauchi village with long-term follow-up.

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Lifestyle-related diseases following the evacuation after the Fukushima Daiichi Nuclear Power Plant accident: a retrospective study of Kawauchi village with long-term follow-up.

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Keywords: metabolic disease, Fukushima Daiichi Nuclear Power Plant accident, medical health check-up, disaster, evacuation

Word Count: 4179

Abstract

Objectives Kawauchi Village lies 20 km west of the Fukushima Daiichi Nuclear Power Plant. On March 16th 2011, evacuation was ordered due to the threat of radiological exposure, and was lifted in April 2012. In this study, we aimed to evaluate the pre- and post-disaster health status of the Kawauchi villagers, measured by routine yearly physical exams.

Methods We analyzed the annual health examination data of residents of Kawauchi village from 2008 to 2013, as available from the Japanese National Health Insurance system. Data from 2011 was not available due to the disaster. As the health data included the same subjects repeatedly from year-to-year, the sample was non-independent, and generalized estimated equation modeling was used. A pre-disaster time period (2008-2010) was categorized for comparison with post-disaster 2012 and 2013. The outcome examined was the prevalence of metabolic disease, and was adjusted for confounding factors.

Results Data for 20.6% to 25.9% of the total residents were available in this period. In 2013, the prevalence of metabolic syndrome (from 17.0% to 25.2%, $p<0.001$), diabetes (from 11.3% to 17.0%, $p<0.001$), dyslipidemia (from 43.2% to 56.7%, $p<0.0001$), hyperuricemia (from 5.2% to 8.4%, $p=0.006$), and chronic kidney disease (from 16.1% to 26.7%, $p<0.001$) were all found to be elevated significantly compared to pre-disaster years, while that of obesity or hypertension did not change.

Conclusions The present follow-up study for Kawauchi Village revealed an increase in lifestyle-related disease following the March 2011 disaster and subsequent evacuation, and that this trend still continues two years later.

(249 words // 250 total)

Strengths and limitations of this study

Kawauchi Village consists of the first residents returning to their homes following evacuation from the 2011 Tohoku Earthquake/Tsunami disaster. This study revealed that the risk of various lifestyle-related diseases increased following the disaster and evacuation and that this trend was continuing two years later.

The data consists of all residents of the village that attended their yearly health consultation, in accordance with the Japanese National Healthcare System. As such, there may be an inherent selection bias.

INTRODUCTION

On March 11th, 2011, an historic magnitude 9.0 earthquake struck the northeastern coast of Japan. Located in the mountains, Kawauchi Village, in Fukushima Prefecture, escaped major damage from both the earthquake and subsequent tsunami. However, the village lies 20 km west of the Fukushima Daiichi Nuclear Power Plant, and was bisected by the March 16th government-ordered mandatory evacuation. The entire village population relocated to nearby evacuation centers, such as Koriyama City. The government authorized return to the village a year later, in April 2012. By April 2013, 1299 of the original 2816 villagers had returned (46.1%), with more than 70% of returnees being above the age of 50. The fallout surrounding the evacuation, including potential radiological exposure, increases in unemployment, loss of living area, and disintegration of families and other social support systems, has constituted innumerable challenges to the returning population. [1]

Numerous studies, both within and outside of Japan, have demonstrated the health impact of disasters and their subsequent personal, environmental, and societal responses. After the Great Hanshin Earthquake struck Kobe City in 1995, mean blood pressure increased significantly for both those patients who were living in the disaster area, as well as those in the surrounding region. In the former, the elevation in blood pressure peaked in the first week and lasted for 4 weeks, but then returned to baseline within 6 weeks of the disaster.[2] Similar temporary hypertension was reported after Hurricane Katrina, with HbA1c levels also increasing throughout the observational period (6-16 months post-disaster).[3] A recent study on the Fukushima region demonstrated the short-term impact of the disaster on metabolic measures within evacuated populations, including differences delineated among those evacuating due to radiological threat and those whose evacuation was du e to the destruction of their homes by tsunami. Significantly higher body weight, body mass index, waist circumference, and HbA1c, as well as lower high-density lipoprotein (HDL) cholesterol levels, were found 5 months following the earthquake.[4] An evaluation of diabetes prevalence in the region examined 27,486 people who were residents of the 12 municipalities surrounding the Fukushima Daiichi power plant, of which Kawauchi Village is a part. Comparing data from before and after the disaster, the evacuated population was found to have a higher incidence of diabetes than those who remained unevacuated.[5]

However, the majority of studies available report only short-term observations, with follow-up typically running less than a year. With the exception of temporary hypertension, little research has examined whether post-disaster metabolic changes return to baseline over time.[6]

The triple-threat of earthquake, tsunami, and radiological damage from the Tohoku disaster is unprecedented. However, studies have demonstrated that the risk of radiological exposure and consequential increase in cancer rate in the Tohoku region around the nuclear power plant is low.[7-10] As the majority of international attention has been focused on radiological threat to the Tohoku population, it is possible if not likely that changes in metabolic health measures may be overlooked in the region.

In this study, the major objective is to evaluate the pre- and post-disaster health status of Kawauchi villagers who underwent their yearly medical checkup in accordance with the Japanese National Health Insurance system guidelines, over a multi-year followup period. This is the first study to evaluate the long-term impact of the disaster, evacuation, and return, on post-evacuation village-returnee health status.

METHODS

Population Data

This retrospective study was approved by the ethical review board of the Graduate School of Medicine at Kyoto University (approval number E1809). Japanese ethical guidelines provide for waiver of informed consent for research use of existing medical records after anonymization. A descriptive and analytical epidemiological study was conducted using medical examination data. The yearly national health screening obtains substantial information about individual residents, and is used for health prevention as dictated by the Japanese Ministry of Health, Labor, and Welfare. Japanese National Healthcare System medical examination data, taken by physicians in Kawauchi Village and surrounding evacuation centers from 2008 through 2010, and 2012 through 2013, were obtained. Data from 2011 was excluded due to a low participation rate immediately following the disaster and evacuation. Access to Japanese National Healthcare System data for Kawauchi Village was obtained with permission of the Kawauchi Village mayor. Villagers were offered the opportunity to individually withhold their medical data from the study. The National Healthcare Insurance system covers villagers older than 40, including self-employed citizens and their families, as well as retirees.

Healthcare records included birthdate, age, gender, height, weight, body mass index (BMI), systolic and diastolic blood pressure, waist circumference, blood glucose, hemoglobin A1c (HbA1c), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglyceride (TG), aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ-glutamyl transpeptidase (γ-GTP), and from 2010 estimated glomerular filtration rate (eGFR) and serum creatinine. Due to a change in the measurement of HbA1c from the Japan Diabetes Society (JDS) standard to the National Glycohemoglobin Standardization Program (NGSP) reference value from 2008 to 2012, the HbA1c values were shifted to NGSP-equivalent values for comparison purposes.[11]

Questionnaire

Lifestyle-related factors were collected by questionnaire and confirmed by interview, and include sleep patterns, dietary changes, smoking and drinking habits and approximate amount consumed, exercise habits, and medications for blood pressure, diabetes, hypercholesterolemia, and other diseases. Information was further confirmed by interview.

Definitions of Lifestyle-related Disease

Metabolic syndrome was defined as the presence of any three abnormal findings of five risk factors [12]: (1) a waist circumference ≥ 90 cm in males or ≥ 80 cm in females, (2) a TG ≥ 150 mg/dL (1.7 mmol/L), (3) a HDL-C < 40mg/dL (1.0 mmol/L) in males, < 50mg/dL (1.3 mmol/L) in females, (4) a systolic blood pressure ≥ 130 and/or diastolic blood pressure ≥ 85 mmHg (with antihypertensive pharmaceutical usage in a subject treated as an alternate indicator), (5) a fasting glucose ≥100mg/dL (with pharmaceutical treatment for elevated glucose as an alternate indicator).

Obesity was defined as a body mass index (BMI) ≥ 25 kg/m^2.[13]

Hypertension was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg, or if patients were undergoing pharmaceutical treatment for hypertension.[14]

Diabetes was defined as a fasting plasma glucose level ≥ 126 mg/dL (7.0 mmol/L) and/or an HbA1c level ≥ 6.5% (NGSP), or if the patient was undergoing treatment for elevated glucose.[15]

Dyslipidemia was defined as a HDL-C < 40 and/or LDL-C ≥ 140 and/or TG ≥ 150, or when treatment for lipidemia was noted.[16]

Hyperuricemia was defined as a uric acid measurement > 7.0 mg/dL.[17]

Chronic Kidney Disease (CKD) was defined as an eGFR < 60 mL/min/1.73m^2.[18]

Statistical methodology

Continuous variables were evaluated using ANOVA and Tukey's HSD test to identify differences due to aging. Significance was defined as a p-value less than 0.05. Statistica 12 software (StatSoft, Tulsa, USA) was used.

As the health data from 2008 to 2013 included the same subjects repeatedly, the sample was considered non-independent and generalized estimating equation modeling was used.[19] The pre-disaster time period (2008-2010) was categorized for comparison to the post-disaster 2012 and 2013. The presence or absence of lifestyle-related disease was treated as dependent, with medical examination consultation year, age at time of visit, and gender independent, with adjustment for both age and gender. An unstructured correlation structure was used to account for correlation among repeated measures on the same subjects. The least-squares means and odds ratio, adjusted for age and gender, was used for repeated measure logistic regression analysis. Significance was set to a level of 0.05. SAS 9.3 (SAS Institute Inc., Cary, USA) was used for analysis.

RESULTS

Demographics

Subjects with missing information regarding the use of medications were excluded from this study. When waist circumference (WC) and fasting cholesterol (FBC) were excluded, over 80% of the total population had all needed data available for analysis (online supplementary appendix 1 (Table S1) provides the full list of results). There was no significant difference seen in the excluded population pre- and post-disaster for either WC nor FBC. Data for obesity, high blood pressure, diabetes, and lipid abnormalities were available in more than 80% of the population (online supplementary appendix 1 (Tables

S2-S5) provides the full list of results). For CKD and hyperuricemia, information availability prior to the earthquake was poor, as those evaluations were not recommended by Kawauchi Village (online supplementary appendix 1 (Tables S6 and S7) provides the full list of results). Overall, we could not determine any systemic bias with regard to data coverage of the population pre- and post-disaster.

From 2008 to 2013 (excluding 2011), medical examinees (percentage of total population) numbered 777 (24.3%), 797 (25.7%), 779 (25.9%), 674 (24.1%), and 576 (20.6%), respectively (Table 1). "Returnee" was defined as a person who returned to the village from evacuation centers in Koriyama City. Patient screening occurred in both Kawauchi village or Koriyama city. In 2012, 64% of Kawauchi medical records available were for returnees vs 36% who remained evacuated; in 2013, 83% belonged to returnees. The average age was significantly different only between 2008 and 2012. No significant differences in gender ratio were seen.

Table 1 Number of participants in Kawauchi Village Health Checkup under national health insurance system

Examination year	2008	2009	2010	2011	2012	2013
Population	3192	3100	3004	2895	2801	2794
Participants number	777	797	779	Disaster	674	576
%	24.3	25.7	25.9		24.1	20.6
In Kawauchi	777	797	779	-	431	477
Evacuated (Koriyama City)	-	-	-	-	184	99
Evacuated (Fukushima Prefecture)	-	-	-	-	26	-
Evacuated (Elsewhere)	-	-	-	-	33	-
Age (Mean±SD)	68.6 ±11.0	68.3 ±11.3	68.0 ±11.2	-	66.7 ±11.7	68.3 ±10.9
ANOVA p=0.016	A#	AB#	AB#	-	B#	AB#
Gender (Male/Female) Chi-square test p=0.704	42%/58%	43%/57%	41%/59%	-	44%/56%	43%/57%

#: Means that do not share a letter are significantly different. For example, there is no statistical difference between A and AB, while there is a significant difference between A and B.

Interview Questionnaire Analysis

The results of the health exam interview questions are summarized in Table 2. No significant differences were seen in self-reported rates of physical activity, alcohol consumption, or tobacco consumption. However, a significant decline was noted in reported sleep quality, and dietary habits became less regular.

Table 2 Results of self-reported lifestyle-related factors assessment by using medical questionnaire

Examined year		2008	2009	2010	2012	2013	Chi-square test	
Test items	Question (Answer choices)	percentage (%) (n)					p-value	
Physical activity	Do you do exercise that makes you sweat for at least 30 minutes twice a week, and have you been doing this for at least 1 year? (Yes/No)	35/65 (n=720)	40/60 (n=557)	38/62 (n=552)	41/59 (n=511)	42/59 (n=411)	0.17	
Alcohol consumption	How often do you drink alcohol? (Everyday/Occasionally/Rarely/Never)	21/18/18/44 (n=739)	20/21/21/39 (n=779)	20/20/21/39 (n=760)	23/20/17/41 (n=649)	19/20/20/40 (n=572)	0.146	
Tobacco consumption	At present, do you have a smoking habit? (Yes/No)	13/87 (n=745)	14/86 (n=787)	12/88 (n=765)	12/88 (n=649)	14/86 (n=574)	0.66	
Sleep patterns	Do you feel you get sound sleep and get enough rest? (Yes/No)	81/19 (n=720)	77/23 (n=565)	74/26 (n=555)	69/31 (n=518)	67/33 (n=437)	0.0001	*
Dietary habits	Skip breakfast 3 times a week (Yes/No)	6/94 (n=719)	7/93 (n=561)	5/95 (n=553)	6/94 (n=519)	11/89 (n=437)	0.0143	*
	Take additional foods after dinner	10/90 (n=721)	14/86 (n=563)	14/86 (n=553)	10/90 (n=515)	14/86 (n=43	0.0779	

	3 times a week (Yes/No)					8)		
	Eating dinner 2 hours before sleep 3 times a week (Yes/No)	27/73 (n=720)	27/73 (n=559)	22/78 (n=551)	22/78 (n=510)	23/77 (n=435)	0.035	*
Medications	Antihypertensive (Yes/No)	50/50 (n=729)	51/49 (n=768)	49/51 (n=758)	51/49 (n=645)	53/47 (n=573)	0.6009	
	Antidyslipidemic (Yes/No)	18/82 (n=729)	18/82 (n=767)	19/81 (n=757)	23/77 (n=642)	26/74 (n=570)	0.0028	*
	Antidiabetic (Yes/No)	8/92 (n=729)	8/92 (n=767)	6/94 (n=757)	9/91 (n=644)	9/91 (n=572)	0.2756	
	Diagnosis of chronic renal failure or dialysis treatment (Yes/No)	0.4/99.6 (n=729)	0.3/99.7 (n=767)	0.3/99.7 (n=757)	0/100 (n=639)	0.3/99.7 (n=572)	0.4013	

Medication status for cholesterolemia significantly changed after the disaster, which resulted from increased prevalence of cholesterolemia. No significant change was observed in prevalent of hypertension, diabetes, or CKD (Table 2).

Changes in laboratory value averages

The trend of the average values of each examined item is listed in Table 3. During the study period, a significant change was seen in all values except for AST and creatinine. Abdominal circumference also showed an increasing trend. On comparing medical results from 2012 to any of the pre-earthquake years available, body weight, BMI, fasting blood glucose, TG, ALT, and γ-GTP were significantly increased, while systolic blood pressure and eGFR decreased significantly. On comparing 2013 to all pre-earthquake years, body weight, fasting blood glucose, HbA1c, and TG had all substantially increased, while diastolic blood pressure, systolic blood pressure, and eGFR were significantly decreased. These differences were tested in relation to patient self-reported physical activity and antihypertensive pharmaceutical usage, but there were no significant correlations noted (Table 2).

Table 3 Demographics of the total Kawauchi Population

Examined year	2008		2009		2010		2012		2013		ANOVA	
Test items	Mean±SD (n) Tukey's HSD test										p-value	
Height	152.2±9.8 (684)	A	152.7±9.6 (666)	A	153.1±9.4 (650)	AB	154.6±9.7 (572)	B	154.6±9.6 (488)	B	<0.0001	*
Weight	55.6±10.4 (684)	A	55.8±10.5 (666)	A	55.8±10.5 (650)	A	58.7±11.1 (572)	B	58.1±11.3 (488)	B	<0.0001	*
BMI	23.9±3.4 (684)	A	23.9±3.5 (666)	A	23.7±3.5 (650)	A	24.5±3.7 (572)	B	24.2±3.6 (488)	AB	<0.0001	*
Waist circumference	84.3±9.8 (381)	A	84.5±9.5 (382)	AB	85.7±9.1 (391)	ABC	86.3±9.7 (390)	BC	87.4±9.4 (296)	C	<0.0001	*
Systolic blood pressure	135.6±14.7 (684)	A	133.0±17.5 (666)	B	134.6±17.1 (650)	AB	126.6±14.3 (572)	C	126.2±14.8 (488)	C	<0.0001	*
Diastolic Blood Pressure	76.3±9.2 (684)	A	75.2±9.7 (666)	AB	75.9±10.8 (650)	AB	74.5±9.2 (572)	B	71.4±9.9 (488)	C	<0.0001	*
eGFR	–	–	–	–	72.1±13.4 (391)	A	68.8±13.9 (615)	B	66.0±12.8 (534)	C	<0.0001	*
Blood Glucose	97.4±16.5 (596)	A	96.8±18.3 (544)	A	96.5±16.0 (556)	A	101.0±21.4 (508)	B	103.3±20.2 (425)	B	<0.0001	*
HbA1c	5.5±0.6 (676)	A	5.5±0.7 (659)	A	5.5±0.6 (643)	A	5.6±0.7 (572)	A	5.8±0.8 (488)	B	<0.0001	*
HDL-C	60.1±14.7 (676)	A	59.7±14.5 (659)	A	58.2±14.1 (643)	AB	56.3±14.4 (572)	B	56.7±13.5 (488)	B	<0.0001	*
LDL-C	114.9±26.7 (676)	AB	113.6±26.2 (659)	A	114.9±27.0 (643)	AB	116.8±31.3 (572)	AB	118.6±29.8 (488)	B	0.033	*
TG	97.0±52.7 (676)	A	92.9±60.0 (659)	A	95.8±55.4 (643)	A	109.3±81.0 (572)	B	109.9±69.7 (488)	B	<0.0001	*
AST	25.8±8.3 (676)	–	27.0±59.3 (659)	–	24.1±7.6 (643)	–	27.3±11.9 (572)	–	25.5±9.4 (488)	–	0.29	
ALT	19.8±9.5 (676)	AB	19.6±17.9 (659)	AB	18.9±9.4 (643)	A	23.3±17.2 (572)	C	21.5±13.9 (488)	BC	<0.0001	*
γ-GTP	31.0±34.6 (676)	AB	29.9±34.3 (659)	A	27.9±27.5 (643)	A	37.4±53.2 (572)	C	36.8±52.0 (488)	BC	<0.0001	*
Blood Creatinine	–	–	–	–	0.75±0.23 (391)	–	0.77±0.18 (615)	–	0.78 ±0.18 (534)	–	0.06	
Uric Acid	5.08±1.33 (380)	AB	5.00±1.29 (382)	A	5.00±1.33 (391)	A	5.29±1.41 (615)	B	5.26±1.39 (534)	B	<0.0001	*

#: Means that do not share a letter are significantly different. For example, there is no statistical difference between A and AB, while there is a significant difference between A and B, or AB and C, etc.

Lifestyle-related diseases

Table 4 shows the trends in prevalence of lifestyle-related factors determined by the least squares mean test, adjusted for age and sex, using repeated measure logistic regression analysis with generalized estimating equations. A significant increase was seen in the prevalence of metabolic syndrome, diabetes, dyslipidemia, hyperuricemia, and chronic kidney disease in the two years following the disaster, even with adjustment for age and gender. Table 5 shows that the odds ratio for 2012, in comparison with pre-earthquake health values, indicates significantly elevated metabolic syndrome, obesity, diabetes, dyslipidemia, hyperuricemia, as well as increased prevalence of chronic kidney disease. Meanwhile, hypertension significantly decreased. For 2013, the odds ratio indicated significant increases in metabolic syndrome, diabetes, dyslipidemia, and hyperuricemia, and the prevalence of CKD was elevated, in comparison with the pre-disaster period. However, significant differences in obesity and hypertension were not seen.

Table 4 Trends in prevalence of lifestyle-related diseases

Examined year	pre-earthquake	2012	2013	Trend test	
Test items	prevalence of lifestyle-related diseases (95% CI)			p-value	
Metabolic syndrome	17.0% (15.0-19.2)	24.2% (21.0-27.7)	25.2% (21.9-29.0)	<0.0001	*
Obesity	35.3% (32.4-38.3)	39.7% (36.3-43.3)	36.9% (33.4-40.5)	0.344	
Hypertension	65.7% (62.7-68.5)	61.8% (58.2-65.2)	63.7% (59.9-67.4)	0.246	
Diabetes	11.3% (9.6-13.4)	14.7% (12.4-17.3)	17.0% (14.4-20.0)	<0.0001	*
Dyslipidemia	43.2% (40.3-46.1)	53.9% (50.2-57.6)	56.7% (52.8-60.6)	<0.0001	*
Hyperuricemia	5.2% (3.9-6.9)	10.0% (7.8-12.7)	8.4% (6.3-11.3)	0.006	*
Chronic kidney disease	16.1% (12.7-20.1)	21.7% (18.5-25.3)	26.7% (23.0-30.8)	<0.0001	*

*: $p<0.05$

Table 5 Odds ratio and 95% confidence intervals (CI) of lifestyle-related diseases after the Great East Japan Earthquake

Examined year	2012 vs pre-earthquake	2013 vs pre-earthquake	2013 vs 2012
Test items		odds ratio (95% CI)	
Metabolic syndrome	1.55* (1.29-1.88)	1.64* (1.35-2.01)	1.06 (0.87-1.28)
Obesity	1.21* (1.06-1.38)	1.07 (0.93-1.24)	0.89* (0.79-0.99)
Hypertension	0.85* (0.75-0.96)	0.92 (0.80-1.06)	1.09 (0.94-1.25)
Diabetes	1.35* (1.13-1.61)	1.6* (1.32-1.95)	1.19* (1.02-1.39)
Dyslipidemia	1.54* (1.33-1.78)	1.72* (1.47-2.02)	1.12 (0.95-1.32)
Hyperuricemia	2.03* (1.50-2.75)	1.69* (1.16-2.45)	0.83 (0.59-1.17)
Chronic kidney disease	1.45* (1.09-1.92)	1.91* (1.43-2.54)	1.32* (1.10-1.57)

*: $p<0.05$

When 2013 was compared to 2012, metabolic syndrome, diabetes, and chronic kidney disease were significantly increased, but obesity had significantly reduced.

DISCUSSION

On review of the available Kawauchi Village medical records, a significant increase in the prevalence of lifestyle-related diseases was found. Increases were noted in metabolic syndrome, diabetes, dyslipidemia, hyperuricemia, and chronic kidney disease following the disaster period. On the other hand, obesity only increased significantly in 2012, and hypertension was significantly reduced. Previous studies of the region had found an increase in diabetes due to evacuation,[5] and our evaluation of Kawauchi Village, which was fully evacuated, reinforces this result. Further, the increase in diabetes continued over the long term, into 2013. This may indicate that it was not the combined stresses of the disaster and evacuation alone, but additional stress relating to trouble following return, including a perceived threat from the nearby Fukushima nuclear power plant.

The nuclear accident impacted Kawauchi Village in a multitude of ways. The changes in population demographics, ongoing evacuation areas, and shuttering of businesses resulted in a diminishment of communal resources. Significant portions of the village, including commercial and welfare institutions, health care facilities, schools, and others, were dependent on the adjacent nuclear power plant in the neighboring Tomioka Town area, and, as they closed with the changing makeup of the region, there were few if any replacements. Consequently, younger members of the village are not returning, and this has lead to a demographic collapse. As of April 2013, only 26% of former residents below the age of 50 had returned to the village, and 58% of those villagers who have returned are 50 years or older. In particular, working-age parents and their children have not returned. This has lead to both a rapid aging in the village, as well as causing separation of families and subsequent diminishment in communal support. Furthermore, residents were unable to farm the land in 2012, potentially leading to a diminishment in physical activity among returnees; thankfully, residents were able to resume rice planting in 2013. Taken together, social and mental stress in concert with decreased physical activity may have triggered and continued a universal increase in the prevalence of metabolic illness in the years following the disaster.

Curiously, systolic blood pressure (in 2012 and 2013) and diastolic blood pressure (in 2013) underwent significant decreases, despite no reported change in usage of antihypertension medications, or, as reported by physicians in the village, any noticed change in the kind of antihypertensives generally being provided. Previous reports have shown that blood pressure tends to increase immediately following a disaster, but stabilize in the weeks and months thereafter.[2-3] As our report looked primarily at long-term outcomes over a year after the disaster period, it would not be possible to detect these short-term changes in blood pressure. Moreover, why systolic and diastolic blood pressure appeared to improve in the population following evacuation remains undetermined, and will require more study.

The rate of diabetes increasing in a post-disaster population, though expected, is concerning. Focused attention on those residents with pre-diabetic and diabetic symptomologies, and/or those exhibiting poor sleep and mental stress, may allow health officials to prevent development or worsening of diabetes within the population.[20-21] However, systemic resources in Kawauchi and the region, and thus the ability to offer population-wide support, remain limited. Notably, the conditions in which the residents were living did not worsen from 2012 to 2013, and may, in fact, have improved; unfortunately, though, the rate of lifestyle disease continued to increase. Ongoing health improvement efforts in Kawauchi and the surrounding region may thus need to focus on improving the lifestyle of residents on an individual level, in addition to efforts to support rebuilding of the community, regenerate industry and livelihoods, and bring back younger members of the population.

There were limitations to this study. The data consists of all residents of the village that attended their yearly health examination offered under the Japanese National Healthcare System. Thus, there may be a selection bias in the population. It is conceivable that, if the healthiest individuals in the village were the ones to undergo health screening, then the actual health status in the village may be substantially worse than seen here.[22] Also, even adjusting for age and gender, it is possible that the significant increase seen in lifestyle disease is due to this bias. Reversely, there may be a possibility of underestimation, if those participants more concerned about their health attended the health examination significantly more than non-participants. We cannot predict in which direction this bias may work.

Further, measurements of patient physical activity, alcohol consumption, tobacco consumption, and medication usage, among others, were obtained by self-report or interview, and were not explicitly measured; no differences between these were seen pre- and post-disaster. There remains a possibility for individual overestimation of physical activity and underestimation of tobacco/alcohol consumption.[23] Further, as specific questionnaires were used individualized follow-up was unavailable, and so it is possible that other unidentified causes may be involved in the increase in lifestyle disease. It must be noted that in order to properly diagnose chronic kidney disease using eGFR, a decrease must be observed over more than 3 months.[18] However, in our study, only single data points at yearly intervals were available, and so the diagnosis is imperfect. In addition, eGFR was not included in the National Healthcare System data prior to 2010. As such, changes seen over the earthquake time period may have been background changes already occurring prior to the disaster. Because a social epidemiological approach was not taken here, future study taking into account specifically the loss of industry and individual livelihood, and subsequent changes in habits and lifestyle should be taken, to better grasp the full picture of what changes are occurring in the disaster environment.

Conclusions

On examination of Kawauchi Village, it appears that the health status of the villagers has continued to deteriorate in the aftermath of the Tohoku earthquake, tsunami, and Fukushima Daiichi Nuclear Power Plant accident. Kawauchi Village and its residents are undergoing difficulties associated with regional de- and re-generation following the disaster and subsequent evacuation. It is not enough to focus on individual lifestyle diseases, but comprehensive preventative measures must be established to combat lifestyle disease development.

Contributors

AK, DE, and MO performed the statistical analysis and drafted the manuscript. KI and KHH performed the statistical analysis and helped in drafting and revising the manuscript. AK designed the study. All the authors read and approved the final manuscript.

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Competing interests None declared.

Ethical approval This study protocol was approved by the ethical review board of the Graduate School of Medicine at Kyoto University (approval number E1809, 23 July 2013). Japanese ethical guidelines provide for waiver of informed consent for research use of existing medical records after anonymization. Access to Japanese National Healthcare System data for Kawauchi Village was obtained with permission from the Mayor of Kawauchi Village.

Data sharing statement No additional data are available.

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Table S1 Demographics of Kawauchi Population with/without missing data for metabolic syndrome

		2008			2009			2010			2012			2013			p value	p value for age	
																	%	Included	Missing
Total (inclusion criteria: three of 5 items are available)																			
		n	Included	Excluded	n	Included	Excluded	n	Included	Excluded	n	Included	Excluded	n	Included	Excluded			
Male	%	329	93	7	340	91.5	8.5	316	90.8	9.2	2[illegible]9	89	11	246	89	11	0.3684		
Female		448	82.6	17.4	457	76.2	23.8	463	76.9	23.1	3[illegible]5	81.6	18.4	330	81.5	18.5	0.0493		
	Age		69.2±10.9	62.6±10.1		70.1±10.7	66.6±7.9		69.7±10.1	66.8±9.6		68.8±11.0	62.1±10.2		70.1±10.4	62.1±8.9		0.53	0.1104
			69.9±10.7	61.2±9.7		69.9±10.8	58.4±10.2		69.3±11.1	58.9±10.5		67.2±11.8	58.7±11.1		69.6±10.7	59.0±8.9		0.0084	0.3937
WC missing			available	missing		available	missing		available	missing		available	missing		available	missing			
Male	%		54.4	45.6		53.8	46.2		57.6	42.4		58.5	41.5		52.4	47.6	0.533		
Female			45.1	54.9		43.5	56.5		45.1	54.9		57.3	42.7		50.6	49.4	0.0004		
	Age		62.4±8.9	76.3±7.9		63.4±8.5	77.2±7.1		64.0±7.8	76.9±7.8		62.9±8.5	75.3±10.2		63.3±7.5	75.8±9.5		0.4719	0.3184
			62.5±8.6	73.3±10.4		62.9±8.9	70.4±12.6		62.1±8.6	70.9±12.6		61.8±9.7	70.8±13.2		63.1±7.9	72.3±12.1		0.5489	0.0568
FBG missing			available	missing		available	missing		available	missing		available	missing		available	missing			
Male	%		81.5	18.5		74.7	25.3		76.3	23.7		78.3	21.7		74.8	25.2	0.2094		
Female			73.21	26.79		63.5	36.5		68	32		73.1	26.9		73	27	0.0042		
	Age		69.0±10.7	67.7±12.1		69.9±10.5	69.3±10.6		69.4±10.2	69.7±9.5		68.5±10.7	66.3±12.2		69.5±10.5	68.5±10.6		0.6561	0.3729
			69.8±10.7	64.6±10.9		69.6±10.8	62.8±12.2		69.1±11.3	62.3±11.5		66.9±11.4	62.1±13.3		69.1±10.7	63.8±11.7		0.014	0.4529
HDL missing			available	missing		available	missing		available	missing		available	missing		available	missing			
Male	%		93	7		91.5	8.5		90.8	9.2		89	11		89	11	0.3684		
Female			82.6	17.4		76.2	23.8		76.9	23.1		81.6	18.4		81.5	18.5	0.0493		
	Age		69.2±10.9	62.6±10.1		70.1±10.7	66.6±7.9		69.7±10.1	66.8±9.6		68.8±11.0	62.1±10.2		70.1±10.4	62.1±8.9		0.53	0.1104
			69.9±10.7	61.2±9.7		69.9±10.8	58.4±10.2		69.3±11.1	58.9±10.5		67.2±11.8	58.7±11.1		69.6±10.7	59.0±8.9		0.0084	0.3937
TG missing			available	missing		available	missing		available	missing		available	missing		available	missing			
Male	%		93	7		91.5	8.5		90.8	9.2		89	11		89	11	0.3684		
Female			82.6	17.4		76.2	23.8		76.9	23.1		81.6	18.4		81.5	18.5	0.0493		
	Age		69.2±10.9	62.6±10.1		70.1±10.7	66.6±7.9		69.7±10.1	66.8±9.6		68.8±11.0	62.1±10.2		70.1±10.4	62.1±8.9		0.53	0.1104
			69.9±10.7	61.2±9.7		69.9±10.8	58.4±10.2		69.3±11.1	58.9±10.5		67.2±11.8	58.7±11.1		69.6±10.7	59.0±8.9		0.0084	0.3937
BP missing			available	missing		available	missing		available	missing		available	missing		available	missing			
Male	%		93.3	6.7		91.8	8.2		92.1	7.9		89	11		89	11	0.238		
Female			84.2	15.8		77.5	22.5		77.5	22.5		81.6	18.4		81.5	18.5	0.0485		
	Age		69.2±10.9	62.1±10.0		70.1±10.7	66.4±8.0		69.8±10.0	65.7±9.7		68.8±11.0	62.1±10.2		70.1±10.4	62.1±8.9		0.525	0.2142
			70.0±10.6	60.2±9.5		69.9±10.7	57.7±10.1		69.3±11.0	58.6±10.4		67.2±11.8	58.7±11.1		69.6±10.7	59.0±8.9		0.0073	0.6134

Table S2 Demographics of Kawauchi Population with/without missing data for obesity

		2008			2009			2010			2012			2013			p value	p value for age	
																	%	Included	Missing
Total (inclusion criteria: BMI is available)																			
		n	Included	Excluded	n	Included	Excluded	n	Included	Excluded	n	Included	Excluded	n	Included	Excluded			
Male	%	329	93.3	6.7	340	91.8	8.2	316	92.1	7.9	29[illegible]	89	11	246	89	11	0.237		
Female		448	84.2	15.8	457	77.5	22.5	463	77.5	22.5	37[illegible]	81.6	18.4	330	81.5	18.5	0.0485		
	Age		69.2±10.9	62.1±10.0		70.1±10.7	66.4±8.0		69.8±10.0	65.7±9.7		68.8±11.0	62.1±10.2		70.1±10.4	62.1±8.9		0.525	0.2142
			70.0±10.6	60.2±9.5		69.9±10.7	57.7±10.1		69.3±11.0	58.6±10.4		67.2±11.8	58.7±11.1		69.6±10.7	59.0±8.9		0.0073	0.6134

Table S3 Demographics of Kawauchi Population with/without missing data for hypertension

		2008			2009			2010			2012			2013			p value	p value for age	
																	%	Included	Missing
Total (inclusion criteria: BPs are available or taking medication for hypertension)																			
		n	Included	Excluded	n	Included	Excluded	n	Included	Excluded	n	Included	Excluded	n	Included	Excluded			
Male	%	329	95.1	4.9	340	94.1	5.9	316	95.6	4.4	299	93.7	6.3	246	94.7	5.3	0.8324		
Female		448	86.6	13.4	457	82.3	17.7	463	83.2	16.8	375	88.8	11.2	330	89.4	10.6	0.0077		
	Age		69.3±10.8	58.8±8.8		70.0±10.6	65.3±8.4		69.7±9.9	63.4±11.1		68.7±10.8	57.8±9.5		69.8±10.3	58.5±8.2		0.5699	0.0626
			69.8±10.6	59.3±9.2		69.3±10.8	56.9±10.3		69.0±11.0	56.8±10.4		66.9±11.7	55.0±10.4		69.0±10.7	56.4±8.5		0.0076	0.2769
BP missing			available	missing		available	missing		available	missing		available	missing		available	missing			
Male	%		93.3	6.7		91.8	8.2		92.1	7.9		89	11		89	11	0.237		
Female			84.2	15.8		77.5	22.5		77.5	22.5		81.6	18.4		81.5	18.5	0.0485		
	Age		69.2±10.9	62.1±10.0		70.1±10.7	66.4±8.0		69.8±10.0	65.7±9.7		68.8±11.0	62.1±10.2		70.1±10.4	62.1±8.9		0.525	0.2142
			70.0±10.6	60.2±9.5		69.9±10.7	57.7±10.1		69.3±11.0	58.6±10.4		67.2±11.8	58.7±11.1		69.6±10.7	59.0±8.9		0.0073	0.6134
HT medication missing			available	missing		available	missing		available	missing		available	missing		available	missing			
Male	%		96.4	3.6		96.8	3.2		97.5	2.5		95	5		99.2	0.8	0.0438		
Female			92	8		96.1	3.9		97.2	2.8		96.3	3.7		99.7	0.3	<0.0001		
	Age		69.2±10.8	57.0±8.9		70.0±10.5	62.6±9.6		69.6±9.9	62.0±12.2		68.4±10.9	60.3±10.8		69.3±10.6	64		0.4507	0.6799
			69.0±11.0	61.2±7.7		67.3±11.8	62.1±10.4		67.2±11.6	57.9±14.6		66.1±11.8	53.6±14.6		67.7±11.2	56		0.0095	0.1872

Table S4 Demographics of Kawauchi Population with/without missing data for diabetes

		2008			2009			2010			2012			2013			p value	p value for age	
																	%	Included	Missing
Total (inclusion criteria: blood tests are available or taking medication for diabetes)																			
		n	Included	Excluded	n	Included	Excluded	n	Included	Excluded	n	Included	Excluded	n	Included	Excluded			
Male	%	329	93	7	340	92.1	7.9	316	91.1	8.9	299	90.3	9.7	246	90.7	9.3	0.7423		
Female		448	82.8	17.2	457	77.5	22.5	463	77.8	22.2	375	83.2	16.8	330	82.7	17.3	0.0564		
	Age		69.2±10.9	62.6±10.1		70.1±10.7	66.2±7.7		69.7±10.1	66.5±9.[illegible]		68.7±10.9	62.0±10.6		70.0±10.3	61.6±9.3		0.4895	0.1665
			69.9±10.7	61.2±9.7		69.7±10.8	58.3±10.4		69.3±11.0	58.7±10.6		67.1±11.7	58.3±11.4		69.5±10.7	58.9±9.0		0.0078	0.3508
FBG missing			available	missing		available	missing		available	missing		available	missing		available	missing			
Male	%		81.5	18.5		74.7	25.3		76.3	23.7		78.3	21.7		74.8	25.2	0.2094		
Female			73.2	26.8		63.5	36.5		68	32		73.1	26.9		73	27	0.0042		
	Age		69.0±10.7	67.7±12.1		69.9±10.5	69.3±10.6		69.4±10.2	69.7±9.[illegible]		68.5±10.7	66.3±12.2		69.5±10.5	68.5±10.6		0.6561	0.3729
			69.8±10.7	64.6±10.9		69.6±10.8	62.8±12.2		69.1±11.3	62.3±11.5		66.9±11.4	62.1±13.3		69.1±10.7	63.8±11.7		0.014	0.4529
HbA1c missing			available	missing		available	missing		available	missing		available	missing		available	missing			
Male	%		93	7		91.5	8.5		90.8	9.2		89	11		89	11	0.3684		
Female			82.6	17.4		76.2	23.8		76.9	23.1		81.6	18.4		81.5	18.5	0.0493		
	Age		69.2±10.9	62.6±10.1		70.1±10.7	66.6±7.9		69.7±10.1	66.8±9.[illegible]		68.8±11.0	62.1±10.2		70.1±10.4	62.1±8.9		0.53	0.1104
			69.9±10.7	61.2±9.7		69.9±10.8	58.4±10.2		69.3±11.1	58.9±10.5		67.2±11.8	58.7±11.1		69.6±10.7	59.0±8.9		0.0084	0.3937
DM medication missing			available	missing		available	missing		available	missing		available	missing		available	missing			
Male	%		96.4	3.6		96.8	3.2		97.5	2.5		94	6		98.8	1.2	0.0302		
Female			92	8		95.8	4.2		97	3		96.8	3.2		99.7	0.3	<0.0001		
	Age		69.2±10.8	57.0±8.9		70.0±10.5	62.6±9.6		69.6±9.9	62.0±12.2		68.5±11.0	61.3±10.1		69.3±10.6	63.3±1.2		0.4711	0.6443
			69.0±11.0	61.2±7.7		67.4±11.8	62.1±10.1		67.2±11.6	59.8±15.7		66.1±11.8	51.4±14.7		67.7±11.2	56		0.0091	0.0927

Table S5 Demographics of Kawauchi Population with/without missing data for dyslipidemia

		2008			2009			2010			2012			2013			p value %	p value for age Included	p value for age Missing
Total (inclusion criteria: blood tests are available or taking medication for dyslipidemia)																			
		n	Included	Excluded	n	Included	Excluded	n	Included	Excluded	n	Included	Excluded	n	Included	Excluded			
Male	%	329	93	7	340	92.1	7.9	316	91.1	8.9	299	90.3	9.7	246	90.7	9.3	0.7423		
Female		448	82.8	17.2	457	77.5	22.5	463	77.8	22.2	375	83.2	16.8	330	82.7	17.3	0.0564		
	Age		69.2±10.9	62.6±10.1		70.1±10.7	66.2±7.7		69.7±10.1	66.5±9.7		68.7±10.9	62.0±10.6		70.0±10.3	61.6±9.3		0.4895	0.1665
			69.9±10.7	61.2±9.7		69.7±10.8	58.3±10.4		69.3±11.0	58.7±10.[illegible]		67.1±11.7	58.3±11.4		69.5±10.7	58.9±9.0		0.0078	0.3508
Blood test missing			available	missing		available	missing		available	missing		available	missing		available	missing			
Male	%		93	7		91.5	8.5		90.8	9.2		89	11		89	11	0.3684		
Female			82.6	17.4		76.2	23.8		76.9	23.1		81.6	18.4		81.5	18.5	0.0493		
	Age		69.2±10.9	62.6±10.1		70.1±10.7	66.6±7.9		69.7±10.1	66.8±9.6		68.8±11.0	62.1±10.2		70.1±10.4	62.1±8.9		0.53	0.1104
			69.9±10.7	61.2±9.7		69.9±10.8	58.4±10.2		69.3±11.1	58.9±10.[illegible]		67.2±11.8	58.7±11.1		69.6±10.7	59.0±8.9		0.0084	0.3937
DL medication missing			available	missing		available	missing		available	missing		available	missing		available	missing			
Male	%		96.4	3.6		96.8	3.2		97.5	2.5		94.3	5.7		98	2	0.1667		
Female			92	8		95.8	4.2		97	3		96	4		99.7	0.3	<0.0001		
	Age		69.2±10.8	57.0±8.9		70.0±10.5	62.6±9.6		69.6±9.9	62.0±12.[illegible]		68.4±11.0	61.1±10.4		69.4±10.4	59.0±10.7		0.4572	0.6978
			69.0±11.0	61.2±7.7		67.4±11.8	62.1±10.1		67.2±11.6	59.8±15.[illegible]		66.1±11.8	54.0±14.2		67.7±11.2	56		0.0098	0.2488

Table S6 Demographics of Kawauchi Population with/without missing data for chronic kidney disease

		2010			2012			2013			p value	p value for age	
											%	Included	Missing
Total (inclusion criteria: eGFR is available)													
		n	Included	Excluded	n	Included	Excluded	n	Included	Excluded			
Male	%	316	57.6	42.4	299	90.3	9.7	246	89.8	10.2	<0.0001		
Female		463	45.1	54.9	375	92	8	330	94.9	5.1	<0.0001		
	Age		64.0±7.8	76.9±7.8		68.8±10.9	60.8±10.1		70.1±10.3	61.4±8.9		<0.0001	<0.0001
			62.1±8.6	70.9±12.6		66.3±11.8	57.5±13.2		68.2±11.0	56.7±9.0		<0.0001	<0.0001

Table S7 Demographics of Kawauchi Population with/without missing data for hyperuricemia

		2008			2009			2010			2012			2013			p value	p value for age	
																	%	Included	Missing
Total (inclusion criteria: blood test is available)																			
		n	Included	Excluded	n	Included	Excluded	n	Included	Excluded	n	Included	Excluded	n	Included	Excluded			
Male	%	329	84.4	15.6	340	53.8	46.2	316	57.6	42.4	29[illegible]	90.3	9.7	246	89.8	10.2	<0.0001		
Female		448	44.9	55.1	457	43.5	56.5	463	45.1	54.9	37[illegible]	92	8	330	94.9	5.1	<0.0001		
	Age		62.4±8.9	76.3±7.9		63.4±8.5	77.2±7.1		64.0±7.8	76.9±7.8		68.8±10.9	60.8±10.1		70.1±10.3	61.4±8.9		<0.0001	<0.0001
			62.5±8.5	73.2±10.4		62.9±8.9	70.4±12.6		62.1±8.6	70.9±12.6		66.3±11.8	57.5±13.2		68.2±11.0	56.7±9.0		<0.0001	<0.0001

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract written in line 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found written in lines 27-47
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported written in lines 68-95
Objectives	3	State specific objectives, including any prespecified hypotheses written in lines 96-98
Methods		
Study design	4	Present key elements of study design early in the paper written in lines 108-109
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection written in lines 111-115
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up written in lines 111-115 *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable written in lines 118-131, 135-154
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group written in lines 111-113
Bias	9	Describe any efforts to address potential sources of bias written in lines 113-115, 161-162
Study size	10	Explain how the study size was arrived at written in lines 111-113
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why written in lines 158-160
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding written in lines 161-172
		(*b*) Describe any methods used to examine subgroups and interactions We considered it was not readily possible in this study due to the reduced statistical power.
		(*c*) Explain how missing data were addressed written in lines 135-136

		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed not applicable *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses It was not used in this study.

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed written in lines 176-179
		(b) Give reasons for non-participation at each stage written in lines 111-115
		(c) Consider use of a flow diagram shown in Table 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders shown in Table 1
		(b) Indicate number of participants with missing data for each variable of interest shown in Table 1,2,3
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) shown in Table 1
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time shown in Table 2,3
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included shown in Table 4,5
		(*b*) Report category boundaries when continuous variables were categorized written in lines 162-164; and 137-154
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses It was not used in this study.
Discussion		
Key results	18	Summarise key results with reference to study objectives written in lines 222-226
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias written in lines 268-289
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence written in 226-267
Generalisability	21	Discuss the generalisability (external validity) of the study results written in lines 226-231,
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based written in lines 302-303

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.