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ORIGINAL ARTICLE

The effect of the Kasuya CKD network on prevention of the progression of chronic kidney disease: successful collaboration of a public health service, primary care physicians and nephrologists—community based cohort study

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Abstract

Background In 2012, we established a CKD network in collaboration with the public health service, primary care physicians, and nephrologists in the Kasuya area. The aim of this study was to clarify if our CKD network was effective in preventing CKD progression.

Methods 1591 subjects, who had CKD in health checks in 2012 were included in this study. The slope of estimated glomerular filtration rate (eGFR) was compared before and after 2012. Parameters at the first health check visit before 2012, visit in 2012, and the last visit after 2012, were compared. Paired t test, analysis of variance for repeated measurements, and the Friedman test were used for the analysis.

Results Mean age was 65 years. There were 781 men and 810 women. Mean eGFR was 59 ml/min/1.73 m^2. The mean slope of eGFR before 2012 was −1.833 ml/min/1.73 m^2/year and significantly reduced to − 0.297 after 2012. Low-density lipoprotein cholesterol showed a significant serial lowering. Uric acid was significantly elevated in 2012 compared to the first visit and had decreased by the last. The dipstick urinary protein significantly increased in 2012 compared to the first visit and decreased by the last. The number of current smokers showed a significant reduction over time. On the other hand, systolic blood pressure (SBP) and HbA1c significantly elevated at the last visit.

Conclusion The Kasuya CKD network may be effective in preventing CKD progression.

Keywords Chronic kidney disease · Network · Public health · Primary care physicians · Nephrologists · Collaboration

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Introduction

Chronic kidney disease (CKD) is an established risk factor for end stage kidney disease (ESKD), cardiovascular disease (CVD), and all-cause mortality [1, 2]. Based on the annual survey of the Japanese Society for Dialysis Therapy, the number of chronic dialysis patients in Japan continues to increase every year [3]. Therefore, the prevention of CKD progression is an urgent public health priority.

A nationwide screening program of Specific Health Check and Guidance program targeting people 40–74 years of age, was started in April 2008 to facilitate the early detection of high-risk subjects for CKD and CVD. Since CKD remains asymptomatic until a later stage, health checks play an important role in early detection and the start of treatment of CKD to prevent progression.

In 2012, we developed a unique network system for CKD in the collaboration with the public health service, primary care physicians, nephrologists, and urologists in Kasuya area in Fukuoka, Japan. The aim of this study was to clarify if our CKD network was effective in the prevention of progression of CKD.

Method

Evaluated parameters at a specific health check

Height, body weight, body mass index (BMI), and waist circumference, blood pressure (BP), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fast blood sugar, uric acid, creatinine, estimated glomerular filtration rate (eGFR), hemoglobin A1c (HbA1c), urinary protein, urinary occult blood, and urinary sugar, were measured at a health check. eGFR was calculated by the following formula: eGFR (ml/min/1.73m^2) = $194 \times Cr^{-1.094} \times Age^{-0.287}$ (If female $\times 0.739$) [4]. Medications, medical history, and lifestyle such as smoking, walking, exercise, eating habits, drinking, and sleep were evaluated by questionnaires.

The Kasuya CKD network

Six towns (Shingu, Kasuya, Sasaguri, Shime, Sue and Umi) excluding Hisayama town and one city (Koga) were included in the Kasuya CKD network. Hisayama town was excluded, since it has its own health care system in collaboration with Kyushu University since 1961.

The flow of Kasuya CKD network is shown in Fig. 1. Public health service does the health check of the residents, finds the participants with CKD, and recommends them to visit primary care physicians by sending a notification letter. The primary care physicians and nephrologists collaboratively play their own role in managing the participants according to the severity of CKD and order the public nurses to give health guidance to participants, if necessary.

Flow of Kasuya CKD network in 2012

The detailed flow of participants who visited at a health check in 2012 is shown in Fig. 2. Among 41,302 residents aged between 40 and 74 years old, 11,945 (29%) participated in a health check. CKD was diagnosed in 1700 participants (14%), among whom, 1681 were recommended to visit primary care physicians. Out of these 1681 participants, 742 (44%) were taking some medications. The remaining 19 participants were recommended to visit nephrologists immediately. Out of them, 16 (84%) were taking some medications.

Participants included in the present study

Out of 1681 participants who had CKD and were recommended to visit a primary care physician in 2012, 1591 participants with available health check data were included in the study.

Endpoints

Primary endpoint was the change in the slope of eGFR. The slope of eGFR before 2012 (between 2008 and 2012) and after 2012 (between 2013 and 2017) was compared.

Secondary endpoint was the change in the parameters measured at health checks, and the answers to the questionnaires. Each parameter at the first health check visit before 2012, visit in 2012 and the last visit after 2012, were compared. To evaluate the changes in answers to the questionnaires, the answer number was converted to point.

Statistics

The slope of eGFR decline was calculated using the principle of the least-squares methods in a linear regression model. Paired t test was used to compare the slope of eGFR. The parametric data at the three visits were compared using analysis of variance for repeated measurements followed by multiple comparisons by Bonferroni method. Non-parametric data at the 3 visits were compared using the Friedman test followed by paired Wilcoxon test. $P < 0.05$ was estimated as statistically significant. In comparison of non-parametric data between two among three visits, $P < 0.0167$ was estimated as statistically significant.

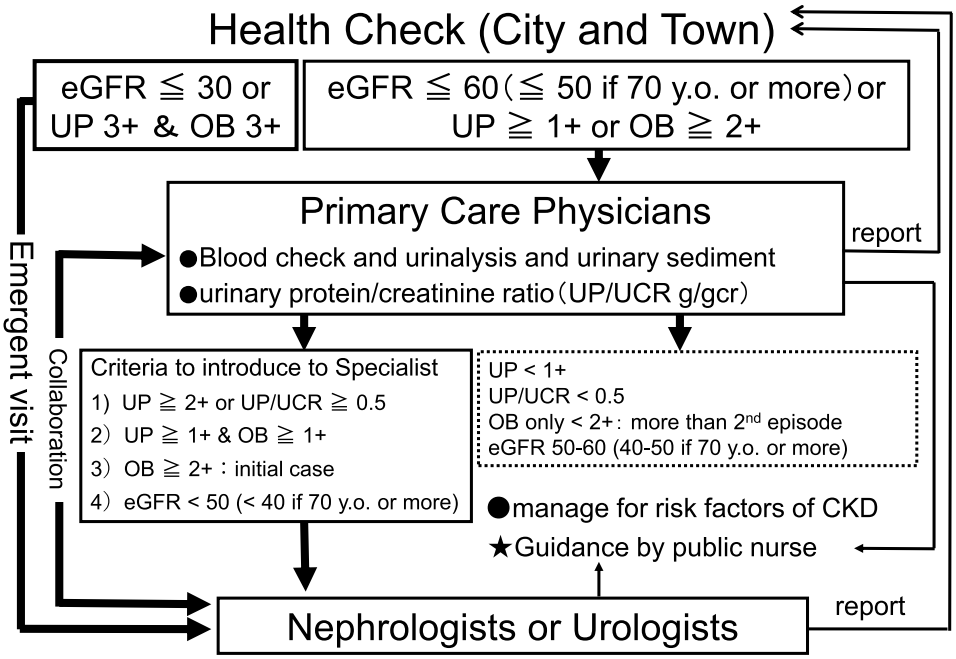

Fig. 1 Kasuya CKD network system. Towns or city do a health check for residents aged from 40 to 74. If eGFR is less than 30 ml/min/1.73m^2, or both urinary protein and occult blood is 3+, participant are recommended by the public health service to visit a nephrologist immediately by sending a notification letter with a list of nephrologists to visit. If eGFR is between 30 and 60 ml/min/1.73m^2 or urinary protein 1+ or more, or urinary occult blood 2+or more, the participants are recommended to visit their Primary Care Physicians by sending a notification letter with a list of primary care physicians to visit. Primary Care Physicians should re-check the blood and urine. If urinary protein 2+or more, or urinary protein-creatinine ratio (UP/UCR) 0.5 or more, or both urinary protein and occult blood 1+or more, or eGFR is less than 50 ml/min/1.73m^2 (less than 40 in participants 70 years old or elder), the participants are recommended by their primary care physicians to visit a nephrologist. If the urinary occult blood is 2+or more for the first time, the participants are recommended to visit a urologist. Primary Care Physicians take care of the rest of the participants to control the risk factors of CKD and/or their lifestyle. Primary Care Physicians or nephrologists or urologists should inform the public health office how to manage and treat the participants and can order the public nurses to give health guidance to residents, if necessary. *eGFR* estimated glomerular filtration rate, *UP* urinary protein, *OB* urinary occult blood, *UP/UCR* urinary protein-creatinine ratio, *y.o.* years old

Results

Clinical characteristics at a health check in 2012

Clinical characteristics in 2012 are shown in Table 1. Mean age was 65 years old. There were 781 men and 810 women. Mean systolic and diastolic BP were 126 and 75 mmHg, respectively. Mean LDL-C was 126 mg/dl. Mean uric acid was 5.8 mg/dl. Mean eGFR was 59.0 ml/min/1.73m^2. The percentage of participants with CKD Stage 1, 2, 3a, 3b, 4 and 5 was 3.2, 26.1, 62.0, 8.0, 0.6, and 0.1, respectively. Urinary protein was negative in 74.4% of participants. Urinary occult blood was negative in 66.2%. Urine sugar was negative in 97.9% of participants. Clinical characteristics in 2012 in each gender are shown in Supplemental Table 1. All parameters showed gender differences.

Answers to questionnaires at a health check in 2012

The answers to questionnaires at a health check in 2012 are shown in Table 2. The percentage of participants who were taking antihypertension, antihyperglycemic, and cholesterol reducing medicines were 35, 8, and 22, respectively. Participants who were diagnosed as CKD previously were only 1%. The current smokers were 15%. Around 50% of participants had a habit of exercise or walking. The percentage of participants with bad eating habits such as late dinner, eating snack after dinner, or missing breakfast was 14, 10 and 10, respectively. Fifty- three percent of participants had no drinking habits and 73% of participants could sleep well. The percentage of participants who intend to improve their lifestyle was 72 and 49% of participants wanted to use health guidance services.

Changes in the slope of eGFR before and after 2012

The slope of eGFR before 2012 and after 2012 is shown in Table 3. The mean slope of eGFR before 2012 was − 1.833 ml/min/1.73m^2/years and was significantly reduced to − 0.297 after 2012. In the participants with CKD stage G2, G3a and G3b in 2012, the slope of eGFR before 2012 was − 1.569, − 2.016 and − 2.877, and significantly

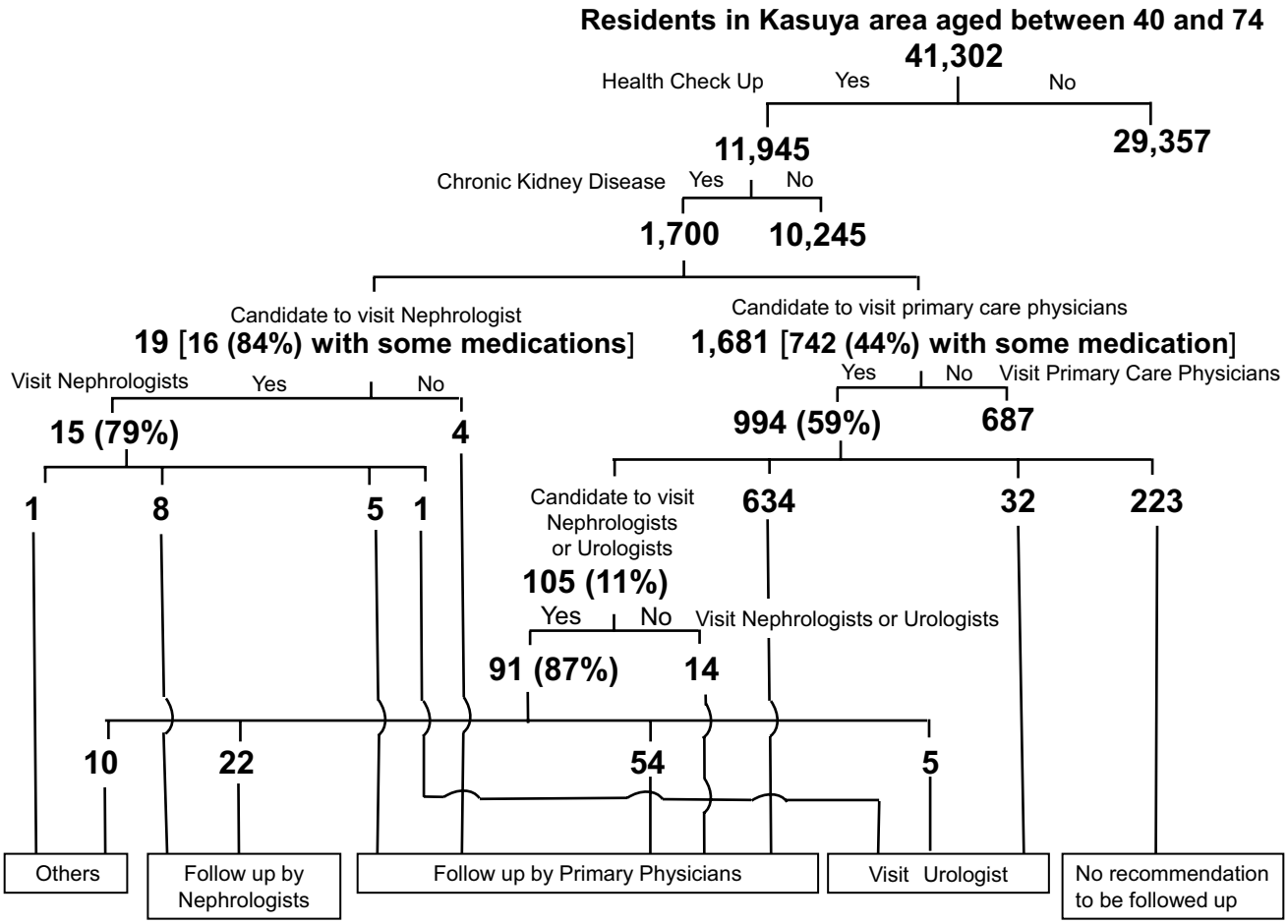

Fig. 2 A detailed flow of participants who visited a health check in 2012. Among 41,302 residents aged between 40 and 74 years old in the Kasuya area, 11,945 (29%) participated a health check. CKD was diagnosed in 1700 participants (14%), among whom, 1681 participants were recommended to visit their primary care physicians. Out of these 1681 participants, 742 (44%) were taking some medications. And out of them, 994 participants (59%) visited their primary care physicians, 105 participants were candidate for visiting nephrologists, and 91 participants (87%) visited a nephrologist. The 19 participants, out of whom, 16 (84%) were taking some medications, were recommended to visit a nephrologist immediately. Out of 19, 15 participants (79%) complied

decreased to − 0.272, − 0.122 and − 0.957 after 2012, respectively. In the participants with CKD stage G 4 or 5, the slope of eGFR before 2012 was − 2.773 and reduced to − 1.700 ml/min/1.73m^2/year after 2012. However, there was no significant difference. The number of data was only 4 in this group. In the participants with CKD Stage G1 in 2012, the slope of eGFR had significantly worsened from 2.368 before 2012 to − 2.226 ml/min/1.73m^2/year after 2012.

The slope of eGFR was compared according to visiting primary care physicians in 2012 or not. The slope of eGFR after 2012 was significantly slower than those after 2012 irrespective of visiting to primary care physicians in 2012. The slope of eGFR before and after 2012 was compared according to using health guidance after visiting primary care physicians in 2012 or not. Although the slope of eGFR after 2012 was significantly slower than those before 2012 irrespective of utility of health guidance, the slope of eGFR after 2012 was almost zero in the participants who used health guidance.

Changes in the parameters measured at health checks

The parameters at the first visit, in 2012, and the last visit, are shown in Table 4. Systolic BP significantly lowered in 2012 compared to the first visit but it was significantly elevated at the last. Diastolic BP lowered significantly in 2012 and at the last visit compared to the first. TG significantly decreased in 2012 and the last visit compared to the first. HDL-C was significantly elevated at the last visit compared to the first. LDL-C showed significant and serial lowering from the first visit to the last. HbA1c was significantly elevated at the last visit compared to the first and in 2012. Uric acid was significantly elevated in 2012 compared to the first

Table 1 Clinical characteristics in 2012

	Number of data	Mean		SD
Age, years old	1591	65	±	7
Men (%)	781	(49)		
Height (cm)	1591	159.6	±	8.2
Body weight (Kg)	1591	58.9	±	10.9
BMI (Kg/m^2)	1591	23.0	±	3.4
Waist circumference (cm)	1590	84.2	±	9.1
SBP (mmHg)	1591	126	±	17
DBP (mmHg)	1591	75	±	11
TG (mg/dl)	1591	117	±	71
HDL-C (mg/dl)	1591	62	±	17
LDL-C (mg/dl)	1591	126	±	33
FBS (mg/dl)	1534	99	±	20
HbA1c (%)	1589	5.4	±	0.7
Uric acid (mg/dl)	1591	5.8	±	1.5
Cr (mg/dl)	1591	0.91	±	0.23
eGFR (ml/min/1.73m^2)	1591	59.0	±	13.7
CKD Stage 1 / 2 / 3a / 3b / 4 / 5 (%)	1591	3.2 / 26.1 / 62.0 / 8.0 / 0.6 /0.1		
Urinary protein −/±/ 1 +/ 2 +/ 3 +(%)	1591	74.4 / 4.3 / 16.4 / 4.0 / 0.9		
Urinary occult blood −/±/ 1 +/ 2 +/ 3 +(%)	1591	66.2 / 6.5 / 5.6 / 15.8 / 5.8		
Urine sugar −/±/ 1 +/ 2 +/ 3 +(%)	1591	97.9 / 0.3 / 0.8 / 0.4 / 0.6		
Visit primary care physicians (%)	909	57.1		
Received special health guidance service after visiting primary care physician (%)	141	15.5		

SD standard deviation, BMI body mass index, SBP systolic blood pressure, DBP diastolic blood pressure, TG triglyceride, HDL-C high density lipoprotein cholesterol, LDL-C low density lipoprotein cholesterol, FBS fast blood sugar, HbA1c hemoglobin A1c, Cr serum creatinine, eGFR estimated glomerular filtration ratio, CKD chronic kidney disease

visit and it decreased at the last. Urinary protein and occult blood significantly increased in 2012 compared to the first visit and significantly decreased at the last visit compared to the first and 2012. Urine sugar significantly increased at the last visit compared to 2012. BMI, waist circumference and fast blood sugar did not show any significant changes.

Changes in the answers to the questionnaires

The answers to the questionnaires at the first visit, in 2012, and the last visit are shown in Table 5. The participants who are taking antihypertensive medicines, antihyperglycemic medicine, and cholesterol reducing medicine significantly and sequentially increased from the first visit to the last. A history of stroke showed a significant serial increase. The participants who were informed they had CKD significantly increased in 2012 and at the last visit compared to the first. Habitual current smokers significantly and sequentially decreased from the first visit to the last. 10 kg or more weight gain compared to 20 years old, significantly decreased at the last visit compared to the first. Habitual exercise significantly increased at the last visit compared to the first. Walking for 1 h or more a day, significantly increased in 2012 and at the last visit compared to the first. Fast walking significantly increased in 2012 and at the last visit compared to the first. A weight gain/loss of 3 kg or more in the past year, significantly decreased in 2012 and at the last visit compared to the first. Fast eating increased in 2012 compared to the first visit. Eating snacks after dinner significantly decreased in 2012 and at the last visit compared to the first. A late dinner or missing breakfast did not change. Drinking frequency did not change. The quantity of alcohol intake significantly decreased. The quality of sleep and the intention to improve the lifestyle did not change. The participants, who want to utilize health guidance, significantly decreased.

Discussion

In the present study, we found the slope of eGFR significantly decreased after the establishment of the CKD network (2013–2017), compared to before (2008 and 2012). These

Table 2 Answers to questionnaires at a health check in 2012

Question number	Questionnaire	Total		n	(%)
1–3	Are you taking the following medicines at present?				
1	Antihypertensive medicines	1591	1. Yes	564	(35)
2	Insulin injection or antihyperglycemic medicines	1591	1. Yes	127	(8)
3	Cholesterol reducing medicines	1591	1. Yes	354	(22)
4	Have you been told by a physician that you have suffered a stroke* or have you ever received treatment for stroke?	1559	1. Yes	68	(4)
5	Have you been told by a physician that you suffer from heart diseases**or have you ever received treatment for heart diseases?	1559	1. Yes	135	(9)
6	Have you been told by a physician that you suffer from chronic kidney disease or kidney failure or have you ever received treatment for chronic renal failure (dialysis)?	1559	1. Yes	21	(1)
7	Have you been told by a physician that you suffer from anemia?	1559	1. Yes	160	(10)
8	Are you currently a habitual smoker? ***	1591	1. Yes	242	(15)
9	Has your body weight increased by 10 kg or more since the age of 20 years?	1394	1. Yes	524	(38)
10	Have you performed exercise with slight sweating for 30 min or more, at least twice a week, for more than one year?	1392	1. Yes	649	(47)
11	Do you walk, or engage in some physical exercise equivalent to walking, for one hour or more a day?	1394	1. Yes	678	(49)
12	Do you walk faster than people who are of nearly the same age and the same sex as you?	1394	1. Yes	727	(52)
13	Did you experience a weight gain/loss of 3 kg or more in the past year?	1393	1. Yes	288	(21)
14	Do you eat faster than others?	1395	1. Fast	410	(29)
			2. Normal	877	(63)
			3. Slow	108	(8)
15	Do you eat dinner within 2 h before sleep at least three times a week?	1395	1. Yes	196	(14)
16	Do you eat any snacks after dinner (a bedtime snack, other than three regular meals) three times or more a week?	1395	1. Yes	133	(10)
17	Do you miss breakfast three times or more a week?	1394	1. Yes	143	(10)
18	How often do you drink alcoholic beverages**** ?	1590	1. Everyday	400	(25)
			2. Sometimes	349	(22)
			3. Rarely drink(cannnot drink)	841	(53)
19	How much sake do you drink a day?*****	894	1. Less than 180 ml	565	(63)
			2. 180-360 ml	211	(24)
			3. 360-540 ml	98	(11)
			4. More than 540 ml	20	(2)
20	Do you sleep well and get a sufficient amount of rest?	1395	1. Yes	1020	(73)

Table 2 (continued)

Question number	Questionnaire	Total		n	(%)
21	Do you intend to improve your lifestyle, including fitness and dietary habits?	1387	1. I do not intend to improve them	387	(28)
			2. I intend to improve them (within about 6 months)	411	(30)
			3. I intend to improve them soon (within about one month). I have already started doing so	125	(9)
			4. I have already attempted to improve them (for less than 6 months)	139	(10)
			5. I have already attempted to improve them (for more than 6 months)	325	(23)
22	Do you utilize health guidance services to improve your lifestyle, if available?	1584	1. Yes	777	(49)

Total: total number of respondents to corresponding questionnaire

n: number of respondents who selected corresponding answer

*: cerebral hemorrhage, cerebral infarction, etc.

**: angina pectoris, myocardial infarction, etc.

***: "A current habitual smoker" is defined as a person who has smoked a total of 100 cigarettes or more, or has a history of smoking for more than 6 months, and has been smoking for the past one month

****: sake, distilled spirit, beer, whiskey, wine, etc.

*****: Alcohol content equivalent to a small bottle of sake (180 ml): an average sized bottle of beer (about 500 ml), a glass of distilled spirit (35 proof liquor, 80 ml), a glass of whiskey (60 ml), two glasses of wine (240 ml)

Table 3 Changes in the slope of eGFR before and after 2012

	Number of pairs	eGFR Slope between 2008 and 2012 (ml/min/1.73m^2/year)		eGFR Slope between 2013 and 2017 (ml/min/1.73m^2/year)		Difference in paired sample				*t* value	*p* value
		Mean	SD	Mean	SD	Mean	SD	95% confidence interval			
								Lower limit	Upper limit		
Total	979	− 1.833	4.027	− 0.297	3.017	− 1.536	5.118	− 1.857	− 1.215	− 9.393	0.000
CKD Stage in 2012											
1	32	2.368	8.764	− 2.226	6.880	4.594	10.506	0.806	8.381	2.473	0.019
2	237	− 1.569	4.886	− 0.272	3.495	− 1.297	5.995	− 2.065	− 0.530	− 3.331	0.001
3a	632	− 2.016	3.128	− 0.122	2.466	− 1.894	4.186	− 2.221	− 1.567	− 11.377	0.000
3b	74	− 2.877	3.546	− 0.957	2.705	− 1.920	4.163	− 2.884	− 0.955	− 3.966	0.000
4 or 5	4	− 2.773	4.772	− 1.700	1.158	− 1.073	5.151	− 9.269	7.123	− 0.417	0.705
Visit primary care physicians in 2012											
Yes	585	− 1.849	4.093	− 0.247	3.163	− 1.602	5.298	− 2.032	− 1.172	− 7.312	0.000
No	394	− 1.809	3.931	− 0.370	2.789	− 1.439	4.842	− 1.919	− 0.959	− 5.899	0.000
Receive special health guidance service in 2012 after visiting primary care physicians											
Yes	89	− 2.046	3.643	0.073	2.633	− 2.119	4.925	− 3.157	− 1.082	− 4.060	0.000
No	496	− 1.813	4.170	− 0.304	3.248	− 1.509	5.362	− 1.982	− 1.036	− 6.268	0.000

SD standard deviation

results may suggest that the CKD network system in Kasuya area successfully prevented the progression of CKD. There have been several reports concerning the effect of community-based CKD screening and prevention programs in various community settings [5–7]. The design of these studies was a control study, comparing CKD progression

Table 4 Changes in the parameters at the first visit before 2012, visit in 2012, and the last health check visit after

	Number of data	First Visit			2012			Last Visit			*p*
		mean		SD	mean		SD	mean		SD	
BMI (Kg/m^2)	1105	**23.0**	±	3.4	**22.9**	±	3.4	**22.9**	±	3.4	0.178
Waist circumference (cm)	1104	**84.0**	±	9.2	**84.0**	±	9.0	**84.2**	±	9.3	0.406
SBP (mmHg)	1105	**128**[b,c]	±	19	**125**[a,c]	±	17	**129**[a,b]	±	18	0.000
DBP (mmHg)	1105	**77**[b,c]	±	11	**75**[a]	±	11	**75**[a]	±	11	0.000
TG (mg/dl)	1104	**122**[b,c]	±	82	**114**[a]	±	66	**114**[a]	±	65	0.000
HDL-C (mg/dl)	1103	**61**[c]	±	16	**62**	±	16	**62**[a]	±	17	0.001
LDL-C (mg/dl)	1103	**128**[c]	±	31	**126**[c]	±	33	**120**[a,b]	±	31	0.000
FBS (mg/dl)	972	**99**	±	19	**98**	±	19	**99**	±	18	0.551
HbA1c (%)	1065	**5.4**[c]	±	0.8	**5.4**[c]	±	0.7	**5.8**[a,b]	±	0.6	0.000
Uric acid (mg/dl)	1098	**5.6**[b]	±	1.4	**5.8**[a,c]	±	1.4	**5.7**[b]	±	1.3	0.000
Urinary protein (0–3)	1103	**0.206**[b,c]	±	0.514	**0.267**[a,c]	±	0.539	**0.135**[a,b]	±	0.420	0.000
Urinary occult blood (0–3)	1041	**0.455**[b,c]	±	0.809	**0.568**[a,c]	±	0.928	**0.218**[a,b]	±	0.563	0.000
Urine sugar (0–3)	1103	**0.031**	±	0.267	**0.027**[c]	±	0.226	**0.056**[b]	±	0.356	0.005

SD standard deviation, *BMI* body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *TG* triglyceride, *HDL-C* high density lipoprotein cholesterol, *LDL-C* low density lipoprotein cholesterol, *FBS* fast blood sugar, *Hb* hemoglobin

[a]Significantly differ compared to the first visit

[b]Significantly differ compared to visit in 2012

[c]Significantly differ compared to the last visit

As for the comparisons of urinary findings between two points among three points, $p < 0.0167$ was defined to be statistically significant

between the participants with a various special intervention and those with usual care, and the delaying of the progression of CKD by special intervention was evident. In our study, we established the network for CKD in collaboration with the public health service, primary care physicians, and nephrologists, in which members of each part played their own role very well. We clearly demonstrated that if the network works functionally, CKD progression can be prevented successfully.

The frequencies of health checkup were various among the participants and might have an influence on the slope of eGFR. Thus, we compared the slope of eGFR before and after 2012 according to the frequencies of health checkup as shown in the Supplemental Table 2. The slope of eGFR after 2012 significantly reduced compared to those before 2012 in most combinations of the frequencies of health checkup, although the pairs in some combinations did not show any significant difference probably due to the small number of the data. Kakio et al. reported a prospective study concerning an effect of health checkup system for CKD and found that the improvement of CKD stage was found regardless of the frequency of receiving health checkup [8]. They concluded that receiving a health checkup itself and notification of one's own health condition could exert a protective effect on kidney function. Their data were compatible with our results. In addition to the effect of network, receiving a health checkup itself might have some effect on slowing eGFR slope.

In the present study, the slope of eGFR significantly decreased after 2012 irrespective of visiting primary care physicians in 2012. There should be some reasons for this result. First, some of the participants who did not visit primary care physicians in 2012 might visit them after 2012 because the network continued to recommend the participants with CKD visiting primary care physicians every year. Second, the recommendation to visit primary care physicians itself might increase the participant's health awareness and might have some effect on slowing of eGFR slope.

In the present study, the slope of eGFR significantly reduced after 2012 irrespective of receiving special health guidance in 2012. There might be several reasons of this result. First, the participant who did not receive special health guidance visited primary care physicians in 2012. Thus, they were managed by the physicians even though they did not receive health guidance. Second, the participants who did not receive special health guidance in 2012 might receive it after 2012. Unfortunately, data on health guidance visits after 2012 were not available, so this possibility was not evident. Since the slope of eGFR after 2012 was nearly zero in the participants who received health guidance in 2012, we felt that there might be some effect of health guidance on slowing eGFR slope. However, the definite evidence

Table 5 Changes in the answers to the questionnaires at the first visit before 2012, visit in 2012, and the last health check visit after 2012

Question number	Questionnaire		n	First Visit	2012	Last Visit	P for among 3 visits
1–3	Are you taking the following medicines at present?						
1	Antihypertensive medicines	1. Yes (%)	1105	27.5	35.4	43.3	
		(Mean point of answer number ± SD)		**1.72**[b,c] ± 0.45	**1.65**[a,c] ± 0.48	**1.57**[a,b] ± 0.50	0.000
2	Insulin injection or antihyperglycemic medicines	1. Yes (%)	1105	5.3	7.5	8.9	
		(Mean point of answer number ± SD)		**1.95**[b,c] ± 0.23	**1.92**[a,c] ± 0.26	**1.91**[a,b] ± 0.28	0.000
3	Cholesterol reducing medicines	1. Yes (%)	1105	14.8	22.9	29.3	
		(Mean point of answer number ± SD)		**1.85**[b,c] ± 0.36	**1.77**[a,c] ± 0.42	**1.71**[a,b] ± 0.46	0.000
4	Have you been told by a physician that you have suffered a stroke* or have you ever received treatment for stroke?	1. Yes (%)	1039	3.1	4.2	5.7	
		(Mean point of answer number ± SD)		**1.97**[b,c] ± 0.17	**1.96**[a,c] ± 0.20	**1.94**[a,b] ± 0.23	0.000
5	Have you been told by a physician that you suffer from heart diseases**or have you ever received treatment for heart diseases?	1. Yes (%)	1040	7.4	7.1	7.9	
		(Mean point of answer number ± SD)		**1.93** ± 0.26	**1.93** ± 0.26	**1.92** ± 0.27	0.562
6	Have you been told by a physician that you suffer from chronic kidney disease or kidney failure or have you ever received treatment for chronic renal failure (dialysis)?	1. Yes (%)	1039	0.3	1.6	2.0	
		(Mean point of answer number ± SD)		**2.00**[b,c] ± 0.05	**1.98**[a] ± 0.13	**1.98**[a] ± 0.14	0.000
7	Have you been told by a physician that you suffer from anemia?	1. Yes (%)	945	10.7	10.5	10.8	
		(Mean point of answer number ± SD)		**1.89** ± 0.31	**1.90** ± 0.31	**1.89** ± 0.31	0.932
8	Are you currently a habitual smoker? ***	1. Yes (%)	1105	16.5	13.9	10.7	
		(Mean point of answer number ± SD)		**1.84**[b,c] ± 0.37	**1.86**[a,c] ± 0.35	**1.89**[a,b] ± 0.31	0.000
9	Has your body weight increased by 10 kg or more since the age of 20 years?	1. Yes (%)	866	37.8	36.7	33.6	
		(Mean point of answer number ± SD)		**1.62**[c] ± 0.49	**1.63** ± 0.48	**1.66**[a] ± 0.47	0.010
10	Have you performed exercise with slight sweating for 30 min or more, at least twice a week, for more than one year?	1. Yes (%)	851	45.5	48.8	52.5	
		(Mean point of answer number ± SD)		**1.55**[c] ± 0.50	**1.51** ± 0.50	**1.47**[a] ± 0.50	0.000
11	Do you walk, or engage in some physical exercise equivalent to walking, for one hour or more a day?	1. Yes (%)	850	46.7	51.6	53.8	
		(Mean point of answer number ± SD)		**1.53**[b,c] ± 0.50	**1.48**[a] ± 0.50	**1.46**[a] ± 0.50	0.001
12	Do you walk faster than people who are of nearly the same age and the same sex as you?	1. Yes (%)	846	50.5	54.4	55.4	
		(Mean point of answer number ± SD)		**1.50**[b,c] ± 0.50	**1.46**[a] ± 0.50	**1.45**[a] ± 0.50	0.007
13	Did you experience a weight gain/loss of 3 kg or more in the past year?	1. Yes (%)	849	26.4	20.3	18.3	
		(Mean point of answer number ± SD)		**1.74**[b,c] ± 0.44	**1.80**[a] ± 0.40	**1.82**[a] ± 0.39	0.000
14	Do you eat faster than others?	1. Fast (%)	850	26.6	28.5	27.9	
		2. Normal (%)		65.1	65.6	64.6	
		3. Slow (%)		8.4	5.9	7.5	
		(Mean point of answer number ± SD)		**1.82**[b] ± 0.56	**1.78**[a] ± 0.54	**1.80** ± 0.56	0.033
15	Do you eat dinner within 2 h before sleep at least three times a week?	1. Yes (%)	851	14.9	14.1	15.0	
		(Mean point of answer number ± SD)		**1.85** ± 0.36	**1.86** ± 0.35	**1.85** ± 0.36	0.726
16	Do you eat any snacks after dinner (a bedtime snack, other than three regular meals) three times or more a week?	1. Yes (%)	822	13.1	9.4	9.6	
		(Mean point of answer number ± SD)		**1.87**[b,c] ± 0.34	**1.91**[a] ± 0.29	**1.90**[a] ± 0.30	0.002

Table 5 (continued)

Question number	Questionnaire		n	First Visit	2012	Last Visit	P for among 3 visits
17	Do you miss breakfast three times or more a week?	1. Yes (%)	850	10.0	9.6	9.5	
		(Mean point of answer number ± SD)		**1.90** ± 0.30	**1.90** ± 0.30	**1.90** ± 0.29	0.884
18	How often do you drink alcoholic beverages**** ?	1. Everyday (%)	954	25.6	23.9	24.3	
		2. Sometimes (%)		20.5	23.2	23.2	
		3. Rarely drink (cannot drink) (%)		53.9	52.9	52.5	
		(Mean point of answer number ± SD)		**2.28** ± 0.85	**2.29** ± 0.83	**2.28** ± 0.83	0.718
19	How much sake do you drink a day?*****	1. Less than 180 ml (%)	443	53.2	57.0	62.0	
		2. 180-360 ml (%)		30.3	29.0	28.5	
		3. 360-540 ml (%)		11.5	11.1	7.5	
		4. More than 540 ml (%)		5.0	2.9	2.0	
		(Mean point of answer number ± SD)		**1.68**[b,c] ± 0.86	**1.60**[a,c] ± 0.80	**1.50**[a,b] ± 0.72	0.000
20	Do you sleep well and get a sufficient amount of rest?	1. Yes (%)	850	76.8	74.3	75.7	
		(Mean point of answer number ± SD)		**1.24** ± 0.42	**1.26** ± 0.44	**1.25** ± 0.43	0.302
21	Do you intend to improve your lifestyle, including fitness and dietary habits?	1. I do not intend to improve them. (%)	846	25.5	28.0	28.6	
		2. I intend to improve them (within about 6 months). (%)		32.3	28.5	30.0	
		3. I intend to improve them soon (within about one month). I have already started doing so. (%)		13.8	8.3	9.8	
		4. I have already attempted to improve them (for less than 6 months). (%)		9.3	9.6	6.9	
		5. I have already attempted to improve them (for more than 6 months). (%)		19.0	25.7	24.7	
		(Mean point of answer number ± SD)		**2.64** ± 1.44	**2.76** ± 1.57	**2.69** ± 1.55	0.741
22	Do you utilize health guidance services to improve your lifestyle, if available?	1. Yes (%)	957	60.2	48.1	40.2	
		(Mean point of answer number ± SD)		**1.40**[b,c] ± 0.49	**1.52**[a,c] ± 0.50	**1.60**[a,b] ± 0.49	0.000

The answer number of questionnaire is converted to the point

n: number of respondents to corresponding questionnaire

SD standard deviation

*: cerebral hemorrhage, cerebral infarction, etc.

**: angina pectoris, myocardial infarction, etc.

***: "A current habitual smoker" is defined as a person who has smoked a total of 100 cigarettes or more, or has a history of smoking for more than 6 months, and has been smoking for the past one month

****: sake, distilled spirit, beer, whiskey, wine, etc.

*****: Alcohol content equivalent to a small bottle of sake (180 ml): an average sized bottle of beer (about 500 ml), a glass of distilled spirit (35 proof liquor, 80 ml), a glass of whiskey (60 ml), two glasses of wine (240 ml)

[a]Significantly differ compared to the first visit; $p < 0.0167$

[b]Significantly differ compared to visit in 2012; $p < 0.0167$

[c]Significantly differ compared to the last visit; $p < 0.0167$

of the effectiveness of health guidance was not found in the present study.

In the present study, LDL-C showed significant lowering from the first to the last visit. The positive relationship between LDL-C and the progression of CKD has been reported in several studies [9, 10]. The significant decrease in the slope of eGFR after 2012 in our study might be due to, at least partly, significant decrease in LDL-C.

In the present study, urinary protein significantly increased in 2012 compared to the first visit, and significantly decreased at the last. The impact of urinary protein on the progression of CKD in the general population has been reported [11, 12]. A significant decrease of proteinuria at the last visit compared to 2012 might associated with the significant slowing of eGFR slope after 2012 in our study.

We found the significant improvement of lifestyle such as decreased current habitual smoker, less body weight fluctuation, increment of exercise habits, decrease of alcohol intake, and decrease of taking snack after dinner. Currently smoking has been reported as a risk in new development of proteinuria [13], or CKD [14], or a risk of rapid decline of eGFR [13]. Wakasugi et al. reported an association between the changes in overall lifestyle, including the smoking status, BMI, physical activity, alcohol consumption, and healthy eating habits, and the incidence of proteinuria in population-based retrospective study [15]. The improvement of lifestyle found in our study might contribute a significant reduction of proteinuria and eGFR slope. Decreased alcohol intake might relate to the reduction of uric acid.

In our study, HbA1c significantly increased at the last visit compared to the first and 2012. Diabetic kidney disease (DKD) was the top cause of ESKD in Japan [3]. To clarify the relation between glucose intolerance and CKD progression, we analyzed the changes in eGFR slope before and after 2012 according to the presence or absence of glucose intolerance in 2012 as shown in Supplemental Table 3. Glucose intolerance was defined as HbA1c 6% or more or taking antihyperglycemic medicine. The participants with glucose intolerance were further divided into two groups: with/without antihyperglycemic medicine. Participants with antihyperglycemic medicine did not show any change in HbA1c and those without medicine showed a significant increase in HbA1c. Although the eGFR slope showed a significant decrease after 2012 in the participants without glucose intolerance, the improvement of eGFR slope was not significant in those with glucose intolerance. Surprisingly, the eGFR slope deteriorated in the participants with glucose intolerance without medicine, although the difference was not significant. These data suggest that glucose intolerance is a strong risk factor for the progression of CKD. We should strengthen the management for glucose intolerance in our area. We are planning to establish the collaborative network for CKD and DKD from April in 2022.

In the present study, SBP significantly decreased in 2012 compared to the 1st visit but significantly increased at the last compared to the first visit and 2012. Hypertension is recognized as a strong predictor for the progression of CKD. Several community-based studies concerning the association of BP and incidence of CKD [16], or progression of CKD [17] have been reported. To clarify the relation of BP to eGFR slope, we analyzed changes in eGFR slope before and after 2012 according to the presence or absence of hypertension in 2012 as shown in Supplemental Table 4. Hypertension was defined SBP 140 mmHg or more or taking antihypertension medicines. The participants with hypertension were divided into two groups: with/without medicines. In all groups, SBP decreased in 2012 and elevated at the last visit. The eGFR slope significantly decreased after 2012 in all groups. The slope of eGFR both before and after 2012 was lower in the participants without hypertension in 2012 than in those with hypertension. These data suggest that hypertension is a risk factor for the progression of CKD. Strict BP control may be a problem to be solved in our area.

The participants who were informed that they had CKD was only 2% at the last visit, although they increased compared to the first. We should strengthen the enlightenment of CKD in general population.

The slope of eGFR significantly deteriorated after 2012 in the participants in CKD stage G1 in 2012. To clarify the reason of this unexpected result, we analyzed the clinical characteristics, and their lifestyle in this group as shown in the Supplemental Tables 5 to 8. The characteristics of this group included less percentage of men, high degree of urinary protein and occult blood, less percentage of visiting primary care physicians, high percentage of current smoker, less habitual exercise, high bad eating habit, high alcohol intake, and less good sleep. LDL-C was unchanged, and current smoker did not decrease. These data suggest that bad lifestyles with no improvement might be the reason why the eGFR slope deteriorated in this group. The education concerning their lifestyle should be strengthened even in the participants with CKD Stage G1.

We have several limitations in the present study. Firstly, we included the participants who were diagnosed as CKD in 2012 only. There is a possibility of misclassification of eligible patients due to a diagnosis at a single point. Secondly, in the analyses of eGFR slope, according to the visit primary care physicians, or utility of a health guidance, we stratified the participants only based on the data in 2012. Thus, some participants who did not visit the primary care physician in 2012 may have visited them afterwards. The same situation could occur concerning the utility of health guidance.

In conclusion, a significant decrease in the slope of eGFR after the establishment of the CKD network in the present

study suggested that the Kasuya CKD network is effective in prevention of the progression of CKD. A significant decrease in LDL-C, and the improvement of bad lifestyle after the establishment of the CKD network might contribute to the slower decline of eGFR. The collaboration of public health service, primary care physicians and nephrologists played the key role in the successful results.

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Declarations

Conflict of interest The authors have declared that no conflict of interest exists.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee at National Hospital Organization Fukuoka-higashi Medical Center (IRB approval number 29-2-2) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent We made public information concerning this study on the web (http://fukuokae.hosp.go.jp) and ensured the opportunities for the research subjects to refuse utilizing their personal information.

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