الأطفال مضادات حيوية بدون وصفات طبية (نسبة الأرجحية: 0.7؛ فاصلة الثقة 95%: 0.6 – 0.8).

الاستنتاج كان معدل انتشار استخدام المضادات الحيوية لصغار الأطفال بدون وصفات طبية عالياً في آولان باتار. ونظراً لأن هذا يؤدي إلى اتساع نطاق مقاومة البكتريا للمضادات الحيوية والمشاكل الصحية ذات الصلة، فإن نتائج هذه الدراسة لها آثار مهمة لتوعية العامة وتعزيز نظم بيع المضادات الحيوية في منغوليا.

Resumé

Enquête sur l'utilisation d'antibiotiques non prescrits chez les enfants d'une communauté urbaine de Mongolie

Objectif Estimer la prévalence et identifier les déterminants de l'utilisation sans prescription d'antibiotiques chez les enfants en Mongolie.

Méthodes Une étude communautaire transversale a été menée dans 10 sous-districts d'Oulan Bator, la capitale de la Mongolie. Nous avons utilisé un questionnaire structuré pour collecter des données à partir d'un échantillon aléatoire de 540 ménages comptant au moins un enfant âgé de moins de 5 ans. La régression logistique a été utilisée pour identifier les facteurs associés à l'usage abusif d'antibiotiques.

Résultats Sur 503 adultes référents ayant pris part à cette enquête, 71% étaient des mères; 42,3% (intervalle de confiance de 95%, IC: 37,8–46,9) des soignants avaient utilisé des antibiotiques non prescrits pour traiter les symptômes de leur enfant au cours des 6 mois précédents. Les symptômes fréquemment soignés étaient la toux (84%), la fièvre (66%), l'écoulement nasal (65%) et le mal de gorge (60%). L'amoxicilline était l'antibiotique le plus communément utilisé (58%). Les pharmacies étaient la principale source (86%) d'approvisionnement des antibiotiques non prescrits. L'administration d'antibiotiques sans ordonnance par les mères de famille était largement associée au fait que ces médicaments étaient conservés à domicile (rapport des cotes, RC: 1,7; IC de 95%: 1,04–2,79), à l'automédication par les soignants (RC: 6,3; IC de 95%: 3,8–10,5) et à l'âge plus élevé de l'enfant (RC: 1,02; IC de 95%: 1,01–1,04). Les adultes référents avec une meilleure connaissance des antibiotiques avaient moins tendance à administrer des antibiotiques non prescrits à leurs enfants (CR: 0,7; IC de 95%: 0,6–0,8).

Conclusion La prévalence de l'utilisation d'antibiotiques non prescrits chez les jeunes enfants était élevée à Oulan Bator. Cet usage abusif entraînant une augmentation de la résistance bactérienne aux antibiotiques, ainsi que des problèmes de santé connexes, nos résultats ont des implications importantes pour l'information du grand public et l'application de réglementations en matière de vente des antibiotiques en Mongolie.

Resumen

Estudio sobre el uso de antibióticos de venta sin receta en los niños en una comunidad urbana de Mongolia

Objetivo Calcular la prevalencia e identificar los factores determinantes para la prescripción de antibióticos de venta sin receta para niños en Mongolia.

Métodos Se realizó un estudio transversal de la comunidad en 10 subdistritos de Ulaanbaatar, la capital de Mongolia. Un cuestionario estructurado nos permitió recopilar los datos de una muestra aleatoria de 540 hogares, con al menos un niño menor de 5 años. Para identificar los factores asociados a la mala utilización de los antibióticos se empleó la regresión logística.

Resultados De los 503 cuidadores participantes, el 71% eran madres; el 42,3% (intervalo de confianza del 95%, IC: 37,8-46,9) de los cuidadores había utilizado antibióticos sin receta en los últimos 6 meses para tratar los síntomas de sus hijos. Los síntomas tratados más habituales fueron: tos (84%), fiebre (66%), mucosidad nasal (65%) y dolor de garganta (60%). El antibiótico más utilizado (58%) fue la amoxicilina. Los antibióticos de venta sin receta se obtuvieron principalmente (86%) en las farmacias. El uso de fármacos de venta sin receta por parte de las madres se asoció de manera significativa a la permanencia de los antibióticos en el hogar (oportunidad relativa, OR: 1,7; CI del 95%: 1,04-2,79), la automedicación de los cuidadores (OR: 6,3; CI del 95%: 3,8-10,5) y a la edad del hijo mayor (OR: 1,02; CI del 95%: 1,01-1,04). Los cuidadores que poseían conocimientos más amplios sobre los antibióticos fueron menos proclives a administrar antibióticos sin receta a los niños (OR: 0,7; CI del 95%: 0,6-0,8).

Conclusión La prevalencia del uso de antibióticos sin prescripción médica en los niños más pequeños fue elevada en Ulaanbaatar. Puesto que dicho uso conlleva un aumento de la resistencia bacteriana a los antibióticos y problemas relacionados con la salud, nuestros resultados tienen implicaciones importantes para la educación pública y para la aplicación de las normativas sobre la venta de antibióticos en Mongolia.

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Duration of maternally derived antibody against measles: A seroepidemiological study of infants aged under 8 months in Qinghai, China

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ABSTRACT

To estimate the sero-prevalence of protective maternal measles antibodies among young infants and examine patterns of waning immunity in one of the poorest provinces in China, infants aged under 8 months and their mothers were randomly selected by multi-stage probabilistic sampling and blood samples were collected. Measles-specific IgG antibodies were measured in all serum samples by enzyme-linked immunosorbent assay. We determined measles-specific antibody titres for 477 pairs of infants and their mothers. After excluding 44 sub-clinical measles infection in infants, the measles antibody titres were ≧1:200, ≧1:800, and ≧1:3200 in 79.2%, 46.9%, and 17.8% of the 433 infants, respectively. The proportion of infants with titre ≧1:800 declined with age from 90.2% in newborns to 45.5% and 14.9% in the fourth and eighth month, respectively. Among the 433 mothers, measles antibody titres were ≧1:800 in 94.0%. Multivariate regression analysis showed that residence, mother's antibody levels and infant's age were significantly associated with infants' having a measles antibody titre ≧1:800. The relatively rapid decay of protective antibody in infants suggests that an earlier administration of the first dose of measles vaccination should be considered in China and a high quality interventional study is needed to decide the optimal schedule of measles immunization.

1. Introduction

Measles remains a leading cause of vaccine-preventable deaths globally, particularly in low-income countries. In 2005, more than 20 million cases occurred, and 345,000 people died from measles worldwide, most of whom were children under five years of age [1–3]. These deaths account for 50–60% of the estimated 1.6 million childhood deaths from vaccine-preventable diseases annually [4].

Primary protection against measles at birth is provided by passively acquired maternal antibodies obtained through the placenta and lactation. These measles-specific maternal antibodies decline gradually during the first year of life with the development of the infants' own immune system. Maternal antibodies may neutralize the vaccine antigen before the development of an immune response, if the measles vaccine is administered to infants who still have maternal antibodies. The timing of the vaccination should be, therefore, carefully determined, and the interval between vaccination and the loss of maternally derived antibodies should be minimized to protect children from infection with measles.

In the early 1980s, the World Health Organization (WHO) established a policy for measles immunization which recommended the administration of a single dose of measles vaccine at 9 months of age [5,6]. This recommendation was based on the finding that infants born to naturally infected mothers have a high antibody titre against measles and do not lose protection from maternal antibodies until 7–9 months of age [7]. Thanks to an increase in vaccine coverage in developing countries over the past 20–25 years, there are now more mothers than ever who have not contracted measles but were vaccinated against measles in their childhood. Previous studies show that infants born to those mothers who have been vaccinated can lose protective antibody before 7–9 months of age [5,8–11]. The changes in the epidemiology of and the immunity against measles require a reconsideration of the vaccination policy against measles in developing countries.

Measles vaccination policy and delivery strategies vary considerably among countries. In the early years of the Expanded Program on Immunization (EPI), most countries followed the recommendation from WHO to administer only one dose of measles vaccine. However, since primary vaccination failure occurs in up to 10–15% of infants vaccinated at age 9 months, this strategy has been proven insufficient to prevent measles outbreaks [12]. WHO now recommends a 2 dose measles vaccine program with a 2nd opportunity for measles vaccine being offered during childhood through

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routine services or periodically through mass campaigns targeted at defined age groups.

Measles vaccination was first introduced into China in 1965. It was not until the launch of the national EPI in 1978, however, that the measles vaccination was routinely administered to children. In 1986, the Chinese Government established a nation-wide two-dose regimen which recommended the administration of the first and second dose of measles vaccine to children at 8 months and 7 years of age, respectively [13]. From 2006, the second dose of measles vaccine was advanced to 18–24 months and all measles vaccinations are free of charge. Following the expansion of measles vaccination and the launch of the EPI, the reported cases of measles in China decreased substantially from 3–4 million cases in the 1960s to less than 74,000 in 2000 and mortality from measles has also subsequently declined from 3000–5000 deaths per year in the 1980s to less than 200 in 2000s [14].

Despite such a dramatic reduction in measles mortality in China, measles cases have significantly increased during recent years and periodic outbreaks of measles continue to occur, particularly alarming is the increase of measles cases among infants who are less than 9 months of age [15–17]. Study shows that the reported total cases rose from 74,813 in 2003 to 100,267 in 2006, with the incidence of 7.67 per 100,000 population [18]. Moreover, the age distribution of measles has changed markedly. In 1990s, 1.74% of reported cases occurred among children less than 8 months of age [19]; however, of cases reported during 2003 and 2004, 4.31% and 2.25% occurred among children less than 8 months of age respectively, and during 2005 and 2006, the proportion of cases occurring in children less than 8 months old increased to 7.62% and 10.98% respectively [18]. In a hospital in Shanghai, nearly 60% of 503 hospitalized children with measles in 2005 were younger than 9 months old [20]. These data demonstrate that young infants in China have increased susceptibility to measles virus. This is problematic given the WHO's target of eliminating measles from the Western Pacific Region by 2012.

The present study is the first sero-epidemiological assessment of measles antibodies in women and infants in Qinghai, one of the poorest provinces in China, where measles has remained endemic since the establishment of EPI with quadrennial epidemic cycles. The average incidence of measles during the 1990s was 33 cases per 100,000 in Qinghai, compared with 0.2 per 100,000 in the developed provinces in eastern China [14]. A review of surveillance data from Qinghai Provincial Center for Disease Control and Prevention (CDC) suggests that measles cases among infants (0–12 months old) have been increasing since 2004, without obvious improvement of surveillance quality. In 2007, reported total measles cases were 86 in Qinghai Province, infant cases accounted for 30% (26/86), and cases among infants aged 0–8 months old accounted for 20% of total cases and 65% of infant cases.

The objectives of this study were three-fold: (1) to estimate the sero-prevalence of protection with passively transferred maternal measles antibodies among unvaccinated infants aged less than 8 months and examine the patterns of waning of their maternal antibodies; (2) to identify factors that affect the level of maternally derived measles antibodies in infants; and (3) to provide evidence for public health policies on the optimal age for measles vaccination.

2. Materials and methods

2.1. Study design

A cross-sectional survey was carried out in Xining, the capital of Qinghai Province from January to May 2009. Xining City covers seven counties and has 2.2 million inhabitants, accounting for 40% of the population of Qinghai Province, which has the highest measles incidence in the country. Two-stage probabilistic sampling was employed to select infants aged 0–8 months and their mothers. In the first stage, three counties were randomly selected out of seven, and one rural township which had the largest population was selected from each sampled county. During the study period, there was no measles outbreak in the townships that participated in the study. In the second stage, newborns and infants aged 1 month or older were sampled separately. A sample of newborn children was obtained by recruiting 15–20 consecutive babies born at each county central hospital. For infants aged 1–8 months, immunization records kept in township health centers were used as a sampling frame to randomly select 15–20 children for each month-age group from each township to ensure the representativeness of the sample. Children were recruited into the study if they had never been vaccinated against measles, they had never had clinical measles, and they did not have any severe illness or an acute illness with a rash at the time of the survey. Interviewers visited the home of each sampled child.

A standardized questionnaire was used to interview mothers. The questionnaire included modules on socio-demographic characteristics (e.g. age, ethnicity, educational background, the number of household members, and household income), the mother's history of infection with measles and vaccination (measles vaccine Hu 191 strain was used in Qinghai), and the birth history of children aged 8 months or younger including questions on the place of delivery, birth order, birth weight, breastfeeding habits, and gestational age. Due to the lack of objective records, the questionnaire asked mothers to self-report whether they had vaccinated against measles or had clinical measles during childhood, and if they could not remember, their mothers were contacted to provide this information. We also examined the mother's knowledge regarding measles and its vaccination program. This study was approved by Qinghai Provincial CDC Institutional Review Board, and all mothers gave informed consent for themselves and their infants before surveyed.

2.2. Serological analyses

Blood samples were collected by finger prick from children aged 1 month or older and their mothers. Neonatal blood samples were obtained from the umbilical cord immediately after delivery, and mothers' blood samples were taken by venopuncture. A sterile technique was followed to obtain all blood specimens. The blood specimens were taken to the Qinghai CDC Laboratory and centrifuged at 3000 rpm for 10–15 min. The sera were then pipetted into a sterile tube labelled with a unique identification code and stored at −20 °C until the analysis was completed. Measles specific IgG antibodies were measured in all serum samples by enzyme-linked immunosorbent assay (ELISA). The ELISA kits were obtained from National Laboratory for Measles, Institute of Viral Disease Control and Prevention, China CDC. The semi-quantitative ELISA method defines measles antibody titres as negative, 1:200, 1:800, 1:3200 and 1:12,800. Sub-clinical measles infection in infants was defined as the infants with a four-fold or greater rise in measles antibody titre when the infant's titre is compared with the corresponding maternal antibody titre.

2.3. Statistical analyses

Antibody titres were log-transformed, and the Geometric Mean Titres (GMTs) were calculated in order to compare the differences between groups. Only antibody titres over the limit of detection (≥1:200) were used for the calculation of GMTs. IgG antibody against measles was considered to be seropositive or detectable (assumed to be immune) at 1:200 or greater, protective at 1:800 or greater, and high at 1:3200 or greater [21,22]. Youwang et al.

[21] tested the titre of ELISA IgG measles antibody among 145 persons exposed to measles virus in 3 measles outbreak villages and observed the occurrence of clinical measles cases. They found all clinical measles infection occurred among those with titre ≤1:200, and no clinical measles infection among those with titre ≥1:800, which demonstrated that a measles IgG titre of 1:800 was associated with protection against clinical measles infection. In this paper, the cut-off was chosen based on the assumption that 1:800 correlates with protection against clinical infection in vaccinated individuals and acknowledge that although it is known that passively acquired antibody protects against measles infection, a precise serological correlate has not yet been defined for this situation.

The proportions of children who had detectable and protective measles antibody titres were estimated by single-month age group. The analysis of variance (ANOVA) and *t*-test were used for comparisons of GMTs between groups. The Pearson Chi-square test and the Fisher exact test were used to compare the proportions in each cohort who had detectable and protective measles antibodies.

A logistic regression analysis was performed to examine the change in infants' measles antibodies with age and to investigate the impact of differing factors on infants' antibody decay. A dichotomous dependent variable was created for the infant's antibody levels to indicate whether they were ≧1:800 or not. The impact of age among the infants was examined for each month, using zero month (newborns) as the reference group. The age of the mothers was used as a proxy for their immunization status in childhood, on the assumption that mothers aged 31 or younger (born in 1978 or later) had vaccine induced immunity and were immunized under the EPI program.

3. Results

Of the 503 pairs of infants and their mothers recruited for this study, 26 were excluded from the analysis because the blood specimens of either the mother or infant were inadequate to run serologic tests. 44 (9.2%) were excluded because of sub-clinical measles infection in infants. The final study population included 433 pairs and blood samples were processed for all of them.

The infant female to male ratio was 1:1.1. The mean gestational age was 279.0 (SD 11.5) days. The mean birth weight was 3272.3 (SD 687.3) g, and 5.7% of the children had a low birth weight (<2500 g). None of these low birth weight infants were premature. Three quarters of the 433 interviewed mothers (75.5%) were born after 1978, the year when China's EPI was established and with it, the launching of the routine administration of measles vaccine to all infants. The mean parity was 1.3 (SD 0.5), and 68.6% of the mothers were primiparas.

None of mothers had records of their vaccination status or history of measles infection. The majority of the 433 mothers (65.3%) could not recall whether or not they had been vaccinated against measles during childhood, whereas 68 (15.7%) reported that they had been vaccinated against measles during childhood and 46 (10.6%) confirmed that they had suffered a natural infection of measles.

The measles antibody titre was seropositive, protective, and high in 79.2%, 46.9%, and 17.8% of the 433 infants, respectively. The proportion of infants with detectable (seropositive) measles antibodies decreased with age from 98.0% in newborns to 77.3% at age 4 months and 53.2% at age 8 months. The proportion of infants with protective antibody levels declined with age from 90.2% in newborns to 45.5% and 14.9% in the fourth and eighth month, respectively (Table 1).

The GMTs of detectable measles antibodies in newborns were not statistically different from that of their mothers (newborns

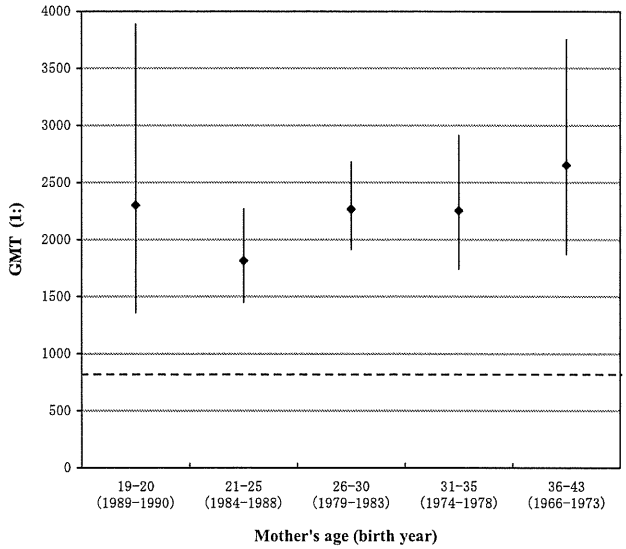

Fig. 1. Distribution of GMTs of measles antibodies in infants 0–8 months in Qinghai, China, 2009. *Note*: Measles antibody titre of 1:800 or greater, defined as protective, is indicated by the dashed line. The points are mean GMTs, and bars are 95% CI.

2294.3 vs. mothers 2870.3, $P = 0.20$). The GMTs in infants decreased dramatically between newborns and infants aged 1 month old. The GMTs fell below the protective antibody level in infants at 3 months of age (GMTs of 1:570.1, 95% CI: 413.1–786.7) (Fig. 1). There were no statistical differences in GMTs between 106 infants whose mothers were born before 1978 and 327 infants born to younger mothers (623.5 vs. 682.9, $P = 0.55$).

Among the 433 mothers, measles antibody titres were equal to or higher than 1:800 in 94.0% (95% CI: 91.3–95.9%) and detectable levels in 99.8% (95% CI: 98.4–100.0%). More than half of the mothers had measles antibody titre ≧1:3200 (59.1%, 95% CI: 54.4–63.7%). The mean antibody titres in mothers did not differ significantly between age groups ($P = 0.87$) (Fig. 2). The mothers of infants with antibody titres ≧1:800 had significantly higher GMT than did mothers of infants with antibody titres lower than 1:800 (3009.2 vs. 1624.4, $P < 0.01$). 26 (6%) mothers had measles antibody titres <1:200.

Table 2 presents the results of logistic regression analysis. After controlling for all other covariates, infants were less likely to have measles antibody titre of ≧1:800 than newborns (<1 month old)

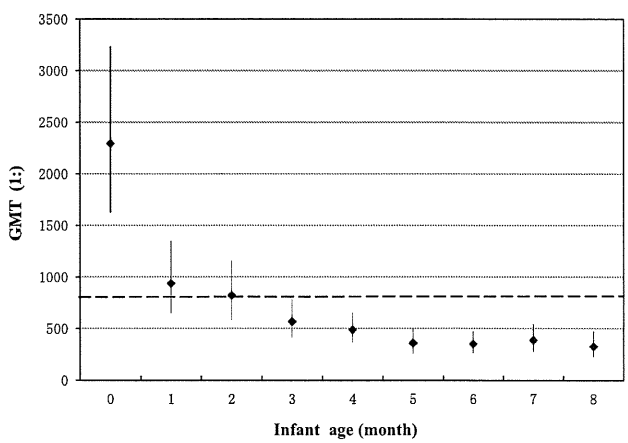

Fig. 2. Distribution of GMTs of measles antibodies in mothers by age in Qinghai, China, 2009. *Note*: Measles antibody titre of 1:800 or greater, defined as protective, is indicated by the dashed line. The points are mean GMTs, and bars are 95% CI.

Table 1
Distribution of measles-specific antibodies among infants aged 0–8 months by age in Xining City, Qinghai Province, China, 2009.

Age (months)	Total	Positive antibody (≥1:200)			Protective antibody (≥1:800)			High antibody (≥1:3200)		
		No.	%	95% CI	No.	%	95% CI	No.	%	95% CI
0	51	50	98.0	(87.4–99.7)	46	90.2	(78.5–95.9)	32	62.7	(48.8–74.8)
1	54	52	96.3	(86.4–99.1)	37	68.5	(55.1–79.4)	16	29.6	(19.0–43.0)
2	49	46	93.9	(82.7–98.0)	33	67.3	(53.2–78.9)	12	24.5	(14.5–38.3)
3	49	45	91.8	(80.2–96.9)	26	53.1	(39.2–66.5)	7	14.3	(7.0–27.1)
4	44	34	77.3	(62.7–87.3)	20	45.5	(31.5–60.1)	2	4.5	(1.1–16.4)
5	40	28	70.0	(54.3–82.1)	10	25.0	(14.0–40.5)	2	5.0	(1.3–17.9)
6	50	34	68.0	(54.0–79.4)	12	24.0	(14.2–37.7)	2	4.0	(1.0–14.6)
7	49	29	59.2	(45.1–71.9)	12	24.5	(14.5–38.3)	2	4.1	(1.0–14.9)
8	47	25	53.2	(39.1–66.8)	7	14.9	(7.3–28.1)	2	4.3	(1.1–15.5)
Total	433	343	79.2	(75.1–82.8)	203	46.9	(42.2–51.6)	77	17.8	(14.5–21.7)

Abbreviation: CI, confidence interval.

by 93% at age 3 months (odds ratio, OR: 0.07, 95% CI: 0.02–0.28, $P<0.001$), 97% at 5 months old (OR: 0.03, 95% CI: 0.01–0.14, $P<0.001$), and 99% at 7 months old (OR: 0.01, 95% CI: 0.00–0.04, $P<0.001$). Infants were more likely to have measles antibody titre of ≧1:800, if they lived in rural areas (OR: 24.62, 95% CI: 8.43–71.94, $P<0.001$) or if their mother had measles antibody titre equal to or greater than 1:3200 (OR: 7.13, 95% CI: 3.67–13.82, $P<0.001$). The likelihood of being protected was higher on average in infants born to mothers who had been born before 1978 (assumed to be naturally infected) than those born to younger mothers, although this difference was not statistically significant (OR: 1.27, 95% CI: 0.64–2.54, $P=0.49$).

Table 2
Odds ratios for the protective levels of passively transferred maternal measles antibodies in infants aged 0–8 months in Xining City, Qinghai Province, China, 2009.

	Not protective (<1:800)	Protective (≥1:800)	OR	95% CI
Residence				
Urban	203	121	1	
Rural	27	82	24.62	8.43–71.94**
Monthly income (log-transformed)			0.85	0.28–2.58
Family member				
>3	121	136	1	
3	108	63	1.37	0.66–2.86
Mother's age (year)				
≤31	179	148	1	
>31	51	55	1.27	0.64–2.54
Mother's antibody				
≤1:800	117	60	1	
≥1:3200	113	143	7.13	3.67–13.82**
Mother's ethnicity				
Han	137	141	1	
Minority	93	62	1.28	0.65–2.52
Mother's education (year)				
≥6	197	168	1	
<6	33	35	1.08	0.47–2.49
Infant's age (month)				
0	5	46	1	
1	17	37	0.32	0.09–1.16
2	16	33	0.26	0.07–0.97*
3	23	26	0.07	0.02–0.28**
4	24	20	0.06	0.02–0.24**
5	30	10	0.03	0.01–0.14**
6	38	12	0.01	0.00–0.05**
7	37	12	0.01	0.00–0.04**
8	40	7	0.01	0.00–0.04**
Gender				
Female	107	98	1	
Male	123	105	0.82	0.46–1.45
Birth weight (g)				
≥2500	213	187	1	
<2500	12	12	0.55	0.16–1.90
Birth order				
First	160	125	1	
2–4	69	75	1.40	0.67–2.92
Gestation age (day)				
≥280	155	138	1	
<280	67	63	1.03	0.54–1.98

Abbreviations: OR, odds ratio; CI, confidence interval.
* $P<0.05$.
** $P<0.001$

4. Discussion

The first cross-sectional study in the capital of one of the poorest provinces in China showed that passively acquired maternal measles antibodies rapidly decreased with age among infants aged 8 months or younger. The measles antibody titres of the majority of the infants had already lower than 1:800 a few months before the 8th month of life, the age for the first dose of measles vaccine under the current policy in China.

The seroprevalence of measles antibodies both in mothers and infants in Qinghai Province is higher than that in other parts of China. Previous serosurveys of mothers and infants aged 8 months or younger in other areas of China reported measles seropositive rates in the range of 84.3–88.5% and 28.9–55.2%, respectively [23–25]. Qinghai Province is located in the north-eastern part of the Qinghai-Tibet Plateau in western China, covering an area of 720,000 km^2. By the end of 2008, the population of Qinghai was 5.38 million, and 70% of inhabitants live in the rural or mountainous areas. Most mothers in this study were unlikely to have been vaccinated, since it is extremely difficult for the providers of health services to reach these rural and mountainous locations. A review of the provincial data by the author found that the measles vaccination coverage was very low at the time when EPI was initially established (data not shown). Mothers were likely to have had a natural measles infection during their lifetime, especially in rural and mountainous areas. Mothers' antibody levels were thus continually boosted due to the high transmission and periodic outbreak of measles in the study area. The association between the higher antibody levels in the infants and rural residence would also suggest that perhaps in the rural areas there are pockets of unvaccinated mothers and more of the mothers had natural disease.

In this study, we found that the concentration of maternally derived measles antibodies in infants was significantly associated with age and the concentration of maternal antibody. This result is consistent with previous study [26]. We did not find a significant difference in average maternal antibody levels between infants born to mothers who reported that they had natural measles infection and those born to mothers who reported that they had vaccination against measles, although several studies have suggested that measles antibody titres induced by vaccination are lower [27–29] and decline earlier in maternal derived antibodies [10,11,27,30–34] than those induced by natural infection. The possible explanation is that mother's history of vaccination and measles natural infection was obtained only through her own recall, without the confirmation of individual health records, moreover, the majority of mothers could not remember clearly whether they had been vaccinated against measles or had natural measles infection during childhood, thus subject to recall bias.

We used a traditional semi-quantitative ELISA method to measure the measles IgG antibodies in infants and their mothers. This method has been widely used in China for many years. In order to compare this traditional method with quantitative measles IgG ELISA assay, Mao et al. [35] retested 92 serum samples from healthy adults that had been tested using the CDC-China assay using the German Vrion/Serion test kit. They found an excellent correlation between the results obtained using each method (Spearman correlation coefficient of 0.963 ($P < 0.000$)). It indicated that the results of measles antibody in our study are reliable.

Measles vaccination has proven to be an extremely successful public health intervention and has already resulted in the remarkable decline of measles in many developing countries. However, the success of measles immunization depends on a number of factors, including the presence of maternal antibodies at the time of vaccination. Maternal antibody is transferred via the placenta during the last trimester of pregnancy and gradually declines during the first year of life when the infant's own immune system develops [36]. Interference by maternal antibodies has been generally thought to be an important issue in the seroconversion following early measles vaccination. The administration of measles vaccine at early age may not be effective because maternal antibodies neutralize the vaccine antigens before the development of a specific immune response [28]. On the other hand, any delay in vaccination may increase the risk of disease complications in infants. It is critical to identify an optimal age for measles vaccination to balance the risk of an early loss of maternal antibodies in the majority of infants with the risk of primary vaccine failure as a result of the presence of maternal antibodies [8].

One of the criteria to determine the optimal age for measles vaccination is the age at which the largest percentage of children lose measles antibodies and at which most respond to vaccine. Our results showed that passively transferred maternal antibodies decline rapidly among infants aged 8 months and younger, and that the mean titres were below 1:800 at 3 months of age. At the same time, 76.0% of infants aged 6 months of age have measles antibody lower than 1:800. In contrast with the developed provinces on the east coast of China, the risk of contracting measles prior to the stipulated age of the first dose of measles vaccine is substantially high in Qinghai Province due to the high incidence and periodic outbreaks of measles. This risk may further increase, once cohorts of vaccinated mothers enter reproductive age.

Although the majority of infants in our study had detectable level of maternal antibodies, previous studies suggest both humoral and cellular immune responses contribute to protection against measles following early vaccination with the currently available vaccine. A study carried out in China from 1991 to 1998 showed that vaccination at the age of 6 months with live attenuated measles vaccine induced a positive immune response in 91.7% of the vaccinated infants [22]. A study on seroconversion rates after administration of the standard Edmonston-Zagreb measles vaccination in infants aged 4.5 months also concluded that, although 28% of infants tested at 4.5 months of age had protective levels of maternal antibodies, 92% had measles antibodies at 9 months of age after early vaccination against measles [5]. Because of the uncertainty about using 1:800 as a serological correlate of protection for passively acquired antibody and because the level of antibody that inhibits vaccine take has not been defined, further studies are needed to understand the dynamics of maternal measles antibody. However, our results suggest that an earlier administration of the first dose of measles vaccine might be considered and that trials of seroconversion of measles vaccine administered before eight months of age may be warranted in China.

This study is one of the few studies that provides solid evidence on the seroprevalence of measles antibodies in a lowly developed area in China with periodic measles outbreaks. Since the majority of infants younger than 8 months had detectible maternal antibody against measles in the study area, more comprehensive trials examining seroconversion following measles vaccination at an early age are needed before lowering the recommended age for the first dose. Immunization programs in China could continue with the current policy of the first measles vaccination at eight months of age and a second opportunity for measles immunization for all children until further results are available.

Measles in young infants usually indicates poor measles control in general. Strategies to give a first dose earlier than 8 months of age during measles outbreak or mass campaign activities, to vaccinate women of childbearing age with measles vaccine will be the another optional ways to resolve the problem of measles cases in infants too young to be vaccinated. In this study, 6% (26/433) mothers had measles antibody titres <1:200. The non-immune mothers may contribute to recurrent epidemics in children and young infants born to these women in Qinghai Province. Achieving an immunization coverage rate of at least 95% with two doses

for all birth cohorts remains the most effective strategy to accelerate and sustain the reduction of mortality from measles and for the elimination of the disease in developing countries.

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50 years of pursuing a healthy society in Japan

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In this Series in *The Lancet*, we review the past 50 years of Japan's universal health coverage, identify the major challenges of today, and propose paths for the future, within the context of long-term population ageing and the devastating crises triggered by the March 11 earthquake. Japan is recognised internationally for its outstanding achievements during the second half of the 20th century, in both improving the population's health status and developing a strong health system. At the end of World War 2, in Japan, life expectancy at birth was 50 years for men and 54 years for women; by the late 1970s, Japan overtook Sweden as the world's leader for longest life expectancy at birth.[1] Japanese women have remained in the number one slot for 25 years, reaching a life expectancy of 86·4 years in 2009 (while Japanese men slipped to fifth longest living that year, at 79·6 years).[2,3]

In 2011, Japan celebrates 50 years of *kaihoken*: health insurance for all. Universal health insurance was achieved in 1961, assuring access to a wide array of health services for the whole population. Since then, benefits have become more egalitarian while health expenditures have remained comparatively low: 8·5% of the gross domestic product and 20th out of countries in the Organisation for Economic Co-operation and Development in 2008.[4] This achievement is all the more remarkable because the percentage of the population aged 65 years or older has increased nearly four-fold (from 6% to 23%) over the past 50 years.[5]

What produced Japan's impressive performance over the past half century? This question is not easily answered, because many factors contributed, including public health policies, high literacy rates and educational levels, the traditional diet and exercise, economic growth, and a stable political environment. Further, buried in the successes of the past 50 years are the roots of Japan's health-care challenges today. This Series examines not only specific factors that have contributed to improved health status but also challenges and opportunities faced today. Here we explore the broader context in which these changes have evolved—and in which Japan's emerging challenges are situated.

With the inauguration of Emperor Meiji in 1868, the Japanese Government embarked on a policy of rapid westernisation throughout society. In health care, the government over time succeeded in changing the basis of medical practice from Chinese to western medicine. Unlike other Asian countries, independent schools or formal qualifications in Chinese medicine were not allowed to co-exist with those teaching western medicine. Moreover, this transition was achieved with minimum cost and limited social disruption.[6]

However, for hospitals, Japan needed to adopt a new method of delivering care, because there were virtually no public or religious institutions that could serve this role. Japan developed hospitals for specific purposes, including teaching and research hospitals, army and navy hospitals, public hospitals for quarantining patients with communicable and venereal diseases, and—the most numerous—private hospitals expanded from clinics. In all four cases, the hospital was regarded as the doctor's workplace, and a doctor served as director with clinical and administrative responsibilities. The medical staff of these

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new hospitals was typically controlled by the professors of prestigious medical schools, notably the University of Tokyo. Physicians were rotated, at the decision of the professor, within the closed network of the university clinical department and its affiliated hospitals.

The most successful of the private hospitals established by physicians continued to expand until they rivalled the large hospitals in the public sector. Thus there was not much distinction between physicians' offices and hospitals, with even large medical centres maintaining outpatient departments, which patients could visit without referrals. There was also not much distinction between specialists and general practitioners. Those who went into private practice continued to regard themselves as specialists, but they mostly provided primary care because they did not have access to hospital facilities. This basic structure continues today.

In 1945, at the end of the war, Japan was confronted with widespread devastation: major cities had been destroyed and two cities were completely wiped out; an estimated 3·2 million people had died; and deep poverty and malnutrition scarred the entire country. Japan's surrender, in August, 1945, was followed by 7 years of US occupation that sought to restructure the health-care system as part of its goal of democratising the fabric of society.

These endeavours had mixed results. On the one hand, to address the population's health problems, the occupying forces strengthened community health institutions, which advanced the control of infectious diseases. Astounding gains in health status occurred in the immediate post-war years. Between 1947 and 1955, average life expectancy increased by nearly 14 years.[7]

These achievements have been attributed to public health policies that were started before the war, facilitated during the occupation along with social reconstruction efforts, and expanded by the Japanese Government after regaining sovereignty in 1952. Importantly, these early post-war health gains occurred before Japan's period of rapid economic growth, but while Japan was expanding employee-based health insurance and community health insurance, both of which already covered over 70% of the population during the war (in 1943). There was also continuity in medical education: the hierarchical structure, with the University of Tokyo at the top, remained intact.

In addition to its impressive health gains, Japan achieved unprecedented economic growth starting in the 1960s. But Japan also saw major setbacks to health in some population groups. Disastrous pollution problems erupted in the 1960s, with serious health consequences for locally affected populations.[8] The lessons learnt led to Japan taking a lead in environmental health. Since the late 1970s, Japan's health gains have captivated the attention of researchers from various disciplines who sought to explain how the country achieved the world's longest life expectancy.

Japan is currently undergoing several sociocultural changes that are challenging the formation of contemporary society. These changes include the rise of part-time and temporary employment for young workers, a growing number of young women who postpone marriage and child-bearing, the ever-expanding number of people who are elderly, an increasing sense of widening inequality in income, and diversity in values that weaken the national myth of homogeneity.[9] One manifestation of these changes is Japan's low fertility rate. Total fertility has declined in Japan to 1·37 livebirths per woman—about the same rates as in Italy and Germany, slightly greater than those in Singapore and South Korea, and much less than the replacement rate.[10] Japan's low fertility combines with low mortality to drive the rapid ageing of the population. People aged 65 years and older made up 20% of the population in 2005, and this group is expected to increase to 40% by 2050. This changing demographic structure has profound implications for many social institutions, including the health-care system, the financing of health care, and how to care for older people.

Japan is now confronting major challenges to its health system in the midst of major political and economic stagnation. The country has slogged through 20 years of economic non-growth, accumulating a huge national debt. Japan's percentage of global gross domestic product rose steadily from 3·9% in 1960, to 18·0% in 1994, but since has declined to 8·3% in 2008.[11] The time of Japan as number one—the 1960s and 1970s—is long over.[12] Unemployment is rising, and income inequality has increased since the late 1980s. The conservative Liberal Democratic Party, the country's dominant political party that held power almost continuously for 54 years, lost heavily in the 2009 Lower House elections and is now the opposition party. This political economy context complicates Japan's efforts to reform its health system today. But the fluid

political situation might also open new opportunities for structural change in how Japan operates, and expands the potential for policy innovation in the health system.

Over the past 50 years, Japan has transformed its health-care system through incremental changes that have been largely successful in expanding universal coverage and containing costs, while increasing fairness, and reducing inequities across different health plans. The basic premise of egalitarian and community-based health care has led to the construct of human security, which is now the core of Japanese diplomacy.[13] But during this time Japan also postponed certain structural changes in its health-insurance plans; these accumulated problems have become harder to avoid, along with the continued expansion of the elderly population and the public debt.

This Series addresses major achievements and challenges now confronting Japan's health system. Nayu Ikeda and colleagues[14] analyse Japan's success in extending life expectancy and the sources of its mortality reductions. Naoki Ikegami and colleagues[15] explain how Japan achieved universal coverage and reduced inequities in different health plans, to remove the risk of financial impoverishment from health-care costs. Hideki Hashimoto and colleagues[16] examine how the health-care system has been able to contain costs while still maintaining standards of quality of care. Nanako Tamiya and colleagues[17] explore Japan's main policy to address its rapidly ageing population: the public long-term-care insurance programme established in 2000. Rayden Llano and colleagues,[18] examine Japan's efforts to expand its role in global health, to provide policy guidance and not just funding. Finally, Kenji Shibuya and colleagues[19] pull together the main lessons for Japan and other countries.

This Series contributes analysis and recommendations to five crucial health-policy debates in Japan. The country's current political circumstances offer opportunities for a bipartisan reform of the health-care system. Japan's concept of human security might provide the key values for confronting both domestic and global conundrums in health policy. We are confident that Japan—the first non-western country to achieve economic development and universal health coverage—has the capacity to resolve these problems in ways that will provide lessons for the world.

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lower than in other high-income countries.[5] Given poor measures on quality of care, further reduction in mortality may require that Japan revamp its health-care system. Economic stagnation and rising income inequality could also be part of the explanation of recent trends.

What lessons can be drawn from the experience of Japan? Drawing from Ikeda and colleagues' analysis, I make four observations. First, strong government action at relatively low national income per capita (Japan in the 1950s) in a comparatively educated population can result in implementation of effective infectious disease control programmes. The critical necessity for high levels of educational attainment[6] should not be underestimated. Second, the main effects of the health-care system in explaining accelerated mortality decline were probably through public health action and primary care management of key risks such as blood pressure. These make up a small fraction of health expenditure in any nation. Low health expenditure as a fraction of GDP in Japan associated with excellent health outcomes could be because most health expenditure in other nations contributes little to improved population health outcomes. Third, Japan has benefited enormously from favourable risk factors for ischaemic heart disease and some cancers. Japan already had lower death rates from ischaemic heart disease than the other eight nations in the 1950s. Favourable risk factor endowment must be taken into consideration when undertaking any type of assessment of health system performance. Fourth, in an era of economic stagnation, political turmoil, ageing populations, and inadequate tobacco control, Japan does not seem to be effective in addressing its new set of health challenges. It will take more than universal access to a low-spending, high-volume health system to tackle these challenges. Without concerted action, Japan, like the USA[7] is likely to continue dropping in the global mortality league tables. Although the relative decline will not be as severe as we are witnessing in the USA, it is a cautionary tale that success in the past does not guarantee top performance in the future.

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Development of a disaster cardiovascular prevention network

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The magnitude 9·0 Great East Japan Earthquake that hit Tohoku in the northeast region of the main island, Honshu, on March 11, 2011, was followed by a devastating tsunami that has killed 15 538 people to date and left 7060 missing. Japan's Disaster Medical Assistance Team, which was developed on the experience of the 1995 Great Hanshin-Awaji (Kobe) Earthquake, went into action immediately. However, the unique nature of the 2011 disaster made it more challenging than its predecessors, as witnessed by the fact that the process of recovery has been far from satisfactory and is expected to be extensive.[1,2] The experience of similar events in the past suggests that survivors will have acute injuries and infections and will be at an increased risk of chronic illness, such as cardiovascular disease or mental ill health.[3]

Major cardiovascular events, such as stroke and myocardial infarction, occur more frequently in survivors of disasters and the effect can last months after the event. An increased incidence of cardiac events (myocardial infarction and sudden death within 24 h of onset) and stroke was reported in communities around the epicentre of the Great Hanshin-Awaji Earthquake in the 3 months after the event.[4,5] Moreover, the frequency of cardiovascular disease in every community was positively correlated with the magnitude of

Reuters

earthquake-induced damage.[4,5] A disaster can trigger cardiovascular events through sympathetic nervous activation and potentiation of acute risk factors.[6,7] In particular, blood pressure increases during and in the aftermath of a disaster, probably because of sympathetic activation by fear and increased salt sensitivity from insomnia and a disrupted circadian rhythm.[7]

The tsunami-hit areas in Tohoku have some of the most rapidly ageing populations in Japan with a high prevalence of hypertension and diabetes; residents in these areas have little access to high-quality facility-based services.[8] Because of the unprecedented scale of the 2011 disaster (earthquake, tsunami, and nuclear crisis) pre-existing disorders such as hypertension and diabetes might be aggravated in survivors, leading to increased risk of cardiovascular disease.[9,10] Despite such concerns, no rapid or systematic assessment of the health status of survivors had occurred 2 months after the earthquake, partly because of the logistical difficulties involved, but mainly because of the absence of preparedness and coordination between Japanese central and local government, medical communities, and non-governmental organisations and voluntary groups.[8] Uncoordinated small-scale surveys that have been undertaken in affected areas have provoked much controversy and debate about the ethical implications of doing research into populations of survivors.[11]

To better assess and reduce risks for disaster-associated cardiovascular events, we developed the web-based Disaster Cardiovascular Prevention (DCAP) network on the basis of previous studies,[4–7,12] and have begun to implement it in the survivors of the 2011 disaster. The DCAP system entails calculation of a risk score to identify survivors at high risk of cardiovascular events and promote preventive behaviours. Our initial DCAP assessment aimed at prevention of excess morbidity and mortality in 386 survivors living in shelters in the towns of Minamisanriku, Ishinomaki, and Kesennuma in May, 2011. We used a real-time feedback survey and after completion of a DCAP risk score sheet asked individuals to undertake behavioural components on a score sheet of prevention measures.

We noted that individuals had lowest ratings on the preventive score component for diet, sleep quality, blood pressure control, and bodyweight. Analysis of blood and urine suggested that high salt intake was widespread in survivors, as was hypercoagulability and increased blood glucose concentration. Our survey highlights the potentially urgent need to introduce a system to monitor the health status of survivors in other locations affected by this disaster. We intend to follow up individuals who were assessed and have DCAP scores to assess the validity and reliability of the scores in terms of prediction of cardiovascular events.

In the difficult circumstances after the Great East Japan Earthquake, the DCAP network provided monitoring devices to assess cardiovascular risks in survivors, allowing preventive interventions to be made by participating health facilities and supporting blood pressure control by public health nurses on the basis of DCAP scores. This system can be extended to other health conditions and will aid the integration of traditional facility-based care with multidisciplinary and community-based primary care in the areas affected by tsunamis. A network of health-care provision will also promote empowerment and connectedness in survivors who can otherwise become isolated.

We hope that the DCAP network will be integrated into the community reconstruction plan in Japan in the coming months. Tohoku should not be regarded as an isolated and powerless region but as a pilot for the future Japanese health system, in which innovative technology-driven primary care can connect patients, service providers, and the community and help to integrate health services and research and development. We believe that this unique network will contribute to more effective cardiovascular protection in survivors and

also provide a model for primary care in other settings around the world with restricted access to services and health care.

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Japan: Universal Health Care at 50 Years 1

What has made the population of Japan healthy?

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People in Japan have the longest life expectancy at birth in the world. Here, we compile the best available evidence about population health in Japan to investigate what has made the Japanese people healthy in the past 50 years. The Japanese population achieved longevity in a fairly short time through a rapid reduction in mortality rates for communicable diseases from the 1950s to the early 1960s, followed by a large reduction in stroke mortality rates. Japan had moderate mortality rates for non-communicable diseases, with the exception of stroke, in the 1950s. The improvement in population health continued after the mid-1960s through the implementation of primary and secondary preventive community public health measures for adult mortality from non-communicable diseases and an increased use of advanced medical technologies through the universal insurance scheme. Reduction in health inequalities with improved average population health was partly attributable to equal educational opportunities and financial access to care. With the achievement of success during the health transition since World War 2, Japan now needs to tackle major health challenges that are emanating from a rapidly ageing population, causes that are not amenable to health technologies, and the effects of increasing social disparities to sustain the improvement in population health.

Introduction

Japan has caught the attention of the rest of the world because of the tremendous success it has achieved in improving the health status of its population in the 20th century. The improving health status of the Japanese population was noted as early as the 1920s when infant mortality rates started to fall.[1] Increased child survival rates were partly possible then through the enhanced education and increasing literacy of mothers—in the early 20th century, with the provision of free compulsory education, almost all girls attended primary schools.[2] However, after World War 2, Japan showed its strength in improving the health of its population. The country was devastated after its defeat. Per person gross domestic product was roughly international $3400 in 1950 (table), which is similar to that in India today (Gakidou E, Institute for Health Metrics and Evaluation, personal communication). The health status of the population was also poor—in 1947, male life expectancy in Japan at birth was only 50 years and female life expectancy was 54 years.[5]

Rapid economic growth started in the late 1950s and life expectancy started to increase at an unprecedented rate. Within a few decades Japan had caught up with and eventually surpassed many other developed nations (figure 1; figure 2). Since 1986, Japan has ranked first in terms of female life expectancy at birth, with the highest ever recorded worldwide life expectancy of 86 years in 2009.[9] The country had also maintained the best healthy life expectancy at birth in 2007 (73 years for men and 78 years for women).[10] With a low rate of total fertility, the proportion of people aged 65 years and older has quadrupled during the past 60 years to 23% in 2010,[4] making the Japanese people the oldest population in the world. Despite the ageing population, Japan's health expenditure is only 8·5% of gross domestic product, which put it in 20th position in terms of expenditure among the countries of the Organisation for Economic Co-operation and Development in 2008.[6]

What has made the population of Japan healthy? How has Japan achieved the longest life expectancy at birth worldwide? Will the Japanese population continue to be

Key messages

- The early establishment of free compulsory primary education and a social insurance system before World War 2 and universal health insurance coverage in 1961 enabled the provision of equal opportunities for health promotion.
- Disparities in health across regions and socioeconomic groups are fairly small in this homogeneous and egalitarian society and have narrowed over time with increased average population health. However, the downward trend in socioeconomic inequality in health has been less obvious since the 1990s, which has coincided with income inequality gradually increasing.
- Japanese life expectancy at birth increased rapidly in the 1950s and early 1960s as a result of decreased mortality rates for communicable diseases in children and young adults, which was largely attributable to the government's strong stewardship in investing in key interventions for public health.
- Stroke mortality reduction was one of the major drivers of the sustained extension of Japanese longevity after the mid-1960s. The control of blood pressure improved through population-based interventions such as salt reduction campaigns and an increased use of cost-effective health technologies such as antihypertensive drugs under universal health insurance coverage.
- Further progress in Japan's longevity primarily depends on prevention of major risk factors for non-communicable diseases such as tobacco smoking and high blood pressure and several cardiovascular risks. Prevention of premature mortality from suicide is also a major challenge for population health.
- A rapidly ageing population as a result of improved survival is challenging Japan's health system in terms of its financing and quality of care. An effective link between medical and long-term care through both top-down and bottom-up approaches is necessary to enhance the welfare of the population throughout the country.

	1950	1960	1970	1980	1990	2000	2005	2010
GDP per person (2005 international $)*	3415	6249	13734	18545	26926	29396	31129	31329
GDP growth rate (%)[3]	NA	12·0†	4·3	2·8	5·6	2·9	1·9	−5·2‡
Total population (×1000)[4]	82199	93189	103710	115915	122251	125720	126393	126536
Population older than 65 years (%)[4]	4·9	5·7	7·0	9·0	11·9	17·2	19·9	22·7
Total fertility rate[4]	3·0	2·0	2·1	1·8	1·5	1·3	1·3	1·4§
Female life expectancy at birth (years)[5]	61·5	70·2	74·7	78·8	81·9	84·6	85·5	86·4
Male life expectancy at birth (years)[5]	58·0	65·3	69·3	73·4	75·9	77·7	78·6	79·6
Total health expenditure (% of GDP)[6]	NA	3·0	4·5	6·4	5·9	7·7	8·2	8·5¶

GDP=gross domestic product. NA=not available. *Gakidou E, Institute for Health Metrics and Evaluation, personal communication. †GDP growth rate in 1961. ‡GDP growth rate for 2009. §Total fertility rate of medium-fertility variant estimate for 2010–15. ¶Total health expenditure for 2008.

Table: **Socioeconomic and demographic characteristics of people in Japan during 1950–2010**

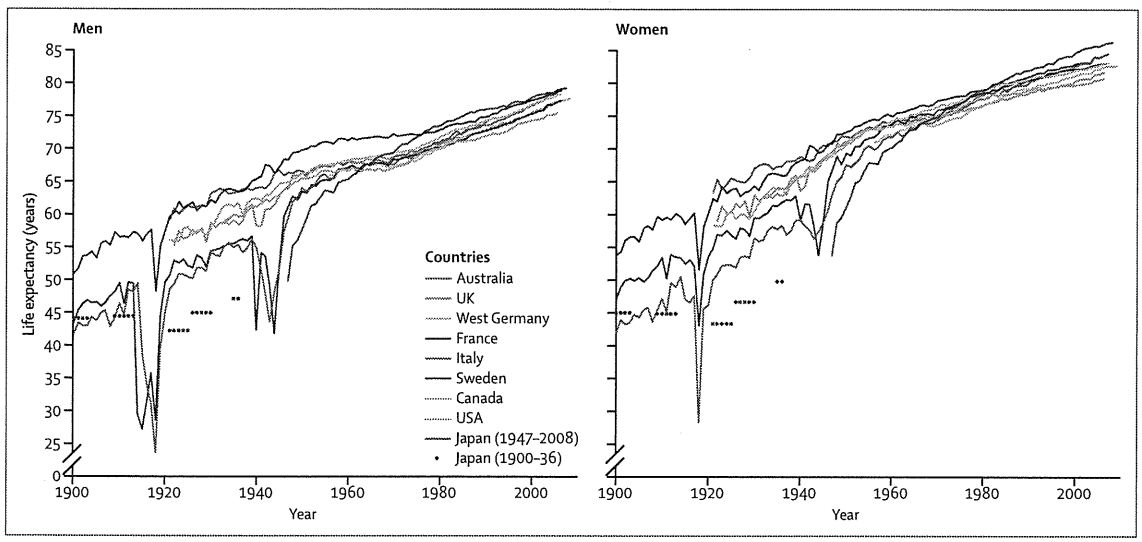

Figure 1: **Trends in life expectancy at birth, 1900–2008**
Data from University of California at Berkeley and Max Planck Institute for Demographic Research[7] and Ministry of Health, Labour and Welfare.[8]

healthy in the future? Understanding what has contributed to making the Japanese population healthy in such a fairly short period is important for global health policy, particularly for countries struggling to improve health. Several aspects of the Japanese lifestyle provide appealing explanations for the first two questions. First, Japanese people give attention to hygiene in all aspects of their daily life. This attitude might partly be attributable to a complex interaction of culture, education, climate (eg, humidity, temperature), environment (eg, having plenty of water and being a rice-eating nation), and the old Shinto tradition of purifying the body and mind before meeting others.[11,12] Second, they are health conscious. In Japan, regular health check-ups are the norm. Mass screening is provided for everyone at school and work or in the community by local government authorities. A systematic check-up of the whole body, referred to as a human dry dock (panel 1), is another type of health screening, which is popular among business people—they stay at clinics or hospitals for several days to undergo thorough physical examinations. Third, Japanese food has a balanced nutritional benefit, and the diet of the Japanese population has improved in tandem with economic development over the five past decades.[15,16]

Healthy lifestyle is, however, only one dimension of Japanese life. Japan is now struggling to deal with several major health challenges, which are partly attributable to the striking changes taking place in the demographic and social structures of its rapidly maturing society. The population is projected to shrink from 128 million in 2005 to 95 million in 2050, while the proportion of people aged 65 years or older is expected to rise to 40%.[17] Since the early 1990s, prolonged political stagnation and economic recession have helped induce a feeling of increasing inequality among this ageing population. Moreover, overweight or obesity is an increasingly serious problem, emanating from a shift towards a western-style diet and sedentary lifestyle. About a third of men aged 30–59 years are overweight or obese,[18] although the prevalence of adult obesity (4%) is well below that in other developed nations.[6]

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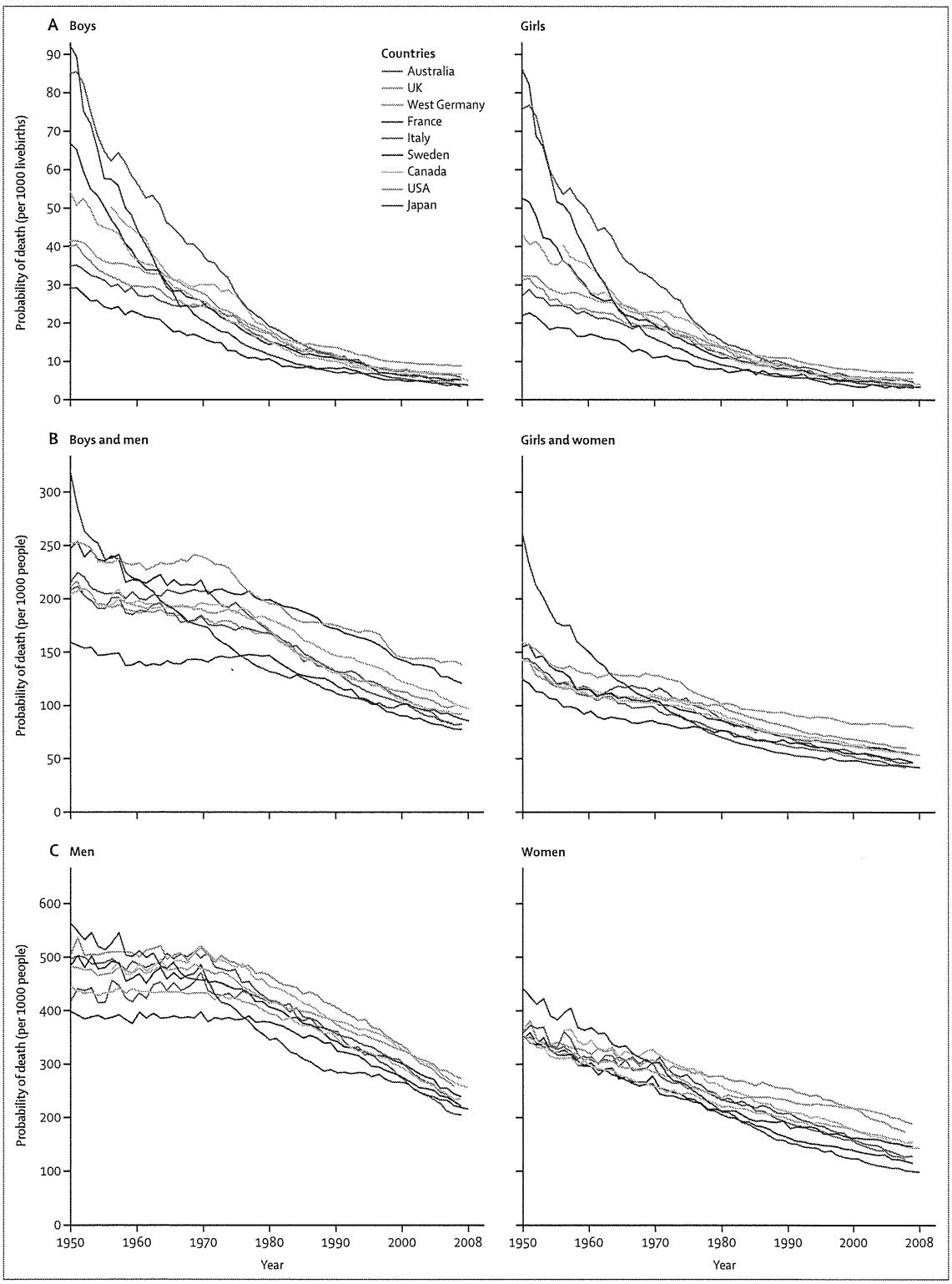

Figure 2: **Trends in the probability of death at age younger than 5 years (A), 15–60 years (B), and 60–75 years (C) in Japan and selected countries during 1950–2008**

Data from University of California at Berkeley and Max Planck Institute for Demographic Research.[7]

Furthermore, the working life of typical salaried workers in Japan seems anything but healthy—often working from early in the morning until late in the evening, 6 days a week. To relieve daily stress, some of them resort to negative health behaviours such as smoking tobacco and getting drunk after work, or even suicide in extreme cases. Death from overwork is also a serious social problem. In the context of these demographic and social challenges, what are the best strategies for Japan to protect the health and wellbeing of its ageing population?

In this first report in the *Lancet* Series, we focus on the improvements in the health of the Japanese population after World War 2. We review and analyse the best available data and evidence for population health in Japan to explore what has made the Japanese people healthy (panel 2). We provide an overview of Japan's population health in terms of the rates and distribution of mortality, and assess possible factors that might account for the longevity of the people in Japan. We also draw attention to the future challenges for Japan in controlling risk factors and social determinants to further enhance the health status of its population. We conclude with the global lessons that can be learned from Japan's experience over the past 50 years.

Panel 1: Human dry dock

The Ningen Dock (or human dry dock) is a comprehensive medical check-up system that is unique to Japan.[13] The Ningen Dock started in 1954 at a hospital in Tokyo. At that time, this service could only be afforded by business and political leaders because it took 6 days of consecutive stay in hospital and cost the equivalent of 3–4 months of a civil servant's starting salary. Advances in automated blood analysers and other testing apparatus reduced the costs, and the 1-day or 1-night stay has become the main type of service. About 3 million people per year are estimated to receive the Ningen Dock at about 1500 medical institutions in the country. A key factor that underpinned the rapid growth in the use of the Ningen Dock was that several companies covered the cost for their employees to ensure their good health.

The Ningen Dock emphasises the importance of a consultation and a post-examination interview. Over 1–2 days, clients undergo a series of medical examinations, such as blood, urine and faecal tests, radiography, and ultrasonography, and a consultation with a doctor about their medical history and lifestyle habits. After the examinations, the doctor explains the results and gives lifestyle advice to the clients.

The Ningen Dock might play a part in the primary prevention of cerebrovascular and cardiovascular diseases through the control of risk factors, such as obesity, hypertension, hyperglycaemia, dyslipidaemia, and hyperuricaemia. It might also be important for secondary prevention through the detection of diseases such as the early stages of cancer. The brain dock with MRI has expanded nationwide since it started in 1988.[14] There has also been a focus on using PET scans to detect the early stages of cancer. However, the cost-effectiveness of the Ningen Dock has been questioned.

Mortality rates in infants and young adults

Most of the increase in longevity in Japan in the past 60 years happened during 1950–65. Life expectancy at birth increased by 10·1 years in men and 11·9 years in women during this time, and these increases accounted for almost 40% of the total increase during 1950–2010 (table). Much of the increase in longevity during this early period was indicative of an enormous reduction in mortality rates in children younger than 5 years and young adults. In 1950, the probability of death before the age of 5 years was greater than 80 per 1000 livebirths and was very high compared with the probabilities of death in other developed countries, but fell to about 20 per 1000 livebirths by 1965 (figure 2). The probability of death in individuals aged 15–60 years was also much higher than in other developed countries, but fell and was on a par with probabilities of death in some developed countries by 1965. Consequently, in the 1950s and early 1960s, lower mortality rates in children younger than 5 years accounted for an increase in male life expectancy at birth of 4·1 years and female life expectancy at birth of 4·3 years, whereas reduced mortality rates in adults younger than 60 years accounted for increases in life expectancies of 3·1 years in men and 4·0 years in women (webappendix p 3).

The health of children younger than 5 years improved greatly in 1950–65 through the control of intestinal or respiratory infections and vaccine-preventable diseases that occurred with a drop in the number of neonatal deaths. The age-standardised mortality rate for communicable diseases, other than tuberculosis, decreased by 90% in children younger than 5 years (webappendix p 7); the age-standardised mortality rates for neonatal illnesses fell from 990 per 100 000 boys to 173 per 100 000 and from 772 per 100 000 girls to 133 per 100 000 during 1953–70 (webappendix p 7). Reduction in mortality rates for infectious diseases, other than tuberculosis, in children younger than 5 years accounted for increases of 2·2 years in male life expectancies at birth and 2·4 years in female life expectancies at birth. The reduction in the mortality rate for neonatal illnesses increased life expectancy by 1·0 year in both sexes (webappendix p 3).

The effect of a reduction in the mortality rate for tuberculosis on the extension of life expectancy at birth in young adults was equivalent to the reduction in mortality rate for other infectious diseases in children younger than 5 years. A 95% reduction in the number of deaths from tuberculosis in adults (aged 15–59 years) in 1950–65 (webappendix p 8) contributed to the increase in life expectancy of 2·4 years in men and 2·3 years in women (webappendix p 3).

See Online for webappendix

These reductions in mortality rates in 1950–65 indicated increasing investment in the public health sector during

Panel 2: Data sources and methods

Mortality trends

To assess trends in mortality rates in Japan since 1950, we used life tables and individual cause of death data that were obtained from different sources (Naghavi M, unpublished).[19,20] Life tables were obtained from the human mortality database at the University of California, Berkeley, CA, USA, and the Max Planck Institute for Demographic Research, Rostock, Germany.[7] We also obtained the individual cause-of-death data for 1950–2008 from the Ministry of Health, Labour and Welfare of Japan,[19] and the Institute for Health Metrics and Evaluation at the University of Washington, Seattle, WA, USA (Naghavi M, unpublished).[20] Japan has had a complete vital registration system since 1899. Although the gold standard is cause of death information from vital registration, a potential bias could be attributable to the inclusion of ill-defined codes (eg, cardiac arrest, heart failure, and senility) and unknown causes. With the algorithm developed by Naghavi and colleagues,[21] ill-defined codes and unknown causes on death certificates were redistributed and the consistency across revisions of the International Classification of Diseases and Related Health Problems (ICD) was checked. We assessed the causes that are amenable to medical care, which was originally proposed by Nolte and McKee,[22] extracting the major causes of death from the list (webappendix p 1), because the ICD avoidable causes of death were no longer applicable to our analysis after redistribution of ill-defined and unknown causes.

Health disparities

We assessed the trend in regional disparities in longevity with data for municipal life expectancy at birth at 5-year intervals during 1985–2005.[23] Municipalities are the smallest administrative units for which life expectancy data at birth are available in Japan. Sample sizes were 3307–3354 in 1985–2000 and 1963 in 2005. The substantial drop in the sample size in 2005 was due to the municipal mergers that were undertaken after 2000. We assessed temporal trends in socioeconomic disparities in the age-standardised all-cause mortality rate in the working population (aged 30–59 years), using vital records from 1980 to 2005. We used occupational status as a measure of the socioeconomic status of individuals. We standardised death rates per 100 000 at 5-year intervals using the Japanese population in 1985 as a standard population.[24] We obtained population data according to occupational status from tables reported in the national census that is undertaken every 5 years.[17,24]

demilitarisation and democratisation in the early post-war years in Japan. 32 health laws were enacted during the first decade after the war.[25] The Japanese Government collaborated with the American occupation forces in scaling up public health interventions at the community level.[26] Water supply coverage and key interventions for maternal and child health rapidly improved after the war (webappendix p 10). The effective provision of essential interventions for child survival, such as access to safe drinking water and institutional delivery, was mediated through a high level of maternal education and health facility provision that had already been achieved before the war.[27] Moreover, free treatment for tuberculosis started in 1952,[28] and included systematic screening with chest radiography and the use of streptomycin. The incidence of tuberculosis decreased sharply at a yearly rate of 11% between 1961 and 1977.[29] Additionally, as elaborated in the second report in this *Lancet* Series,[30] health insurance coverage, which was applied to about 70% of the population before World War 2, ensured access to new interventions such as drugs and vaccines for tuberculosis.

Mortality rates for non-communicable diseases

Even after communicable diseases had been successfully tackled, life expectancy of Japanese people continued to increase steadily. Male and female life expectancies at birth, respectively, increased by 5·7 years and 5·9 years during 1965–80, 3·0 years and 4·0 years during 1980–95, and 3·3 years and 2·9 years during 1995–2008 (figure 1). The risks of people dying at the ages of 15–60 years and 60–75 years fell, becoming one of the lowest in the developed world by 1980 (figure 2).

In 1950, mortality rates for cancers and ischaemic heart disease were already quite low in Japan compared with those in other developed countries, whereas the stroke mortality rate was very high. The age-standardised mortality rates for men with cancers and other neoplasms, ischaemic heart disease, and stroke were 163·8 per 100 000, 143·4 per 100 000, and 363·1 per 100 000, respectively, and for women 137·8 per 100 000, 124·8 per 100 000, and 326·5 per 100 000, respectively (webappendix pp 11–13). The low mortality rates for cancers and ischaemic heart disease in the early post-war years is one of the features of the health transition in the Japanese people. Although it is not known why the mortality rates for non-communicable diseases, other than stroke, were already low at this time, the reasons might be a favourable lipid profile and glucose metabolism, a generally low body-mass index, and other lifestyle factors relating to diet and low to moderate alcohol intake.[31] Indeed, the results of the Ni-Hon-San study[32,33] and the Honolulu Heart Program[34] showed that Japanese Americans (first-generation immigrants) were more likely to develop ischaemic heart disease and less likely to develop stroke than were Japanese people living in Japan, drawing attention to the importance of lifestyle rather than genetic background in determining the risk of disease.[32–34] The sustained increase in life expectancy at birth after the mid-1960s was largely attributable to reduced mortality rates for non-communicable diseases (webappendix p 4). From 1965 to 1980, reduced mortality rates in adults with these diseases had a substantial effect on increasing life expectancy. Reduction in the mortality rate for stroke in people aged 60–74 years increased male life expectancy at birth by 1·1 years and female life expectancy at birth by

1·0 years (webappendix p 4). Reduced mortality rate for stroke in women aged 75 years and older also accounted for a substantial increase (0·9 years) in female longevity.

The fall in stroke mortality rates slowed during 1980–95, while ischaemic heart disease mortality rates continued to fall steadily. Although not decreasing so rapidly as that of stroke, the mortality rate for ischaemic heart disease in adults aged 60–74 years nevertheless constantly decreased in this period (webappendix p 9). Consequently, although improved stroke mortality rates continued to be a major determinant of increased life expectancy, the effect of decreased mortality rates for ischaemic heart disease became pronounced during 1980–95, particularly in elderly women (webappendix p 5). Moreover, a reduction in the mortality rate in women aged 75 years and older had the largest effect on the increase in female life expectancy at birth, accounting for a change of more than 2 years (webappendix p 5). The distribution of the effects of change in mortality rate on increased longevity by age and cause of death was similar for both sexes during 1995–2008 (webappendix p 6).

An improved stroke mortality rate coincided with a reduction in average blood pressure that started in the late 1960s.[19,35,36] The numbers of deaths from stroke associated with high blood pressure have decreased over the past three decades.[37] Two factors that might be important in contributing to the falling trend in blood pressure in the population are the increased coverage of antihypertensive drugs in patients with hypertension and improved lifestyles that include reduced dietary salt intake.[38]

A population-wide approach with easy access to primary care as a result of universal health coverage has proved to be especially successful in reducing the incidence and prevalence of stroke.[39] The national government launched a strategy for the prevention and control of hypertension and stroke in 1969 and applied the strategy nationwide in 1982. This strategy included the measurement of blood pressure for screening high-risk populations, provision of national health insurance coverage for the clinical treatment of hypertension, and population-wide health education for reduction of dietary salt intake and improvement of other lifestyle-related factors. On the basis of this strategy, occupational health acts were enacted in 1972 and community health acts in 1982 to mandate the provision of programmes for primary and secondary prevention, including annual health check-ups. More than 70% of Japanese men aged 45–54 years have some form of health check-up at least once a year.[40]

A reduction in dietary salt intake has been very important for the health improvement of the Japanese population. Average salt intake among middle-aged men decreased from 30 g/day in the 1950s to 14 g/day in the 1980s.[41] Some aspects of a westernised Japanese diet, such as the improved preservation of food might have contributed to the reduction in dietary sodium consumption.[16] These results partly support the claim that both a population-based approach and subsequent advances in modern medical technologies with the scale-up of their access have made a substantial contribution to the improved life expectancy of the Japanese population.

Cultural background

Japan's success in terms of the increased life expectancy of its population is unlikely to have resulted solely from the achievement of good access to health care. Instead, other cultural background factors might be involved. Marmot and Smith[42] hypothesised that the way Japanese people relate to each other and groups might partly account for the longevity of the Japanese population.[42] Results of previous studies have lent support to this hypothesis because strong ties in Japanese communities seem to be associated with improved outcomes in mental health, dental health, and physical functioning, while buffering against the adverse effects of income inequality.[43] More than 50 years of peace and political stability might also have contributed indirectly to Japan's success in population health.

Health inequality

The homogeneous and egalitarian nature of Japanese society is shown in terms of strong educational policies, formal and informal regulations that ensure employment security, and universal access to health care. Disparities in life expectancy at birth between prefectures had started to decrease before World War 2 and continued to decline steadily until they were very low in the 1970s.[2] Indirect evidence suggests that people living in prefectures in the northeast of Japan might have shorter life expectancies than do those living in the prefectures in the southwest.[44] This geographical gradient might be attributable to differences in risk profiles such as a higher prevalence of hypertension and diabetes in the northeastern prefectures that are related to lifestyles, health-care resources, and socioeconomic status. Our additional analysis showed that the variability in life expectancy at birth across municipalities remained low from 1985 to 2005—standard deviations of longevity changed by about 1·0 for male life expectancy and 0·8 for female life expectancy, and were small compared with 2·0–2·5 and 1·5–2·0, respectively, for counties in the USA.[45]

Gaps in all-cause mortality rates for men in different occupational groups were reduced from the early 1960s to the late 1980s, except for workers in the service industry and those working in the agriculture, fishery, and forestry industries.[2] An additional analysis we undertook showed that the downward trend in socioeconomic disparities in mortality rates continued in the early 1990s, and the mortality rates for managers and professionals rose in the late 1990s, which coincided with the Asian financial crisis in 1997 (webappendix p 14).

The rapid reduction in mortality rates in Japan might have been partly attributable to the narrowing gap in income during the period of high economic growth in the 1960s and 1970s.[42] By the 1990s, more than 90% of