# 主論文の要旨

# Estimation of the unvaccinated among those aged less than 25 years according to aimag and its association with incidence of measles outbreak 2015-2016 in Mongolia

各県の 25 歳未満のワクチン未接種者の推定と 2015 年から 2016 年にかけてモンゴルにおいて 発生した麻疹流行との関連

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### [Introduction]

Measles may be potentially eliminable because human are the sole pathogen reservoir, accurate diagnostic tests exist and an effective, practical intervention is available at a reasonable cost. Mongolia had an epidemic of measles in 2015-2016, even though more than 90% of the population have been vaccinated since 1997. According to WHO position paper, the risk of measles outbreaks is determined by the rate of accumulation of susceptible people in the population and WHO advises to take a more extensive assessment of the accumulation of susceptible persons and undertake it in case of countries close to measles elimination.

This study aimed to estimate the proportion of the unvaccinated among those aged less than 25 years in 2015 according to aimag based on the measles vaccine coverage in 1991-2014. Furthermore, the associations between the accumulated unvaccinated proportion (AUP) in 2015 and the incidence of measles in the epidemic in 2015-2016 were examined.

# [Materials and methods]

Mongolia has 22 provinces (aimags) including Ulaanbaatar (Fig. 1). The data of vaccination coverage during 1991-2014 and measles incidence according to aimag were obtained from the National Center for Communicable Diseases, Mongolia. Accumulated unvaccinated proportion (AUP) among those aged 1 to 24 years in 2015 was estimated from the unvaccinated at the 1st dose of 1991 to 2014.

The associations between the estimated AUP and incidence of measles in the epidemic during 2015-2016 were examined with Pearson's correlation coefficients. P values less than 0.05 were considered statistically significant.

### Results

The first dose of unvaccinated proportion of children throughout Mongolia was reduced to nearly one fifteenths from 28.0% in 1991 to 1.8% in 2014. In Ulaanbaatar, the unvaccinated proportion was reduced to one seventh from 20.1% in 1991 to 2.8 % in 2014. The reduction was achieved around 2002 (98.4% of 1991), although the unvaccinated proportion was slightly increased in some aimags after 2002 (Fig. 2 and Table 1).

Govisumber with the smallest target children (7,912 children) had the highest AUP (21.8%), followed by Bayankhongor (20.3%) and Zavkhan (18.6%) aimags. The AUP was low in Selenge (2.7%), Orkhon (3.6%), and Dornod (4.4%) aimags. The AUP in whole country was 8.7% (Table 2).

Among 53,737 measles cases during 2015-2016, 30,164 (56.1%) individuals were reportedly 1 to 24 years old. The city of Ulaanbaatar had the largest number of cases among those aged 1 to 24 years (21,148 cases), followed by Darkhan-Uul (1,421 cases), Uvurkhangai (745 cases), Selenge (668 cases), Dornogovi (492 cases), and Orkhon (468 cases) aimags.

There were no significant correlations between the AUP and measles incidence in 2015-2016 in both among those aged 1 to 24 years (r=-0.167 and p=0.459 and whole population (r=-0.127

and p=0.574), as shown in Fig 3A and 3B.

Although the AUP was relatively low in Ulaanbaatar (5.2%) and Darkhan-Uul (10.0%), the incidence of measles among those aged 1 to 24 years and among the whole population was higher in Ulaanbaatar (50.5 and 26.3 per 1,000, respectively) and Darkhan-Uul (32.2 and 24.1 per 1,000, respectively). Similarly, the incidence among children aged 1 to 4 years, age group effectively protected by recent vaccination, had no correlation with the AUP (r=0.077 and p=0.733).

Then we analyzed the correlation between the unvaccinated density per 1 km<sup>2</sup> of those aged 1 to 24 years in a logarithmic scale and the incidence among those aged 1 to 24 years. The correlation was significant when all 22 aimags were included (r=0.725, p<0.01), while there was no correlation when Ulaanbatar and Darkhan-Uul were removed (r=-0.044, p=0.853), as shown in Fig 4.

# [Discussion]

This is the first report in English on the trends in measles vaccination coverage between 1991-2014 according to aimag collected by Mongolian government.

Measles outbreak might be explained by the accumulation of susceptible person and/or their low immunity status. The trends in the measles vaccination coverage showed that the unvaccinated proportion among the target population was relatively large before 2001, although some aimags had a slightly large unvaccinated proportion possibly due to poor supply of measles vaccine, disruption of vaccine cold chain, absence of registered children moving to another aimag, etc. It indicated that the proportion of children sensitive to measles were high among those aged 15 years or older. However, our examination suggested that the incidence might not be influenced by the range of 2.7% to 21.8% of the AUP among those aged 1 to 24 years.

A total of 1,180,565 (92.3%) children were vaccinated and 97,888 (7.3%) were unvaccinated among 1,278,453 target children during 1991-2014. In order to reduce the unvaccinated children, periodic nationwide measles supplemental immunization activities (SIAs) were implemented 5 times in 1994, 1996, 2000, 2007 and 2012 for the target age groups. The vaccination was administered to 162,751 (74.6%) children of 218,034 target children in 1994, 541,441 (97.5%) of 554,968 target children in 1996, 353,389 (96.1%) of 674,38 target children in 2000, 133,648 (96.9%) of 137,790 target children in 2007, and 522,429 (96.1%) of 560,592 target children in 2012. SIAs should be applied based on precise information from monitoring the susceptible people to prevent an outbreak of measles.

We assumed that the incidence in each aimag was strongly influenced by the proportion of the unvaccinated. However, there was no significant correlation between the AUP and the incidence. There might be two possibilities; 1) the estimated AUP did not reflect the actual proportion of susceptible children due to the problems stated in the following limitations, and 2) the AUP with the range in this study did not influence the incidence according to aimag. Unvaccinated population density of those aged 1 to 24 years had a significant correlation (p<0.01) with measles

incidence among those aged 1 to 24 years. If two highly populated aimags (Ulaanbaatar and Darkhan-Uul), the correlation was not observed (r=-0.044, p=0.853).

There are several limitations in this study. The first was the inaccuracy of the statistical data on the vaccine coverage and measles incidence. Since these were the only available nationwide data, there was no alternative to estimate the coverage and incidence. The second was the movement of people to other areas, mainly from the rural areas to urban areas during 1991-2015. For example, the population in Ulaanbaatar was 600,985 in 1991 and 1,345,500 in 2015, which showed 2.3 times increase in the population of Ulaanbaatar. The third was the age range used for the estimation of the unvaccinated proportion. The vaccine coverage for those aged 25 years or older in 2015 was not available. The fourth was the vaccination coverage of the second dose during 1991-2008 was not available, because the data on the second dose was not collected according to the health statistical regulation. Finally, the number of SIAs was not taken into account, because the number according to aimag was not available.

# [Conclusion]

Unvaccinated proportion among those aged 1 to 24 years in the whole country was reduced to one fifteenth (from 28.0% in 1991 to 1.8% in 2014) during last 25 years. In the range of AUP between 2.7% and 18.5% among those aged 1 to 24 years, the vaccination coverage was not a significant factor for the incidence according to aimag at measles epidemic 2015-2016 in Mongolia. The density of the unvaccinated among those aged 1 to 24 years had a significant correlation with measles incidence 2015-2016, although the correlation disappeared when two highly populated aimags (Ulaanbaatar and Darkhan-Uul aimag) were excluded.