ABSTRACT
Cervical cancer is the second commonest cancer among females in Indonesia. The Global Burden of Disease 2017 study provides the comprehensive estimates of all diseases, including cervical cancer. This study was aimed to give overview of burden of cervical cancer at national and provincial level in Indonesia from 1990 to 2017. This was descriptive study using the GBD 2017 results for cervical cancer incidence, prevalence, deaths, disability-adjusted life-years (DALYs), and risk factors. Cervical cancer incidence in Indonesia rose slightly (17%) from 7.4 to 8.7 per 100,000 women. Prevalence rate rose 20.8% in the same period, from 43.3 to 52.4 per 100,000. Meanwhile, death rate was almost same from 3.3 and 3.7 per 100,000 respectively. DALYs of cervical cancer increased significantly from 211,616 to 303,308. At provincial level, in 2017 the highest prevalence rate and incidence rate were in North Maluku and West Papua. The lowest were in the North Kalimantan and North Sumatera. Incidence rate and death rate of cervical cancer rose from age of 30-34 and peaked at 95+. Meanwhile, prevalence rate and DALYs rate started at age of 25-29 and steadily high at age of 44. Risk factors contributed to cervical cancer were unsafe sex and tobacco.

Keywords: cervical cancer, Burden of Disease, DALY, Indonesia

1. INTRODUCTION
Cervical cancer is the second commonest cancer among females in Indonesia. This disease becomes national concern for the prevention and early detection. Screening of cervical cancer was developed since 2008 and became national program. It was stated in stated in Ministry of Health Decree No 34/2005 (1) and was included in Ministry of Health Strategic Plan 2015-2019 (2). The screening also becomes minimum services standard for women aged of 30-59 (3). Since 2014, the program was also supported by national health insurance (BPJS) through non capitation schene (4). Screening coverage of cervical cancer in Indonesia till 2016 was still low. It was only 5.15% from target, women aged 30-50 years (5), increased from 2.45% in 2014 (6).

Incidence of cervical cancer in Indonesia was 17.3 per 100,000 women (7). In Jakarta Province that has been developing population based cancer registration, the incidence was 9.25 per 100,000 women (8). This incidence is still high even though cervical cancer can be prevented by HPV vaccination and detected early. Unfortunately, the vaccination has not been national program.

Cervical cancer is influenced by many factors, including unsafe sex, delivery status, and marital status (9). Human papilloma virus was the main infection related to cervical cancer. Tobacco is also common risk factors for most of cancers, including cervical cancer. Controlling the risk factors and early detection are the keys for preventable disease like cervical cancer.

National and provincial burden of cervical cancer is needed to determine its prevention and control. The Global Burden of Disease 2017 study provides the comprehensive estimates of all diseases, including cervical cancer, for its prevalence, incidence, death, DALYs, and risk factors. Based on these situations, this study was aimed to give overview of burden of cervical cancer at national and provincial level in Indonesia from 1990 to 2017.
2. METHOD
This was a descriptive study using the Global Burden Study 2017 results for cervical cancer incidence, prevalence, deaths, disability-adjusted life-years (DALYs), and risk factors. The burden were determined for national and 34 provinces in Indonesia. We provided estimates by year and age using standard GBD2017 statistical methods.

3. RESULTS AND DISCUSSION
Cervical cancer incidence in Indonesia rose slightly from 7.4 per 100,000 women in 1990, to 8.7 per 100,000 women in 2017 or increased 17% and ranked number 5 from all cancers. Prevalence rate of the cancer rose 20.8% in the same period, from 43.3 to 52.4 per 100,000, it was rank number 2. Meanwhile, death rate was almost same from 1990 and 2017, with 3.3 and 3.7 per 100,000 respectively. DALYs rate increased only 5% in the period with majority contribution from YLL than from YLD. But in number, it increased significantly from 211,616 to 309,308 (Table 1).

Table 1. Burden of Cervical Cancer in Indonesia, 1990 and 2017

| Burden   | 1990       | 2017       | % Increase** |
|----------|------------|------------|--------------|
| incidence| 13,834     | 22,497     | 17.0         |
| prevalence| 80,407     | 135,149    | 2.8          |
| deaths   | 6,653      | 9,405      | 42.2         |
| DALY     | 211,616    | 309,308    | 47.0         |
| YLL      | 260,643    | 393,675    | 47.0         |
| YLD      | 6,422      | 10,633     | 63.6         |

*rank of the rate among all cancers
**increase of the rate

At provincial level, by 2017 the highest incidence rate and prevalence rate of cervical cancer were in North Maluku and West Papua. The lowest were in the North Kalimantan and North Sumatera (Figure 1).

The highest death rate and DALY rate were in Gorontalo and North Maluku, and the lowest were in North Kalimantan and North Sumatera (Figure 2).

Incidence rate of cervical cancer increased dramatically from age of 30-34 years and peaked at 95+. Meanwhile, prevalence rate rose since age of 25-29, reached the peak at 40-44, than declined after that age (Figure 3).

Meanwhile, death rate of cervical cancer rose from age of 30-34 years and peaked at 95+. Meanwhile, DALYs rate started at age of 25-29 and reached the peak at 70-74 (Figure 4).

Figure 1. Incidence rate and Prevalence Rate of Cervical Cancer in Indonesia, by Province, 2017

Figure 2. Death Rate and DALY of Cervical Cancer in Indonesia, by Province, 2017

Figure 3. Incidence Rate and Prevalence Rate of Cervical Cancer in Indonesia, by Age, 2017

Figure 4. Death Rate and DALY Rate of Cervical Cancer in Indonesia, by Age, 2017
Risk factors contributed to cervical cancer death and DALY were unsafe sex and tobacco. Unsafe sex (3.73 per 100,000) contributed much bigger than tobacco (0.24 per 100,000) (Table 2)

Table 2. Risk Factors contributed to Cervical Cancer in Indonesia, 2017

| Burden | Unsafe Sex | Tobacco |
|--------|------------|---------|
|        | Number     | Rate per 100,000 | Number | Rate per 100,000 |
| Death  | 9,495      | 3.72     | 623    | 0.24 |
| DALY   | 308,369    | 119.82   | 18,385 | 7.12 |

Discussion

Burden of cervical cancer, in term of incidence in Indonesia is still high and rose slightly since 1990 till 2017. This incidence (8.72 per 100,000 women) was lower than estimacy from Global Burden of Cancer (Globocan) which resulted the incidence in 2012 was 17.3 per 100,000 women and 23.4 per 100.00 in 2018 (7,10). In Jakarta province, the incidence was 9.26 per 100,000 (11). In Indonesia, the prevalence of cancer in general was 1.4 per 1000 people in 2013 and 1.79 per 1000 people in 2018 (12,13). In Southeast Asia region, incidence of cervical cancer decreased from rank number 4 in 1990 to number 7 in 2017, when in Indonesia the incidence was still ranked number 5. But the rate in this region was still high for 9.39 per 100,000. Meanwhile, in central Europe, it ranked number 14 and in United States it was rank number 22 by 2017. (14)

Incidence and of cervical cancer in Indonesia which remained high in last 27 years indicates the program of prevention need to be strengthened, especially for prevention through vaccination and early detection. The program of screening on this cancer should be expanded and reach all target. Death rate (3.72 per 100,000) was lower than data from Globocan 2012 (8.2 per 100,000) and globocan 2018 (13.9 per 100,000) (10,15). This difference might cause by different method of data sources and method of analysis. Nevertheless, the burden in term of death brought information that cervical cancer mortality still became problem to be solved. Screening and early detection should be increased to give more chances treatment of cancer in early stage or even in pre cancer stage. Treatment of pre cancer lesion can be conducted in Primary Health Centers (16).

DALY, YLD, and YLL increased slightly from 1990 to 2017. The contribution of YLL was dominant compared with YLD. In Southeast Asia region, DALY of cervical cancer ranked number 8, while in Indonesia still number 7. In The United States, DALY of cervical cancer deceased from 70.2 per 100,000 (rank number 18) to 63.4 per 100,000 (rank number 19). (14,17). It means that cervical cancer was deadly and need effort on treatment. Even though cervical cancer can be prevented and detected early, DALY of this cancer still increased. It implied that all related stakeholders should work together to prevent it.

Burden of cervical cancer in eastern part of Indonesia such as North Maluku and west Papua was the highest, in term of incidence rate and prevalence rate. Meanwhile, this is low in North Kalimantan and North Sumatera. Similarly, death rate were highest in Gorontalo and North Maluku, and the lowest were in North Kalimantan and North Sumatera. This needs more explanation why these rates were high in this part. Data from Basic Health research 2013 and 2018 showed that prevalence of cancer was high in Jogyakarta province (4.1 and 4.86, per 1000) and Central Java province (2.1 per 1000 in 2013 and 2018) and quite high in North Maluku (1.2 and 0.9 per 1000), but it was low in West Papua (0.6 in 2013 and 1.3 per 1000). It was also quite high in North Sumatera (1.0 and 1.5 per 1000). But, the highest DALYs in number were highest in East Java and West Java, and the lowest were in North Kalimantan and West Papua.

Incidence rate and death rate seemed to increase as increase of aged, with dramatic increase from age of 30-34 years and peaked at 95+. This indicates that new cases of cervical cancer are getting young. The government should consider the screening program to the younger women with aged below 30 years. Cervical cancer screening is recommended beginning at age 21 years and continuing through age 65 years for both vaccinated and unvaccinated women. (18,19).

Meanwhile, prevalence rate rose since age of 25-29, reached the peak at 40-44 and then declined after that age. This might be related to high of death rate, as shown in DALY rate and YLL rate. In general population, prevalence of cancer in Indonesia increased at age of 35, peaked at age of 55-64, and declined after age of 55. (13). In term of DALYs, the rate increased at age of 25-29 and steadily high till 44 years and reached the peak at 70-74. It was related to the high prevalence of cervical cancer.

Risk factors associated with cervical cancer were unsafe sex and tobacco. Unsafe sex could be mode of transmission of Human Papilloma Virus, as the main infection related to cervical cancer (9). Tobacco could be the factor that causes the gene mutation to initiate cervical cancer. Mass campaign on safe sex and tobacco control should be strengthened in Indonesia. Tobacco control can be conducted through community movement on healthy live (Germas), (20), and efforts of MPOWER, Monitor (monitor prevenence of smoking, Protect (protect people from smoke), Offer (offer quite smoking), Warn (warn the hamr of smoking), Enforce (ban the smoke advertisement), and Raise taxes of cigarette (21).

Based on the findings, program of early detection should be implemented and expanded. Recent research into alternative approaches for the secondary prevention of cervical cancer offers new possibilities for more affordable and implementable programs, particularly "screen and treat" programs that have been tested in randomized trials in South Africa and India and shown that HPV-based screening coupled with treatment using cryotherapy
significantly reduces the incidence of cervical cancer precursors and cervical cancer. (22).

4. CONCLUSION
The burden of cervical cancer increased slightly from 1990 to 2017. There was difference burden of cervical cancer each province in Indonesia. The burden increase started at age of 25 and peaked at 95+. The main risk factors of cervical cancer were unsafe sex and tobacco.

ACKNOWLEDGMENT
Thank you for Institute of Health Metric and Evaluation (IHME), Head of National Institute of Health Research and Development (NIHRD), Ministry of Health, Head of Center for Humanity and Health Management, NIHRD which supported us to conduct the research.

REFERENCES

[1] Kemenkes. Peraturan Menteri Kesehatan R.I. Nomor 34 tahun 2015 tentang PENangguhan Kanker Payduara dan Kanker Leher Rahim. 2015.

[2] Kemenkes. Keputusan Menteri Kesehatan R.I. Nomor HK.02.02/Menkes/52/2015 tentang Rencana Strategis Kementerian Kesehatan R.I. tahun 2015-2019. 2015.

[3] Kemenkes. Peraturan Menteri Kesehatan No.43 Tahun 2016 tentang Standar Pelayanan Minimal Bidang Kesehatan. 2016;

[4] Kemenkes RI. Peraturan Menteri Kesehatan R.I. Nomor 52 tahun 2016 tentang Standar Tarif Pelayanan Kesehatan dalam Penyelenggaraan Program Jaminan Kesehatan. Jakarta: Kementerian Kesehatan RI; 2016.

[5] Kemenkes. Profil Penyakit Tidak Menular 2016. 2017.

[6] Wahidin M. Deteksi Dini Kanker Leher Rahim dan Kanker Payudara di Indonesia 2007-2014. Bul Jendela Data dan Inf Kesehat [Internet]. 2015;1. Available from: http://www.depkes.go.id/download.php?file=download/pusdatin/buletin/buletin-kanker.pdf mugi wahidin buletin jendela

[7] IARC. Globocan 2012: Country Fast Stat Estimated age-standardised incidence and mortality rates: men Estimated incidence , mortality and 5-year prevalence: men GLOBOCAN 2012 : Country Fast Stat. 2012. p. 1–7.

[8] Wahidin M, Noviani R, Hermawan S, Andriani V, Ardian A, Djarir H. Population-Based Cancer Registration in Indonesia. Asian Pac J Cancer Prev [Internet]. 2012;13:1709–10. Available from: http://journal.waocp.org/article_26398_286f4c cdb00c5644a28ddd01b1b4048d.pdf

[9] Rasjidi I. Epidemiologi Kanker pada Wanita. CV Sagung Seto Jakarta. 2010.

[10] IARC. Globocan 2018: Country-specific, Incidence Method, National Country-specific, Mortality. 2019.

[11] Wahidin M, Noviani R, Hermawan S, Andriani V, Ardian A, Djarir H. Population-based cancer registration in Indonesia. Asian Pacific J Cancer Prev. 2012;13(4).

[12] Kemenkes. Riset Kesehatan Dasar (Riskesdas) 2013. Jakarta; 2013. 1–384 p.

[13] Kemenkes. Riset Kesehatan Dasar (Riskesdas) 2018. 2019.

[14] IHME. Global Burden of Disease 2017. 2018.

[15] IARC. Globocan 2012: Country Fast Stat http://globocan.iarc.fr/old/factsheet.asp. 2012;1–7.

[16] Kemenkes. Pedoman Teknis Pengendalian Kanker Payudara dan Kanker Leher Rahim. 2013;

[17] Kemenkes. Analisis Beban Penyakit Nasional dan Sub Nasional Indonesia 2017. Jakarta; 2018.

[18] Saslow D, Solomon D, Lawson HW, Kulasingam S, Cain J, Francisco AR, et al. American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology Screening Guidelines for the Prevention and Early Detection of Cervical Cancer. J Low Genit Tract Dis. 2014;16(3):175–204.

[19] Screening for cervical cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2012;158(11).
[20] RI P. Instruksi Presiden Nomor 1 Tahun 2017 tentang Gerakan Masyarakat Hidup Sehat. Jakarta; 2017.

[21] WHO. MPOWER: A Policy Package to Reverse Tobacco Epidemic. Geneva: WHO Library Cataloguing-in-Publication Data; 2008.

[22] Denny L, Anorlu R. Cervical Cancer in Africa. 1434 Cancer Epidemiol Biomarkers Prev. 2012;21(9):1434–9.