

# 22. maternal maortality audit based on district

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## Maternal mortality audit based on district maternal health performance in East Java Province, Indonesia



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### ABSTRACT

**Background:** Maternal mortality rate (MMR) in Indonesia is still high, including in East Java Province. Although the successful decline in MMR has been achieved, more action still needed to maintain and accelerate the process. Several factors that affect the maternal mortality, especially referral factor, and districts maternal health services quality, need to analyse. This study was conducted to analyze the correlation between maternal mortality with labour referral and maternal health service quality in 10 regencies/cities in East Java Province, Indonesia

**Methods:** The case-control study among 2 groups of 5 regencies/cities with the highest and lowest MMR in East Java Province in 2015. The indicators used, were maternal referral relay in maternal mortality report, frequencies of antenatal care, labor by health care provider, puerperal health care, obstetric complication management, detection

of high-risk pregnancy by community and healthcare personnel, and family planning program.

**Results:** Total number of maternal mortality in East Java province in 2015 was 531, with MMR were 89,6/100.000 living birth. From the comparative study, we found a significant difference in indicators of high-risk pregnancy detection by healthcare personnel ( $p=0,035$ ) and obstetrics complications management ( $p=0,006$ ). There were no significant differences in frequencies of antenatal care, labor by health care provider, puerperal health care, detection of high-risk pregnancy by community, and family planning program in 10 regencies/cities in East Java Province, Indonesia

**Conclusion:** High-risk pregnancy detection by healthcare personnel and obstetrics complications management were related with MMR in 10 districts in East Java province, Indonesia.

**Keywords:** maternal mortality, MMR, SDGs

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### INTRODUCTION

Indonesia needs address high maternal mortality rate from all sides. Based on WHO estimates in 2013, MMR in Indonesia is 190/100,000 live births. The target of Sustainable Development Goals (SDGs), by 2030, all countries should reduce at least two-thirds of MMR in 2010. Global average MMR target in 2030 is 70/100,000 live births, and no country has more MMR than 140/100,000 live births. To lower maternal mortality, it needs the cooperation of many parties, a policy of births assisted by skilled health personnel should offset by the improved quality of childbirth services. Maternal and child services in Indonesia can be evaluated every month through reports from the local area monitoring of maternal and child health services. The frequency of antenatal visits (K1 and K4), early detection of high-risk pregnancies both by society and by healthcare personnel, childbirth assisted by a trained healthcare personnel, and obstetric complications management is an indicator of *prepartum* and *intrapartum* maternal health services. Some indicators of *postpartum* services include puerperal women care and family planning programs. Among *prepartum*, *intrapartum*, and *postpartum* services will affect

the quality of maternal health services and referral system in an area.<sup>1,3,7,11</sup>

Structuring the region was very important in regulating access to maternal referral in an area to reduce maternal mortality. Maternal referrals system in Indonesia starting from the community, village/private midwives, general physician/primary public health centres, and lastly in the hospital with specialistic services. The success of the maternal referral system is very influenced by the maternal health services quality in an area. Therefore, in this study, we want to analyse the correlation between MMR with labor referral system and districts maternal health services and know the factors affecting incidence of maternal mortality in East Java, Indonesia.<sup>6,10</sup>

### METHODS

The research design used in this study was a case-control study. Five regencies/cities with highest maternal mortality as the case groups and five regencies/cities with the lowest maternal mortality as the control groups. The aims of this study was to analyse the correlation between MMR with labor referral relay in maternal mortality

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report, frequencies of antenatal care visits, child-birth assisted by a trained healthcare personnel, puerperal women care, obstetric complication management, detection of high-risk pregnancy by community and healthcare worker, and also family planning program between two groups.

## RESULTS

### Labor Referral in Maternal Mortality Report in 10 Regencies/Cities in East Java Province, Indonesia

From maternal mortality reports, we found that mostly, all cases of maternal mortality had undergone referral relay 2-3 times before the last place in which maternal mortality happened.

**Table 1** The Number of Referral Relay in 5 Cities/Regencies with the Highest and Lowest MMR in East Java 2015 (Dinkes Provinsi Jawa Timur, 2016)

	Referral Relay					
	0	1	2	3	4	>4x
Bojonegoro Reg.	0	6	9	6	2	0
Situbondo Reg.	2	0	6	3	1	1
Probolinggo Reg.	1	4	15	6	0	0
Lumajang Reg.	3	4	14	3	0	0
Bondowoso Reg.	1	4	6	6	2	0
Madiun City	0	0	0	0	0	0
Madiun Reg.	0	0	4	0	0	0
Sumenep Reg.	0	0	6	1	0	0
Blitar City	0	0	1	0	0	0
Pamekasan Reg.	0	2	6	0	0	0
Total	7	20	67	25	5	1

**Table 2** The Cause of Maternal Mortality In 10 Cities / Regencies with the Highest and Lowest MMR in East Java 2015 (Dinkes Provinsi Jawa Timur, 2016)

	Bleeding	PE/E	Infection	Heart		
				Disease	Emboli	Others
Bojonegoro Reg.	5	7	2	1	0	8
Situbondo Reg.	1	5	2	0	0	5
Probolinggo Reg.	3	8	0	5	0	10
Lumajang Reg.	6	2	1	3	0	12
Bondowoso Reg.	4	1	3	6	0	5
Madiun City	0	0	0	0	1	0
Madiun Reg.	0	1	0	2	1	0
Sumenep Reg.	0	5	1	1	0	0
Blitar City	0	1	0	0	0	0
Pamekasan Reg.	3	2	1	0	0	2
Total	22	32	10	18	1	42

Table 1 showed that relay in labor referral with maternal mortality outcome in 10 regencies/cities were very varied. Referral relay in 10 regencies/cities occurred 0 time with 7 cases (5.6%), 1 time with 20 cases (16%), 2 times with 67 cases (53.6%), 3 times with 25 cases (20%), 4 times with 5 cases (4%), and there was 1 case (0.8%) of maternal mortality occurred after >4 times of referral relay.

Table 2 showed that maternal mortality in 10 regencies/cities in East Java, 2015, were mostly caused by preeclampsia/eclampsia with 32 cases (25.6%). The other cases were bleeding with 22 (17.6%), infection with 10 (8%), heart disease with 18 (14.4%), emboli 1 (0.8%), and others with 42 (33.6%).

Table 3 showed maternal mortality had occurred in the general hospitals with 74 (59.2%), in private hospitals with 24 (19.2%), in public health centers with 3 (2.4%), in the maternity hospital with 3 (2.4%), in midwife practices / Polindes with 1 (0.8%), at patient's home with as 16 (12.8%), and in the journey as many as 4 cases (3.2%).

### Overview of MMR in East Java 2015

In 2015, five regencies/cities with the highest maternal mortality in East Java were Bondowoso Regency with MMR 187.95/100.000 lives birth, Lumajang Regency with MMR 155.73/100.000 lives birth, Probolinggo Regency with MMR 140.62/100.000 lives birth, Situbondo Regency with MMR 137.78/100.000 lives birth, and Bojonegoro Regency with MMR 128.22/100.000 lives birth. While five regencies/cities in East Java with the lowest MMR was Madiun City with MMR 0, followed by the Madiun Regency with MMR 41.88/100.000 lives birth, Sumenep Regency with MMR 44.89/100.000 lives birth, Blitar City with MMR 48.80/100.000 lives birth, and Pamekasan Regency with MMR 59.74/100.000 lives birth.

### Picture of Maternal Health Services in the Regency/City with the Highest and Lowest MMR in East Java 2015

Table 4 shows that five regencies/cities with the highest MMR has K1 coverage which is already quite high (97.31 to 100.21%), but there are 4 regencies with K4 coverage below 90% which are Bondowoso Regency (81.49%), Probolinggo Regency (88.11%), Bojonegoro Regency (88.31%), and Lumajang Regency (89.01%). Delivery by skilled birth attendance coverage and services for *postpartum* mothers in five regencies/cities with the highest maternal mortality has been good enough. As for the indicators of high-risk pregnancy detection, by the community and health personnel showed a moderately high coverage (9.75 to

**Table 3** Place of Maternal Mortality in 5 Cities/Regencies with the Highest and Lowest MMR in East Java 2015 (Dinkes Provinsi Jawa Timur, 2016)

	Place of Mortality						
	Gen Hosp	Priv Hosp	PHC	MH	Mid wife/Polin des	Pt's house	Journ
Bojonegoro Reg.	13	8	0	0	0	1	1
Situbondo Reg.	8	3	0	0	0	2	0
Probolinggo Reg.	17	2	0	0	0	4	3
Lumajang Reg.	8	8	1	2	1	4	0
Bondowoso Reg.	13	1	1	0	0	4	0
Madiun City	0	0	0	0	0	0	0
Madiun Reg.	2	2	0	0	0	0	0
Sumenep Reg.	6	0	0	0	0	1	0
Blitar City	1	0	0	0	0	0	1
Pamekasan Reg.	6	0	1	1	0	0	0
Total	74	24	3	3	1	16	4

\* Gen hosp: general hospital, Priv hosp: private hospital, PHC: public health centre, MH: maternal hospital, Midwife/Polin des: village maternity house, Pt's house: patient's house, Journ: Journey.

**Table 4** Percentage Coverage of Maternal Health Services in the Regency/City with the Highest Maternal Mortality in East Java 2015 (Dinkes Provinsi Jawa Timur, 2016)

Cities/Regencies	K1	K4	SBA	Puer	Compl	HRP Soc	HRP HP	New FP	Active FP	MMR
Bojonegoro Reg.	98.49	88.31	99.28	97.07	124.4	17.75	45.43	0.90	69.89	128.22
Situbondo Reg.	100.21	91.7	97.05	96	116.26	9.75	35.97	10.50	68.72	137.78
Probolinggo Reg.	97.41	88.11	96.54	96.18	133.71	19.1	31.8	10.00	70.91	140.62
Lumajang Reg.	98.67	89.01	98.69	92.63	116.87	15.8	25.63	13.10	69.91	155.73
Bondowoso Reg.	97.31	81.49	86.15	91.53	90.48	11.53	21.48	11.20	72.23	187.95

**Table 5** Percentage Coverage of maternal health services in the regency/city with the lowest maternal mortality in East Java 2015 (Dinkes Provinsi Jawa Timur, 2016)

Cities/Regencies	K1	K4	SBA	Puer	Compl	HRP Soc	HRP HP	New FP	Active FP	MMR
Madiun City	99.68	97.15	98.56	97.43	91.45	11.8	23.09	9.30	56.34	0
Madiun Reg.	97.92	91.83	93.4	92.74	84.04	10.77	20.51	7.50	65.32	41.88
Sumenep Reg.	104.35	94.72	98.83	99.94	85.52	11.02	16.88	18.50	51.78	44.89
Blitar City	91.25	85.56	89.11	86.25	68.3	18.78	24.1	7.60	62.81	48.8
Pamekasan Reg.	100.01	93.82	99.78	97.05	94.44	12.54	20.51	15.10	53.12	59.74

\* K1: 1st antenatal visit, K4: 4th or more antenatal visits, SBA: delivery by skilled birth attendance, Puer: puerperal health care, Compl: obstetric complication management, HRP Soc: detection of high-risk pregnancy by community, HRP-HP: detection of high-risk pregnancy by healthcare worker, New FP: new participant of family planning program, Active FP: active participant of family planning program, MMR: maternal mortality ratio.

45.43%). From the above data we also found that couples of childbearing age using contraception is already quite high (69.89 to 72.23%).

From the data in table 5, the lowest MMR group obtained high K1 coverage (91.25 to 104.35%). For the K4 coverage, only Blitar city that has 85.56% K4 coverage (below the target 90%). For coverage of births attended by skilled health personnel and services for puerperal women, only Blitar city had just under 90% coverage, which amounted to respectively 89.11% and 86.25%. For the indicator

of detection of high-risk pregnancy by community is already above the target of the province (> 10%), but there is one regency with detection of high-risk pregnancy by health personnel coverage is still below the target of East Java province (<20%), which is Sumenep Regency (16.88%). For obstetric complications management by healthcare personnel, Blitar city still has a lower coverage of the target (<80%), while contraceptive coverage in five regencies/cities with the lowest MMR were below 70%.



**Table 6** The Maternal Health Services Indicator in 10 Regencies/Cities with the Highest and Lowest MMR in East Java Province 2015

	Highest MMR		Lowest MMR	
	Mean	S/D	Mean	S/D
K1	98,41	± 1,17	98,64	± 4,76
K4	87,72	± 3,76	92,61	± 4,38
Puer	94,68	± 2,44	94,68	± 5,37
COMPL	116,34	± 16,09	84,75	± 10,13
HRP HP	32,06	± 9,31	21,01	± 2,80
New FP	9,14	± 4,75	11,6	± 4,94
Active FP	89,98	± 1,49	82,1	± 10,93

\* K1: 1st antenatal visit, K4: 4th or more antenatal visits, Puer: puerperal health care, Compl: obstetric complication management, HRP-HP: detection of high-risk pregnancy by healthcare worker, New FP: new participant of family planning program, Active FP: active participant of family planning program

**Table 7** The Mean and Standard Deviations for Delivery by Skilled Birth Attendance and Detection of High-Risk Pregnancy by Community in 5 Regencies/Cities with the Highest and Lowest MMR in East Java Province 2015

	Highest MMR		Lowest MMR	
	Mean	S/D	Mean	S/D
HRP HP	14,78	± 4,01	12,98	± 3,31
SBA	95,54	± 5,37	95,93	± 4,55

\*SBA: delivery by skilled birth attendance, HRP HP: detection of high-risk pregnancy by community

**Table 8** Results of ANOVA Test on the 1st Antenatal Visit, 4th or More Antenatal Visits, Puerperal Health Care, Obstetric Complication Management, Detection of High-Risk Pregnancy by Health Care Worker, New Participant of Family Planning Program, and Active Participant of Family Planning Program

Group	Indicator	Mean ± SD	p-value
Highest MMR	K1	98,41 ± 1,17	0,921
Lowest MMR		98,64 ± 4,76	
Highest MMR	K4	87,72 ± 3,76	0,95
Lowest MMR		92,61 ± 4,38	
Highest MMR	Puer	94,68 ± 2,44	1,000
Lowest MMR		94,68 ± 5,37	
Highest MMR	COMPL	116,34 ± 16,09	0,006
Lowest MMR		84,75 ± 10,13	
Highest MMR	HRP HP	32,06 ± 9,31	0,035
Lowest MMR		21,01 ± 2,80	
Highest MMR	New FP	9,14 ± 4,75	0,446
Lowest MMR		11,6 ± 4,94	
Highest MMR	Active FP	89,9 ± 1,49	0,162
Lowest MMR		82,1 ± 10,93	

\*K1: 1st antenatal visit, K4: 4th or more antenatal visits, Puer: puerperal health care, Compl: obstetric complication management, HRP HP: detection of high-risk pregnancy by a healthcare worker, New FP: new participant of family planning program, Active FP: active participant of the family planning program.

### Analysis of the Differences Between Maternal Health Services Indicator in 5 Regencies/Cities with the Highest MMR Compared to 5 Regencies/Cities with the Lowest MMR in East Java 2015

Samples were divided into two groups, five regencies/cities with the highest maternal mortality included as case group, and five regencies/cities with the lowest MMR entered as a control group. Kolmogorov - Smirnov normality test done first to indicators of maternal health services in the form of 1st antenatal visit, 4th or more antenatal visits, delivery by skilled birth attendance, puerperal health care, obstetric complication management, detection of high-risk pregnancy by community, detection of high-risk pregnancy by health care worker, new participant of family planning program, active participant of family planning program, maternal mortality ratio in each group. On normality test, if the results obtained  $p > 0.05$  then shows normal data distribution.

For normal data distribution, as shown in table 6, showed the K1 coverage indicator mean in the highest MMR group was  $98.41 \pm 1.17$  and in the lowest MMR group was  $98.64 \pm 4.76$ . The K4 coverage indicator mean in the highest MMR group was  $87.72 \pm 3.76$  and in the lowest MMR group was  $92.61 \pm 4.38$ . The puerperal health care indicator mean in the highest MMR group was  $94.68 \pm 2.44$  and in the lowest MMR group was  $94.68 \pm 5.37$ . The obstetric complication management indicator mean in the highest MMR group was  $116.34 \pm 16.09$  and in the lowest MMR group was  $84.75 \pm 10.13$ . The detection of high-risk pregnancy by health care worker indicator mean in the highest MMR group was  $32.06 \pm 9.31$  and in the lowest MMR group was  $21.01 \pm 2.80$ . The new participant of family planning program indicator mean in the highest MMR group was  $9.14 \pm 4.75$  and in the lowest MMR group was  $11.60 \pm 4.94$ . The active participant of family planning program indicator mean in the highest MMR group was  $89.98 \pm 1.49$  and in the lowest MMR group was  $82.1 \pm 10.93$ .

For the abnormally distributed data in table 7 showed the detection of high-risk pregnancy by community indicator mean in the highest MMR group was  $14.78 \pm 4.01$  and in the lowest MMR group was  $12.98 \pm 3.31$ . The delivery by skilled birth attendance indicator mean in the highest MMR group was  $95.94 \pm 5.37$  and in the lowest MMR group was  $95.93 \pm 4.55$ . The MMR mean in the highest MMR group was  $150.06 \pm 23.37$  and in the lowest MMR group was  $39.06 \pm 22.85$ .

After knowing the distribution of the data in the study, then the data will be processed using comparison test. For the normally distributed

**Table 9** The Results of Mann-Whitney U Test on Delivery By Skilled Birth Attendance and Detection of High-Risk Pregnancy by Community Indicators

Group	Indicator	Mean ± SD	p-value
Highest MMR	HRP HP	14,78 ± 4,01	0,754
Lowest MMR		12,98 ± 3,31	
Highest MMR	SBA	95,54 ± 5,37	0,602
Lowest MMR		95,93 ± 4,55	

\*SB: delivery by skilled birth attendance, HRP HP: detection of high-risk pregnancy by community

data, we use one-way ANOVA parametric test, for abnormally distributed data we use Mann-Whitney U non-parametric test.

In the normal distributed data from ANOVA analysis (Table 8) showed that there were no significant differences between the 2 groups in variables: number of antenatal visits (1<sup>st</sup> antenatal visit, 4<sup>th</sup> or more antenatal visits), puerperal health care, new participant of family planning program, and active participant in family planning. We found significant differences between the 2 groups ( $p < 0.05$ ) in obstetric complication management ( $p = 0.006$ ) and detection of high-risk pregnancy by healthcare worker ( $p = 0.035$ ).

In the abnormally distributed data from the analysis of the Mann-Whitney U test (Table 9) showed that there were no significant differences between the 2 groups of skilled birth attendance and detection of high-risk pregnancy by community indicators with each p-value of  $p = 0.754$  and  $p = 0.602$  ( $p > 0, 05$ ). While from the MMR indicators were found significant difference between the 2 groups, with  $p = 0.009$  ( $p < 0.05$ ).

## DISCUSSION

This research was using secondary data that obtained from reports of East Java Provincial Health Office compiled from tiered primary health care, Public Health Center, and from the Regency/City Health Office reports. Although there are guidelines for the collection, processing, and data validation, the actual data quality depends on the understanding and commitment of each person in charge of the program. Thus the data can be inaccurate and lacked reliability needed to guide decisions to be made optimally at national and district level so that it becomes one of the weaknesses in this study.

There were 3 problems related to maternal labor referral system in Indonesia, which was the geographical situation (mostly mountains and islands), the cultural effects, and social economics in which would affect transportation and referral limitations that make it difficult to obtain access to

adequate health care and cases referred often comes too late. There were three risks of delay which first is late deciding to be referred, including late to recognize danger signs, second was late to come to health facilities during emergencies, and the third was late to obtain adequate services by health workers.<sup>5</sup>

The decline in the fertility rate has led to a decrease in the mortality rate, but the decline in fertility rates tend to be static since the mid-1990s, so the maternal mortality must be attributed mainly to other factors that go into the calculation of the cause of mortality. However, this was not to minimize the importance of family planning programs, and they should remain an integral part of safe delivery services that were offered to the pregnant woman in Indonesia. In this study, we found no significant differences in new and active family planning program participant indicators between the two groups. This suggests that efforts to use contraceptives in East Java has been running well, and according to the projection, TFR in East Java in 2015 was 1.97% which already quite small and has exceeded the national target at 2.1% in 2025.<sup>1,8</sup>

In this study, there were significant differences in high-risk pregnancy detection by health personnel and obstetric complication management. In 3-phase model of delays in treatment of obstetric complications, it is known that the delay in referring women with complications can occur in the first phase, that delays to decide to seek care that was also influenced by socio-cultural factors.

In this study showed that in the group with the highest MMR obtained 2 or more maternal relay in maternal mortality cases. This may cause the referral delay of pregnant women who require emergency treatment to the hospital. At home deliveries, the decision to refer the patient and to arrange the transportation was the responsibility of the midwife and the family, and often actions taken were delayed due to financial reasons, clinical judgment, or even religious reasons. Based on the analysis of cases of maternal mortality in East Java Maternal Perinatal Audit conducted in 2012, the problems that arise in the community was 40.91% late detection of high-risk pregnancy, late to take decisions by 22.73%, and late referral amounted to 13.64%. Some contributing factor to it is the level of public education and awareness about health is low.<sup>4,5</sup>

Most causes of maternal mortality in East Java, according to this study, was due to pre-eclampsia and haemorrhage, which the prognosis of both these complications depends on the time of management (time-related). To get the proper quality of obstetric emergency cases management will require the readiness of health infrastructure and qualified human resources. Marriage and pregnancy at an early age

<sup>13</sup> is a risk factor for *preeclampsia* which is the highest cause of maternal mortality. Women who marry at a very young age tend to have lower levels of education and awareness to the risk of pregnancy. East Java BPS data in 2013 showed that women who marry under the age of 17 years in the group of regencies/cities with the highest maternal mortality are Bojonegoro regency 33.27%, Situbondo regency 51.54%, Probolinggo regency 48.09%, Lumajang regency 30.09%, Bondowoso regency 53.26%. This figure was above the average of East Java that is 26.33% and the national rate of 17%. The things mentioned above were closely related to delays in treatment of complications in the first phase.<sup>2</sup>

In this study, we found significant differences in obstetric complications management. It was known that the highest maternal mortality was in the hospital with as many as 98 cases (78.4%), this suggests that maternal mortality can occur due to late referral so that when the patient arrived at the hospital the patient was already in bad condition. Furthermore, the number of mortality occur in hospitals can demonstrate inadequate obstetric complications management in hospitals, both regarding the availability of facilities, health facilities, and trained health personnel. However, the training and skills of health workers in Indonesia were very varied, to perform interventions in emergencies conditions. From the Audit of Maternal Perinatal outcomes in East Java in 2012, it was known that, at the advanced healthcare referral facility, 18% workers competency in maternal emergencies are still lacking, and 12% of them have no specialists to standby at the hospital, especially on holidays. And the other aspects, namely the mode of delivery by Cesarean section was 31.82%, response time more than 30 minutes was 50%, referral communication management that was not functioning properly, and feedback to the public health centre was still lacking.<sup>4,5</sup>

In this study, we found significant differences in detection of high-risk pregnancy by healthcare personnel. Risk approach was an early evaluation to determine any risks that may cause maternal morbidity and mortality. There is no pregnancy without risk. Maybe during pregnancy, there was no risk found, but the danger can be developed at the time of delivery, or during childbirth, which can cause pain, disability, and mortality in the mother or the baby. Quality antenatal care was expected to identify and undertake the management of high-risk pregnancy to ensure good outcomes of pregnancy (mother and baby healthy). In a remote area, the midwife may be the only provider of health services at the village level, working with different ways (government employees, short-term staff contracts,

or private practitioners) with various levels of supervision and referral system support and also lack of training and experience in obstetric emergencies. Additionally, there were also poor communication between midwives and doctors at the hospitals.<sup>9,11</sup>

Most antenatal care program in the world use risk factor assessment system in various forms, which can filter out the entire pregnant women, and provide supervision and care for women with high-risk. To detect high-risk pregnancies mother in East Java, we use the Poedji Rochjati Score Card (KSPR). This card was very applicable and easy to understand by using descriptive image. The score-card will distinguish pregnancy into low-risk pregnancies, high-risk pregnancies, and very high-risk pregnancy. Pregnant women with low-risk pregnancies can give birth in a basic level health facility, while high-risk and very high-risk pregnancy was suggested to give birth in hospitals or advanced healthcare facilities.

So, it was important to detect high-risk pregnant women earlier and make sure they gave birth in a place with a comprehensive healthcare facilities, with adequate emergency obstetric complication care.

## CONCLUSION

<sup>4</sup> High-risk pregnancy detection by healthcare personnel and obstetrics complications management were related with MMR in 10 regencies/cities in East Java province, Indonesia.

## <sup>8</sup> CONFLICT OF INTEREST

All authors declare there is no conflict of interest regarding publication of this manuscript.

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