INTRODUCTION

Antibiotics are chemical substances produced by microorganisms that can inhibit or kill bacteria (Fair & Tor, 2014). Antibiotics usage for an infection in the low and middle-income countries has increased up to 65% from 2010-2015 (Klein et al., 2018). An increase has followed the increase in usage in bacterial resistance. The irrational use of antibiotics, such as treating viral infections and usage on the farm and fisheries, correlates with bacterial resistance (Economou & Gousia, 2015). Furthermore, the patient's compliance in taking their oral antibiotics also contributed to bacterial resistance prevalence (Moradi et al., 2013).

Several studies evaluated the patient's compliance with oral antibiotics have been conducted using various methods. Measuring compliance using objective or subjective methods has its particular limitations (Jin et al., 2008). Examples of objective methods in assessing patient compliance are pill count and Medication Event Monitoring System (MEMS). Pill count is a physical count of the number of pills that remain and compares to the prescription's instruction (Lam & Fresco, 2015). The MEMS is a medication container contains a microelectronic chip that records the date and time of opening of every bottle (Llor et al., 2013). Although MEMS measures compliance accurately, it cannot be used in an everyday situation. Besides, pill count cannot describe specifically the aspects of compliance, such as timing, dosing, and taking compliance (Williams et al., 2013). Hence, a subjective method such as using a questionnaire is preferable because of less cost, non-judgmental, non-threatening, quick, and comfortable in
collecting results (Lam & Fresco, 2015; Llor et al., 2013; Ponto, 2015).

Various questionnaires such as Medication Adherence Questionnaire (MAQ), Medication Adherence Rating Scale (MARS), Patient Medication Adherence Questionnaire (PMAQ), Morisky Medication Adherence Scale (MMAS), etc. have been developed and validated to measure compliance (Morisky et al., 1986; Thompson et al., 2000; Duong et al., 2001). However, the questionnaires have not been translated and validated into Bahasa Indonesia for measuring compliance with oral antibiotics treatment in Indonesia. A study has been conducted to validate the English version of Morisky 3, 4, and 5-item questionnaires in assessing oral antibiotics compliance (Treibich & Ventelou, 2017). In Indonesia, measuring oral antibiotics compliance usually uses pill count. Therefore, there has been no questionnaire developed yet. Hence, developing a standard questionnaire for evaluating oral antibiotics compliance in Bahasa Indonesia is essentials. In developing a questionnaire, validity tests are needed in order to evaluate whether it measures what it is supposed to measure or not (Setia, 2017). Validity tests are classified into two broad categories, viz internal and external validity (Bolarinwa, 2015). Internal validity includes content validity that measures the degree to which the instrument comprehensively assesses the construct of interest usually conducted before external validity. Therefore, this study was conducted to record the developed questionnaire's content validity assessing compliance with oral antibiotics.

**20-KAO Questionnaire**

The 20-KAO questionnaire was developed in Bahasa Indonesia and aimed to assess short-course oral antibiotics usage compliance. The name 20-KAO was developed from 20 items in assessing compliance with oral antibiotics or in Bahasa Indonesia: Kepatuhan Antibiotik Oral (KAO). The questionnaire was developed in four sections and contained 20 questions. Section one contained ten questions to evaluate whether the patients understood the dosage regimens and took their dosage correctly or not and the reasons behind their action in taking the dosage. Section two rated the patient's understanding, compliance, and the reasons in how many times they took the dosage daily through five questions. In the third section, it was assessed how patients gave an interval between their dosages and the reasons why they did it. In the last section, the patient's understanding of the duration of taking the antibiotics, and whether they had stopped taking the antibiotics before it should be stopped, and their reasons to do so. Additionally, patients were also asked to fill in the number of pills left in the questionnaire and if they used other non-prescribed medication.

**Content validation**

The literature shows that the ideal number of content experts needed in a validation study is still controversial. However, the suggestions are between three and ten experts (Polit & Beck, 2006). In this study, a total of six experts were selected. Three of them were academic experts, while three remained were registered pharmacists. These experts' proportion were designed intentionally so that the review results would reflect academic and practical opinions. The academic experts were selected based on their experiences in developing a questionnaire and the pharmacists' experts' experiences in giving patient consultation to improve the patient's compliance. The experts were invited from educational
institutions and community health centers in Surabaya (they were registered pharmacists in Wonokromo, Gayungan, and Kalirungkut Community Health Centers and academic lecturers in clinical as well as community pharmacy at Universitas Airlangga and Akademi Farmasi Surabaya). After getting their approval, the researcher sent an informed consent form, an information cover letter, and the questionnaire attached to the evaluation criteria. The evaluation form contained an explanation of the validation procedure. The experts were requested to provide recommendations for each item, either revisions or deletion. The maximum time for completing the questionnaire for each expert was two weeks, and they were requested to return the result through email or in-person to the researcher. The response from the experts was analyzed through Content Validity Index (CVI), specifically Item Content Validity Index (I-CVI) and Scale-Content Validity Index (S-CVI). The I-CVI was calculated in every item from the number of experts giving 3 or 4 scores divided by the total number of experts, while S-CVI was computed as the average of I-CVI from all the items. The questionnaire would qualify to be content valid if the S-CVI greater than 0.90.

RESULTS AND DISCUSSION
All of the six experts invited were agreed to participate. They were registered pharmacists in Wonokromo, Gayungan, and Kalirungkut Community Health Centers and academic lecturers in clinical and community pharmacy at Universitas Airlangga and Akademi Farmasi Surabaya. All experts are deliberately selected from Surabaya to facilitate communication. The mean age of the experts was 41.5 (SD=9.16) years. After the validation process, the number of question items in the 20-KAO questionnaire remained unchanged. There were 19 out of 20 items that had an I-CVI of 1.00. Therefore, S-CVI was calculated at 0.98 as shown in Table I.

### Table I.

| Section | Item Number | Question description | Expert Raters | I-CVI |
|---------|-------------|----------------------|---------------|-------|
|         |             |                      | 1  | 2  | 3  | 4  | 5  | 6  |       |
| Section I | Q1 | Knowledge of prescribed antibiotic dose at one time | 3 | 4 | 3 | 4 | 3 | 3 | 1.00 |
|          | Q2 | Experience in taking a higher dosage at one time | 4 | 3 | 4 | 3 | 4 | 3 | 1.00 |
|          | Q3 | Reasons for Q2 Answer | 4 | 3 | 4 | 3 | 4 | 3 | 1.00 |
|          | Q4 | Experience in taking a lower dosage at one time | 4 | 3 | 4 | 3 | 4 | 3 | 1.00 |
|          | Q5 | Reasons for Q4 Answer | 4 | 3 | 4 | 3 | 4 | 3 | 1.00 |
|          | Q6 | Knowledge of prescribed antibiotic dose daily | 3 | 4 | 4 | 4 | 4 | 3 | 1.00 |
|          | Q7 | Experience in taking higher dosage daily | 4 | 4 | 4 | 3 | 4 | 3 | 1.00 |
|          | Q8 | Reasons for Q7 Answer | 4 | 4 | 4 | 3 | 4 | 3 | 1.00 |
|          | Q9 | Experience in taking lower dosage daily | 4 | 4 | 4 | 3 | 4 | 3 | 1.00 |
|          | Q10| Reasons for Q9 Answer | 4 | 4 | 4 | 3 | 4 | 3 | 1.00 |
| Section II | Q11| Knowledge of times taken prescribed antibiotics daily | 4 | 4 | 4 | 2 | 4 | 2 | 0.67 |
|          | Q12| Experience in taking more frequent | 4 | 3 | 4 | 3 | 4 | 3 | 1.00 |
Table I showed that the questionnaire had excellent content validity in measuring oral antibiotic compliance.

However, the experts gave some editorial revisions to make the sentences more comfortable to be understood, as presented in Table II.

Table II. Editorial revision of 20-KAO questionnaire

| Item | Question description | Original Question Sentences (Bahasa Indonesia) | After Editorial Revision (Bahasa Indonesia) | After Editorial Revision (English) |
|------|----------------------|-----------------------------------------------|-------------------------------------------|----------------------------------|
| Q1   | Knowledge of prescribed antibiotic dose at one time | Berapa table/kapsul antibiotik yang seharusnya anda konsumsi tiap kali minum? | Berapa jumlah table/kapsul antibiotik yang seharusnya anda konsumsi tiap kali minum? | How many pills of antibiotic should you take at one time? |
| Q2   | Experience in taking higher dosage at one time | Apakah Anda pernah mengkonsumsi lebih dari jumlah tersebut tiap kali minum? | Apakah Anda pernah mengkonsumsi obat antibiotik lebih dari jumlah tersebut tiap kali minum? | Have you taken more antibiotic pills than that at one time? |
| Q3   | Reasons for Q2 Answer | Apa alasankanda? | Apa alasankanda? | Please explain your reasons. |
| Q4   | Experience in taking | Apakah Anda pernah mengkonsumsi | Apakah Anda pernah mengkonsumsi | Have you taken less |
|      |                      |                                               |                                               | antibiotic than that at one time? |

| Q5   | Reasons for Q4 Answer | Apa alasankanda? | Please explain your reasons. |
| Q6   | Knowledge of prescribed antibiotic dose daily | Berapa table/kapsul antibiotik yang seharusnya anda konsumsi dalam satu hari? | Berapa jumlah table/kapsul antibiotik yang seharusnya anda konsumsi dalam satu hari? | Have you taken more antibiotic pills than that in one day? |
| Q7   | Experience in taking higher dosage daily | Apakah Anda pernah mengkonsumsi lebih dari jumlah tersebut dalam satu hari? | Apakah Anda pernah mengkonsumsi obat antibiotik lebih dari jumlah dalam satu hari? | Have you taken less antibiotic pills than that in one day? |
| Q8   | Reasons for Q7 Answer | Apa alasankanda? | Please explain your reasons. |
| Q9   | Experience in taking lower dosage daily | Apakah Anda pernah mengkonsumsi kurang dari jumlah tersebut dalam satu hari? | Apakah Anda pernah mengkonsumsi obat antibiotik kurang dari jumlah dalam satu hari? | Have you taken less antibiotic pills than that in one day? |
| Q10  | Reasons for Q8 Answer | Apa alasankanda? | Please explain your reasons. |
| Q11  | Knowledge of times taken prescribed antibiotics daily | Berapa kali seharusnya Anda minum antibiotik dari pakhemasan tersebut dalam satu hari? | Berapa kali dalam satu hari seharusnya Anda minum antibiotik dari pakhemasan sesuai resep dokter? | Have you taken more frequently than that? |
| Q12  | Experience in taking more frequent | Apakah Anda pernah mengkonsumsi lebih dari itu dalam satu hari? | Apakah Anda pernah mengkonsumsi obat antibiotik lebih dari itu dalam satu hari? | Have you taken more frequently than that? |
| Q13  | Reasons for Q9 Answer | Apa alasankanda? | Please explain your reasons. |
| Q14  | Experience in taking less frequent | Apakah Anda pernah mengkonsumsi kurang dari itu dalam satu hari? | Apakah Anda pernah mengkonsumsi obat antibiotik kurang dari itu dalam satu hari? | Have you taken less frequently than that? |
| Q15  | Reasons for Q10 Answer | Apa alasankanda? | Please explain your reasons. |
| Q16  | The time interval between dosage | Bogaimana Anda memberi jeda waktu dalam meminum antibiotik Anda? | Bogaimana Anda memberi jeda waktu dalam meminum antibiotik Anda? | How do you give interval between your antibiotic dosage? |
Among the 20 items validated, the only item with I-CVI less than 1.00 and significant editorial revision was Q11. The Q11 was developed to assess whether the patients understand how many times they should take their antibiotics or not. Two of the six experts suggested changing the sentence structured because the original sentence was too complicated. Changes in the structure of the questions were then carried out after consultation with these experts. The final form of the 20-KAO questionnaire after the content validity process was shown in Table III.

Table III. The 20-KAO questionnaire

| Identities |                                                                 |
|------------|------------------------------------------------------------------|
| Nama atau Inisial (Name or Initials) | .............................................................................. |
| Jenis Kelamin (Gender) | ☐ Perempuan (Female) ☐ Laki-laki (Male) |
| Usia dalam tahun (Age in y.o) | .............................................................................. |
| Apakah anda memiliki riwayat penyakit? Jika IYA, harap sebutkan. (Do you have comorbid? If YES, please mention it) | .............................................................................. |
| Apakah anda mengkonsumsi obat lain selain yang diresepkan untuk anda? Jika IYA, harap sebutkan. (Do you take any other medications out of prescribed? If YES, please mention it) | .............................................................................. |

| 20-KAO Questionnaire |                                                                 |
|----------------------|------------------------------------------------------------------|
| Bagian 1 (Section 1) |                                                                 |
| 1. Berapa jumlah tablet/ kapsul antibiotik yang seharusnya anda konsumsi tiap kali minum? (How many pills of antibiotic should you take at one time?) | .............................................................................. |
| 2. Apakah Anda pernah mengkonsumsi obat antibiotik lebih dari jumlah tersebut tiap kali minum? (Have you taken more antibiotic pills than that at one time?) | ☐ Ya (Yes) ☐ Tidak (No) |
| 3. Apa Alasan Anda? (Please explain your reasons) | .............................................................................. |
| 4. Apakah Anda pernah mengkonsumsi obat antibiotik kurang dari jumlah tersebut tiap kali minum? (Have you taken less antibiotic pills than that at one time?) | ☐ Ya (Yes) ☐ Tidak (No) |
| 5. Apa Alasan Anda? (Please explain your reasons) | .............................................................................. |
| 6. Berapa jumlah tablet/ kapsul antibiotik yang seharusnya anda konsumsi dalam satu hari? | .............................................................................. |
| Question                                                                 | Yes | No | Reason                                                                 |
|-------------------------------------------------------------------------|-----|----|------------------------------------------------------------------------|
| 7. Apakah Anda pernah mengkonsumsi obat antibiotik lebih dari jumlah dalam satu hari? | ☐   | ☐  |                          | 8. Apa Alasan Anda? (Please explain your reasons) |
| (Have you taken more antibiotic pills than that in one day?)            |     |    |                          |                                                    |
| 9. Apakah Anda pernah mengkonsumsi obat antibiotik kurang dari jumlah tersebut dalam satu hari? | ☐   | ☐  |                          | 10. Apa Alasan Anda? (Please explain your reasons) |
| (Have you taken less antibiotic pills than that in one day?)            |     |    |                          |                                                    |
| 11. Berapa kali dalam satu hari seharusnya Anda minum antibiotik dari puskesmas sesuai peresepan dokter? | ☐   | ☐  |                          | 12. Apa Alasan Anda? (Please explain your reasons) |
| (How many times should you take your antibiotic as prescribed in one day?) |     |    |                          |                                                    |
| 13. Apa Alasan Anda? (Please explain your reasons)                       |     |    |                          |                                                    |
| 14. Apakah Anda pernah mengkonsumsi kurang dari itu dalam satu hari?    | ☐   | ☐  |                          | 15. Apa Alasan Anda? (Please explain your reasons) |
| (Have you taken less frequently than that?)                             |     |    |                          |                                                    |
| 16. Bagaimana Anda memberi jeda waktu dalam meminum antibiotik Anda?     | ☐   | ☐  |                          | 17. Sejak kapan Anda minum antibiotik? (Since when you take your antibiotics course?) |
| (How do you give an interval between your antibiotic dosage?)           |     |    |                          |                                                    |
| 18. Apakah Anda telah berhenti meminum antibiotik Anda sebelum hari ini? | ☐   | ☐  |                          | 19. Apa Alasan Anda? (Please explain your reasons) |
| (Have you stopped your antibiotic course before today?)                 |     |    |                          |                                                    |
| 20. Berapa Jumlah antibiotik anda yang tersisa? (How many pills of antibiotics do you have left?) | ☐   | ☐  |                          |                                                     |

To our knowledge, there had no reported studies developing a questionnaire that evaluated oral antibiotics compliance in Indonesia. A study in Lithuania by Kandrotaite et al. (2013) developed a 91-items
questionnaire adapted from ASK-20, SF-12, and Morisky scale questionnaire to identify the risk of nonadherence to antibiotics treatments. It was said that the developed questionnaire covered the identification of the five-dimension adherence model developed by World Health Organization (Kandrotaite et al., 2013). However, although the developed questionnaire had been discussed with nine professionals, it had not been validated yet. Besides, one of the studies in Indonesia that used questionnaires to measure antibiotics compliance was the study by Muljabar and Supadmi (2014) that used 8-items MMAS. However, the study did not validate the questionnaire directly to patients receiving antibiotics. Therefore, the questionnaire developed in this study could be tested for construct validity and reliability tests. Construct validity is the degree to which an instrument measures the trait or theoretical construct intended to measure, while reliability test is the extent to which a questionnaire produces consistent results on repeated trials (Boateng et al., 2018; Kimberlin & Winterstein, 2008). Construct validity for the 20-KAO questionnaire is essentials to measure how well the targeted respondents give answers as the questionnaire aims to measure, while the reliability test is useful to assess whether the questionnaire will give consistency in results. Future construct validity and reliability test for 20-KAO questionnaire can be done through distribution to the patient’s prescribed antibiotics and then analyze their responses.

CONCLUSION

The 20-KAO questionnaire was found to have excellent content validity based on six experts' reviews. Future construct validity and reliability tests for 20-KAO are needed to be conducted to analyze the respond of targeted respondents and the consistency of the questionnaire.

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REFERENCES

Boateng, G.O., Neilandsm T.B., Fongillo, E.A., Melgar-Quínonez, H.R., & Young, S.L. (2018). Best Practices for Developing and Validating Scales for Health, Social, and Behavioral Research: A Primer. Frontiers in Public Health, 6, 149. doi:10.3389/fpubh.2018.00149

Bolarinwa, O.A. (2015). Principles and methods of validity and reliability testing of questionnaires used in social and health science researches. Nigerian Postgraduate Medical Journal, 22(4), 195-201. doi:10.4103/1117-1936.173959

Duong, M., Piroth, L., Grappin, M., Forte, F., Peytavin, G., Buisson, M., Chavanet, P., & Portier, H. (2001). Evaluation of the Patient Medication Adherence Questionnaire as a tool for self-reported adherence assessment in HIV-infected patients on antiretroviral regimens. HIV Clinical Trials, 2(2), 128-135. doi:10.1310/M3JR-C390-LXCM-F62G

Economou, V. & Gousia, P. (2015). Agriculture and food animals as a source of antimicrobial-resistant bacteria. Infection and Drug Resistance, 8, 49-61. doi:10.2147/IDR.S55778

Fair, R.J. & Tor, Y. (2014). Antibiotics and Bacterial Resistance in the 21st Century. Perspective in Medicinal Chemistry, 6, 25-64. doi:10.4137/PMCSI14459

Jin, J., Sklar, G.E., Oh, V.M.S., & Li, S.C. (2008). Factors affecting therapeutic compliance: A review from the patient’s perspective. Therapeutics and Clinical Risk Management, 4(1), 269-286. doi:10.2147/tcrm.s1458

Kandrotaite, K., Smigelskas, K., Janusauskiene, D., Jievaltas, M., Maciulaitis, R., & Briedis, V. (2013). Development of a short questionnaire...
to identify the risk of nonadherence to antibiotic treatment. *Current Medical Research and Opinion, 29*(11), 1555-1563. doi:10.1185/03007995.2013.835255

Kimberlin, C.L. & Winterstein, A.G. (2008). Validity and reliability of measurement instruments used in research. *American Journal of Health-System Pharmacy, 65*(23), 2276-2284. doi:10.2146/ajhp070364

Klein, E.Y., Boeckel, T.P.V., Martinez, E.M., Pant, S., Gandra, S., Levin, S.A., Goossens, H., & Laxminarayan, R. (2018). Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. *Proceedings of the National Academy of Sciences of the United States of America, 115*(15), E3463-E3470. doi:10.1073/pnas.1717295115

Lam, W.Y. & Fresco, O. (2015). Medication Adherence Measures: An Overview. *BioMed Research International, 2015*, 217047. doi:10.1155/2015/217047

Llor, C., Hernández, S., Bayona, C., Moragas, A., Sierra, N., Hernández, M., & Miravilles, M. (2013). A study of adherence to antibiotic treatment in ambulatory respiratory infections. *International Journal of Infectious Diseases, 17*(3), e168-172. doi:10.1016/j.ijid.2012.09.012

Martinez, J.L. (2017). Effect of antibiotics on bacterial populations: a multi-hierarchical selection process. *F1000Research, 6*, 51. doi:10.12688/f1000research.9685.1

Moradi, M., Hamedi-Shahraki, S., Rezayee, M., & Verdi, M. (2013). Compliance with antimicrobial therapy: Evaluating the related factors. *Journal of Pharmaceutical Care, 1*(2), 60-64.

Morisky, D.E., Green, L.W., & Levine, D.M. (1986). Concurrent and predictive validity of a self-reported measure of medication adherence. *Medical Care, 24*(1), 67-74. doi:10.1097/00005650-198601000-00007

Muljabar, S.M. & Supadmi, W. (2014). Pengaruh Pemberian Informasi Obat terhadap Tingkat Kepatuhan Penggunaan Antibiotika pada Pasien ISPA di Puskesmas Kotagede I Yogyakarta. *Pharmaciana: Jurnal Kefarmasian, 4*(2), 143-149. doi:10.12928/pharmaciana.v4i2.1571

Polit, D.F. & Beck, C.T. (2006). The content validity index: are you sure you know what's being reported? Critique and recommendations. *Research in Nursing and Health, 29*(5), 489-497. doi:10.1002/nur.20147

Ponto, J. (2015). Understanding and Evaluating Survey Research. *Journal of the Advanced Practitioner in Oncology, 6*(2), 168-171.

Setia, M.S. (2017). Methodology Series Module 9: Designing Questionnaires and Clinical Record Forms – Part II. *Indian Journal of Dermatology, 62*(3), 258-261. doi:10.4103/ijd.IJD_200_17

Thompson, K., Kulkarni, J., & Sergejew, A.A. (2000). Reliability and validity of a new Medication Adherence Rating Scale (MARS) for the psychoses. *Schizophrenia Research, 42*(3), 241-247. doi:10.1016/s0920-9964(99)00130-9

Treibich, C. & Ventelou, B. (2017). Validation of a short-form questionnaire to check patients' adherence to antibiotic treatments in an outpatient setting. *European Journal of Public Health, 27*(6), 978-980. doi:10.1093/eurpub/ckx146

Williams, A.B., Amico, K.R., Bova, C., & Womack, J.A. (2013). A proposal for quality standards for measuring medication adherence in research. *AIDS and Behavior, 17*(1), 284-297. doi:10.1007/s10461-012-0172-7