



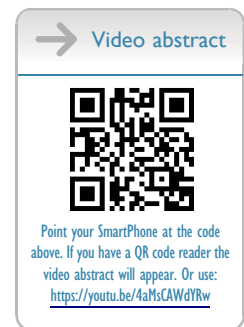


# Effectiveness of Standard Therapy for Acne Vulgaris Based on Clinical Practice Guidelines in Indonesia

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**Purpose:** To evaluate the effectiveness of standard therapy for acne vulgaris based on Indonesian guidelines.

**Patients and Methods:** New patients with acne vulgaris at Dr. Cipto Mangunkusumo National Central General Hospital, the national referral center in Indonesia, who met the criteria were included in this study. Patients were treated with standard therapy for acne vulgaris based on the 2017 guidelines of Dr. Cipto Mangunkusumo Hospital, depending on severity. Changes in the number of non-inflammatory, inflammatory, and total lesions and the proportion of acne severity after three months of therapy were analyzed retrospectively.

**Results:** Among the 131 subjects, 63.4% had moderate acne; 20.6% had mild acne, and 16% had severe acne at baseline. Most patients (29 (22.2%)) received a combination of retinoic acid, benzoyl peroxide, and topical or oral antibiotics. Standard therapies reduced the median of non-inflammatory (25 (5–135) vs 8 (0–53)), inflammatory (10 (0–93) vs 2 (0–22)), and total lesions (41 (10–160) vs 10 (1–71)) at week 12 (all  $p < 0.001$ ). The proportion of acne severity differed significantly after three months, with an increasing proportion of mild acne (20.6% vs 93.1%) and a decreasing percentage of moderate and severe acne (moderate = 63.6% vs 6.1%; severe, 16% vs 0.8%;  $p < 0.001$ ).

**Conclusion:** Standard therapy for acne vulgaris based on the clinical practice guidelines in Indonesia improved acne lesions and severity after 12 weeks. These results support the implementation of national guidelines for acne management in Indonesia, with the practice of improving antimicrobial stewardship.

**Keywords:** acne vulgaris, clinical practice guideline, therapy, Indonesia, effectiveness

## Introduction

Acne vulgaris (AV) is a prevalent chronic inflammatory disorder of the pilosebaceous unit affecting all ages, especially teenagers and young adults, leading to depression and anxiety in more severe cases.<sup>1</sup> It is the third most frequent dermatological cases at the Central and Regional General Hospital in Indonesia.<sup>2</sup> The incidence of AV constituted about 46% of the total new cases at Dr. Cipto Mangunkusumo National Central General Hospital's Cosmetic Dermatology clinic, with over 50% of moderate-to-severe acne. Effective and timely treatment of acne is needed to hasten skin resolution, prevent the formation of new acne and permanent scars, and alleviate the associated psychosocial burden.<sup>1–3</sup> AV management has been challenging because of various diagnostic parameters and treatment options globally accommodating each nation's condition.<sup>3,4</sup>

Several acne guidelines are available in Indonesia, such as the consensus of the Indonesian Acne Expert Meeting (IAEM) in 2015<sup>2</sup>, clinical practice guidelines (CPGs) of the Indonesian Society of Dermatology and Venereology

(INSDV)<sup>5</sup> and Dr. Cipto Mangunkusumo Hospital<sup>6</sup> in 2017, which have similarities in the recommended treatment choices. These national guidelines emanate from the best available evidence and relevant international guidelines with some adjustments; however.<sup>3</sup> To the best of our knowledge, there are no data on the effectiveness of standard therapy for AV based on the national guidelines to date. This study analyzed medical records from 2017 to 2019, as there was a COVID-19 pandemic from 2020 to 2021, thus hindering routine follow-up. The AV guideline in this research referred to the one by Dr. Cipto Mangunkusumo Hospital 2017 in line with the date of outpatient visits, for which therapy was based on this CPG. This paper presents the clinical outcomes of standard regimens in the national guidelines.

## Materials and Methods

### Design and Subjects

This retrospective observational study was conducted using medical records from a national referral hospital in Indonesia. Data of new patients diagnosed with AV in the dermatology outpatient clinic between 2017 and 2019 were extracted. Cases were selected based on the inclusion and exclusion criteria of the total sampling technique. The minimum sample size was determined using the following formula:  $n = (Z_{\alpha}^2 \times p \times q)/d^2$ , where  $z = 1.96$ , confidence level ( $\alpha$ ) = 0.05 and margin of error ( $d$ ) = 10%, which yielded the required minimum sample size of 97.

Patients were eligible if they had complete sociodemographic and clinical information, including age, sex, occupation, level of education, risk factors, diagnosis of AV, and received treatment based on Dr. Cipto Mangunkusumo Hospital's guideline,<sup>6</sup> subject to severity (Table 1). Severity was classified as mild, moderate, and severe.<sup>7</sup> The number of non-inflammatory, inflammatory, and total lesions and acne severity were also recorded at baseline and follow-up. Subjects with less than three times of follow-ups in three months, incomplete medical records, diagnosis without acne

**Table 1** Guideline for the Management of Acne Vulgaris by Dr. Cipto Mangunkusumo National Central General Hospital 2017<sup>a</sup>

| Acne Severity               | Mild  | Moderate   | Severe  |
|-----------------------------|---|--|---|
| First-line topical therapy  | <b>Comedonal</b>  |  |   |
|                             | 1. RA, or<br>2. BPO<br>1x/day, at night   | 1. RA, or<br>2. BPO<br>1x/day, at night  | 1. RA, or<br>2. BPO<br>1x/day, at night   |
|                             | <b>Combination (comedonal/papular/pustular)</b>   |  |   |
|                             | 1. RA + BPO, or<br>2. Antibiotic + BPO, or<br>3. Antibiotic + RA + BPO<br>1x/day, at night                    | 1. RA + BPO, or<br>2. Antibiotic + BPO, or<br>3. Antibiotic + RA + BPO<br>1x/day, at night | 1. RA + BPO, or<br>2. Antibiotic + BPO, or<br>3. Antibiotic + RA + BPO<br>1x/day, at night  |
| First-line oral therapy     | NA  | 1. Doxycycline, or<br>2. Tetracycline  | 1. Doxycycline, or<br>2. Tetracycline   |
| Second-line topical therapy | 1. RA + BPO<br>2. Consider other retinoids<br>3. Topical dapsone 5% - 7.5%<br>4. AA cream                     | 1. RA + BPO<br>2. Consider other retinoids<br>3. Topical dapsone 5% - 7.5%<br>4. AA cream  | 1. RA + BPO<br>2. Consider other retinoids<br>3. Topical dapsone 5% - 7.5%<br>4. AA cream   |
| Second-line oral therapy    | NA  | 1. Erythromycin, or<br>2. Azithromycin, in pregnancy and children < 8 years                | 1. Isotretinoin 0.3–1 mg/kg/day to an accumulative dose of 125–150 mg/kg/day<br>Women: hormonal therapy with oral contraceptive therapy or spironolactone |
| Adjuvant therapy            | Patient education and/ or skin care and/ or skin peels and/ or laser and light therapy and/ or dermocosmetics |  |   |
| Maintenance therapy         | Patient education and/ or skin care and/ or RA 0.01–0.025% and/ or dermocosmetics                             |  |   |

**Notes:** <sup>a</sup>Data from *Clinical Practice Guideline for Acne Vulgaris*, Department of Dermatology and Venereology RSUPN dr. Cipto Mangunkusumo 2017.<sup>6</sup>

**Abbreviations:** RA, retinoic acid; BPO, benzoyl peroxide; NA, not applicable; AA, azelaic acid.

severity, history of steroid consumption or acneiform eruption, acne-associated systemic diseases such as polycystic ovarian syndrome (PCOS), Cushing's syndrome, congenital adrenal hyperplasia, or history of allergy to therapy were excluded from the study. Data from the included subjects were collected through week 12 of the therapy. This study was approved by the Health Research Ethics Committee of Faculty of Medicine Universitas Indonesia-Cipto Mangunkusumo Hospital under dossier number #KET-344/UN2.F1/ETIK/PPM.00.02/2023 and was carried out afterward from April 2023 through July 2023.

## Outcome Measures

Therapy effectiveness was measured as the clinical response demonstrated by the number of non-inflammatory, inflammatory, and total lesions, and the proportion of acne severity at week 12 of standard therapy compared to baseline.

Figure 1 is a flow chart of the retrospective observational study.

## Statistical Analysis

The baseline characteristics and adjuvant therapy, if any, were reported. This study did not analyze the association between risk factors and acne. The normality of the data distribution was examined using the Kolmogorov–Smirnov test. Comparisons of paired continuous data were analyzed using the paired *T*-test or Wilcoxon Signed-Rank test, depending

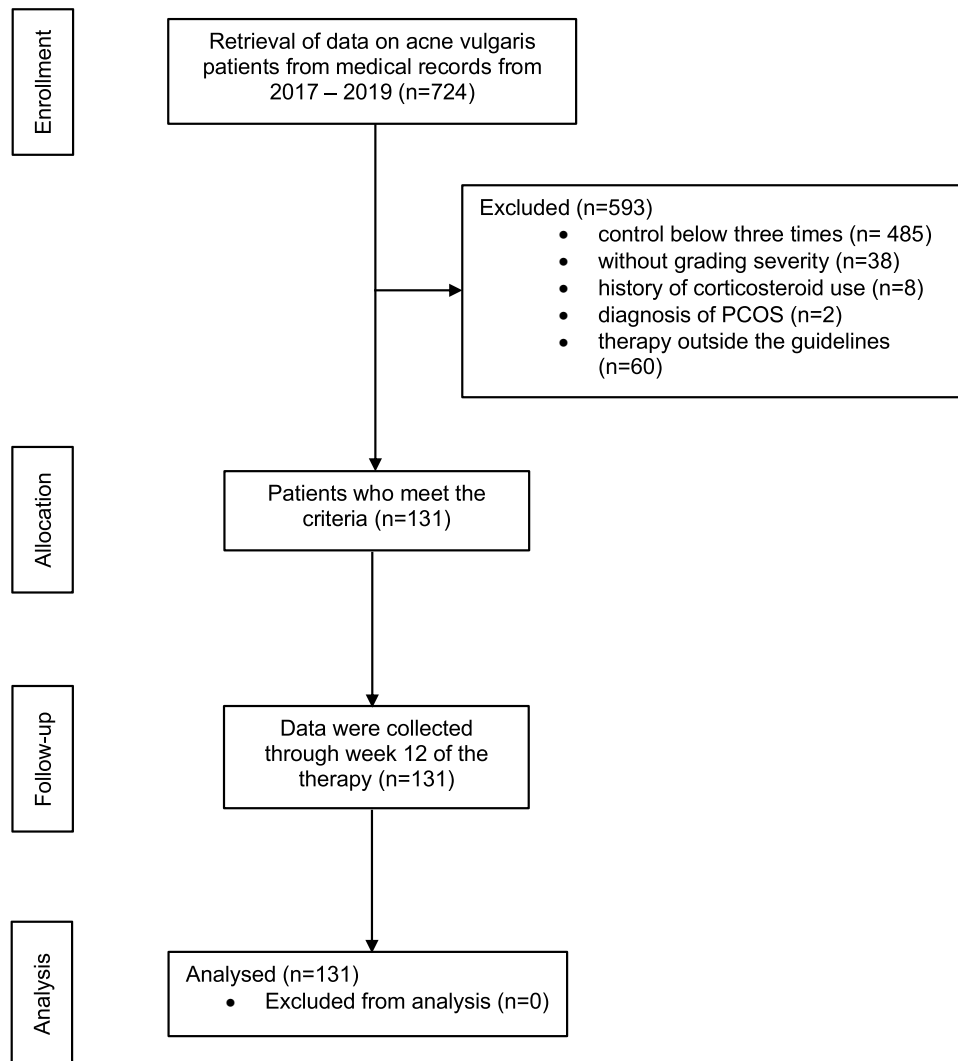


Figure 1 Flow chart of retrospective observational study.

on the data distribution. Paired ordinal data were compared using Wilcoxon Signed-Rank test. All analyses were performed using the SPSS® software version 24, and p-values <0.05.

## Results

### Patient Characteristics

A total of 131 of the 724 eligible patients were included. The reasons for exclusion of 593 subjects were less than three times the control in three months (n = 485), diagnosis of acne without severity (n = 38), history of corticosteroid use (n = 8), diagnosis of PCOS (n = 2), and therapy outside the guidelines due to becoming research subjects at the time of visit (n = 60). The reasons for follow-up non-attendance were not investigated in this study.

Of the 131 patients, most were female (83.2%), between 16 and 20 years of age (34.4%), had an onset of acne <25 years (92.4%), had indoor work (96.9%), had a history of acne therapy (58%), and had normal nutritional status (44.3%). The median age for female was significantly higher than for male (23 (13–45) years vs 19 (12–27) years), p < 0.001). The median duration of AV was 48 months. Most participants presented with moderate acne at baseline (63.4%) (Table 2).

**Table 2** Subjects' Sociodemographic and Clinical Characteristics at Baseline<sup>a</sup>

| Characteristic                          | N = 131     |                         |                      |
|---|-------------|-------------------------|----------------------|
| Year of visit                           |             |                         |                      |
| 2017                                    | 27 (20.6%)  |                         |                      |
| 2018                                    | 61 (46.4%)  |                         |                      |
| 2019                                    | 43 (32.8%)  |                         |                      |
| Sex                                     |             |                         |                      |
| Female                                  | 109 (83.2%) |                         |                      |
| Male                                    | 22 (16.8%)  |                         |                      |
| Age <sup>b</sup>                        |             | <b>Female (n = 109)</b> | <b>Male (n = 22)</b> |
| Median (range) <sup>c</sup>             | 23 (12–45)  | 23 (13–45)              | 19 (12–27)           |
| 11–15 y                                 | 7 (5.3%)    | 4 (3.7%)                | 3 (13.6%)            |
| 16–20 y                                 | 45 (34.4%)  | 34 (31.2%)              | 11 (50.0%)           |
| 21–25 y                                 | 38 (29.0%)  | 33 (30.3%)              | 5 (22.7%)            |
| 26–30 y                                 | 21 (16.0%)  | 18 (16.5%)              | 3 (13.6%)            |
| 31–35 y                                 | 13 (9.9%)   | 13 (11.9%)              | 0 (0%)               |
| 35–40 y                                 | 6 (4.6%)    | 6 (5.5%)                | 0 (0%)               |
| 41–45 y                                 | 1 (0.8%)    | 1 (0.9%)                | 0 (0%)               |
| Age of onset of acne, year              |             |                         |                      |
| Median (range)                          | 18 (10–42)  |                         |                      |
| Age < 25 y                              | 121 (92.4%) |                         |                      |
| Age ≥ 25 y                              | 10 (7.6%)   |                         |                      |
| Level of education                      |             |                         |                      |
| Primary level                           | 2 (1.5%)    |                         |                      |
| Secondary level                         | 79 (60.3%)  |                         |                      |
| Tertiary level                          | 50 (38.2%)  |                         |                      |
| Work settings                           |             |                         |                      |
| Outdoor                                 | 4 (3.1%)    |                         |                      |
| Indoor                                  | 127 (96.9%) |                         |                      |
| Duration of acne, median (range), month | 48 (1–240)  |                         |                      |
| History of acne therapy                 |             |                         |                      |
| Yes                                     | 76 (58.0%)  |                         |                      |
| No                                      | 55 (42.0%)  |                         |                      |

(Continued)

**Table 2** (Continued).

| Characteristic                         | N = 131          |  |  |
|--|------------------|--|--|
| History of acne drug consumption       |                  |  |  |
| Yes                                    | 21 (16.0%)       |  |  |
| No                                     | 110 (84.0%)      |  |  |
| BMI, median (range), kg/m <sup>2</sup> | 21.8 (16.2–36.1) |  |  |
| Nutritional status                     |                  |  |  |
| Underweight                            | 26 (19.8%)       |  |  |
| Normal                                 | 58 (44.3%)       |  |  |
| Overweight                             | 23 (17.6%)       |  |  |
| Obesity I                              | 20 (15.3%)       |  |  |
| Obesity II                             | 4 (3.1%)         |  |  |
| Degree of acne severity <sup>d</sup>   |                  |  |  |
| Mild                                   | 27 (20.6%)       |  |  |
| Moderate                               | 83 (63.4%)       |  |  |
| Severe                                 | 21 (16.0%)       |  |  |

**Notes:** <sup>a</sup>Data are presented in number (%) unless otherwise stated; <sup>b</sup>Distribution of age and age group by sex; <sup>c</sup>*Wilcoxon Rank-Sum* test showed median age of male and female differed significantly ( $p = 0.02$ ); <sup>d</sup>Severity was based on Lehmann grading system.

**Abbreviation:** BMI, body mass index (classified based on Asia-Pacific criteria).

## Treatment

Most patients were prescribed a combination of retinoic acid (RA), benzoyl peroxide (BPO), and topical and oral antibiotics (22.2%), followed by RA, BPO, and topical antibiotics (21.4%) (Table 3). All patients received adjuvant therapy in the form of education on acne and facial cleansers from the attending registrars at the time of the visit. Additionally, 30 subjects (22.9%) received all other adjuvant treatment choices, including chemical peels, corticosteroid injection, comedone extraction, light/laser therapy, and other dermocosmetics.

**Table 3** Standard Treatments for Acne Vulgaris of Subjects<sup>a</sup>

| Standard therapy   | N = 131    |
|--|------------|
| First-line topical therapy (n = 68)  |            |
| RA   | 12 (9.2%)  |
| RA + topical antibiotic  | 7 (5.3%)   |
| RA + BPO   | 21 (16.0%) |
| RA + BPO + topical antibiotic  | 28 (21.4%) |
| First-line topical and oral therapy (n = 49)                                 |            |
| RA + topical antibiotic + Doxycycline  | 6 (4.6%)   |
| RA + BPO + topical antibiotic + Doxycycline                                  | 29 (22.2%) |
| RA + BPO + Doxycycline   | 14 (10.7%) |
| RA + Doxycycline   | 1 (0.8%)   |
| First-line topical and oral therapy and Second-line topical therapy (n = 14) |            |
| RA + AA  | 2 (1.5%)   |
| RA + topical antibiotic + AA   | 1 (0.8%)   |
| RA + topical antibiotic + Doxycycline + AA                                   | 2 (1.5%)   |
| RA + BPO + AA  | 2 (1.5%)   |
| RA + BPO + topical antibiotic + AA   | 4 (3.1%)   |
| RA + BPO + topical antibiotic + Doxycycline + AA                             | 1 (0.8%)   |
| RA + BPO + Doxycycline + AA  | 2 (1.5%)   |

**Notes:** <sup>a</sup>Data are in number (%) of the total included subjects N = 131.

**Abbreviations:** RA, retinoic acid; BPO, benzoyl peroxide; AA, azelaic acid.

## Effectiveness

The median number of non-inflammatory lesions at week 12 was significantly lower than that at the initial visit (8 (0–53) vs 25 (5–135),  $p < 0.001$ ). Similarly, there were significantly lower medians of inflammatory lesions at week 12 than at baseline (2 (0–22) vs 10 (0–93),  $p < 0.001$ ) and total lesion count at week 12 than at baseline (10 (1–71) vs 41 (10–160),  $p < 0.001$ ). The median change in the lesion count was  $>50\%$  (Table 4).

The number of patients with mild acne at week 12 was higher than at baseline (122 (93.1%) vs 27 (20.6%)), whereas the proportion of moderate-to-severe acne was lower at week 12 than at baseline (moderate = 8 (6.1%) vs 83 (63.4%), severe = 1 (0.8%) vs 21 (16%)). This occurred due to an improvement in the severity of acne from moderate and severe acne previously. There was a significant difference in the proportion of acne at week 12 ( $p < 0.001$ ) (Table 5). All subjects with mild acne at baseline had mild acne at 3-month follow-up. Of the 83 patients with moderate acne, 81 (97.6%) had mild acne and 2 (2.4%) had moderate acne at the end of the follow-up period. The percentage of patients with initially severe acne became mild, moderate, and remained to be severe acne was 14 (66.7%), 6 (28.6%), 1 (4.7%), respectively.

## Discussion

This analytical retrospective study is the first to evaluate the effectiveness of standard therapy for acne vulgaris (AV) based on clinical practice guidelines (CPG) in Indonesia. This study used the CPG developed by Dr. Cipto Mangunkusumo National Central General Hospital in 2017, which was developed in reference to another Indonesian guideline by the IAEM in 2015. There is a slight difference in the first-line topical therapy for severe acne when used with oral antibiotics. RA or BPO or its combination with topical antibiotic is an option in Dr. Cipto Mangunkusumo Hospital's CPG.<sup>6</sup> Meanwhile, IAEM 2015 recommends topical antibiotics and reserves BPO for pregnant and breast-feeding patients.<sup>2</sup> Dr. Cipto Mangunkusumo Hospital's CPG is comparable to the CPG for AV in Southeast Asia, which also recommends the combination of oral antibiotics with RA and BPO for moderate to severe acne.<sup>8</sup> Guidelines for AV in Europe,<sup>9</sup> America,<sup>10</sup> China<sup>11</sup> and Singapore<sup>12</sup> recommend the use of oral isotretinoin for severe acne, however this drug has not been approved in Indonesia. Indonesian guidelines have been adjusted for drug availability in Indonesia, environmental and socioeconomic factors, and skin characteristics of Indonesians.<sup>3,13</sup> Thus, the results of this study are applicable in Indonesia and could become the basis for the evaluation of current CPGs.

**Table 4** Lesion Count Changes at Baseline and Week-12

| Type of lesions               | Baseline <sup>a</sup> | Week-12 <sup>a</sup> | Percentage (%) change in lesion count | <i>p</i> value <sup>b</sup> |
|-------------------------------|-----------------------|----------------------|---------------------------------------|-----------------------------|
| Non-inflammatory lesion count | 25 (5–135)            | 8 (0–53)             | 71.4 (9.1–100)                        | <0.001                      |
| Inflammatory lesion count     | 10 (0–93)             | 2 (0–22)             | 81.8 (0–100)                          | <0.001                      |
| Total lesion count            | 41 (10–160)           | 10 (1–71)            | 77.4 (30–84.2)                        | <0.001                      |

**Notes:** <sup>a</sup>Kolmogorov–Smirnov test =  $p < 0.001$ ; data are presented in median (range); <sup>b</sup>Analysis with Wilcoxon Signed-Rank Test for absolute change of non-inflammatory, inflammatory, and total lesion counts.

**Table 5** Proportion of Acne Severity at Baseline and Week-12

| Severity | Baseline   | Week-12     | <i>p</i> value <sup>a</sup> |
|----------|------------|-------------|-----------------------------|
| Mild     | 27 (20.6%) | 122 (93.1%) | <0.001                      |
| Moderate | 83 (63.4%) | 8 (6.1%)    |                             |
| Severe   | 21 (16.0%) | 1 (0.8%)    |                             |

**Notes:** <sup>a</sup>Analysis with Wilcoxon Signed-Rank Test for comparison between the proportion of acne severity between baseline and week-12.

Eighty percent of the subjects were female, and acne was more prevalent in females than in males across all age groups. The prevalence of acne in both sexes declined as age increased, especially after the age of 25. These patterns align with a systematic review,<sup>14</sup> and epidemiological studies in Asia.<sup>15,16</sup> Male acne was most common during adolescence (under 20 years), while acne during adulthood (over 25 years), known as adult acne, was more common in females. A similar prevalence was reported in several previous studies.<sup>3,15,17</sup> Adolescent acne was 85% more common than adult acne. This may be explained by the large number of adolescents and young adults in the sample, and epidemiological studies have shown that adolescent acne is more prevalent than adult acne.<sup>15,17,18</sup> More than 50% of the subjects had a history of acne treatment, and 16% had received systemic acne medication. Patients' beliefs and knowledge about acne may influence health-seeking behavior.<sup>19</sup> The possible reasons for subjects with history of therapy to consult with a dermatologist in the hospital include dissatisfaction with previous treatment, drug side effects, and referral from a general practitioner.<sup>20,21</sup>

The majority of subjects had normal nutritional status. The proportion resembles the epidemiology of nutritional status in Indonesia, where most individuals are of normal status, followed by *overweight* and obesity I, underweight, and obesity II.<sup>22</sup> Most subjects had a secondary education level and worked indoors, which reflects the high number of teenagers and young adults under 25 years of age being students or office employees. A study in Italy found that working in an office was related to a higher risk of acne in adult females, possibly due to environmental and psychological factors.<sup>23</sup>

Most subjects had moderate acne at baseline. The same result was demonstrated in two other studies in Indonesia using the same grading system,<sup>24,25</sup> contrary to the global epidemiological data that depicts mild acne as assessed using the *Global Acne Grading System* to be the most prevalent.<sup>26</sup> The large number of patients with moderate acne in this study may be explained by a higher risk for more severe acne in Asians than in Caucasians,<sup>1,27</sup> and a higher motivation to seek help in more severe cases that negatively affect quality of life and self-esteem,<sup>16,28</sup> hence more severe acne encountered in secondary health facilities or hospitals than in primary health care.<sup>29</sup>

All patients were treated in accordance with the CPG of Dr. Cipto Mangunkusumo Hospital, based on their severity. The most commonly prescribed therapy is a combination of three first-line therapies: RA, BPO, topical antibiotics, and systemic antibiotics. This corresponds to the high proportion of patients with moderate acne. All subjects received at least a selection of first-line topical therapy. First-line topical drugs are recommended only for mild and moderate acne if the inflammatory lesions are less of a concern.<sup>3,8</sup> The use of topical retinoid therapy is also the main of choice in China and Singapore as first-line topical drugs because of its effectiveness.<sup>11,12</sup> An additional systemic antibiotic, doxycycline, was administered for all severe cases and some moderate cases. Doxycycline belongs to the class of tetracyclines, has long been used, and is effective for acne.<sup>30–32</sup> The resistance rate to tetracycline is relatively low in Indonesia, especially doxycycline, compared to macrolides and clindamycin.<sup>33</sup> This supports the use of doxycycline as the first-line antibiotic for acne in Indonesia. This study discovered that combined topical and systemic antibiotics were the most frequently prescribed drugs, which should be avoided to prevent drug resistance.<sup>31,34</sup> Antibiotic resistance is associated with acne therapy failure. This finding may guide the evaluation of acne treatment selection and the implementation of antibiotic resistance prevention efforts in the future.

The second-line therapy included addition of azelaic acid (AA). This practice is quite different from global recommendations and previous studies where AA is used as an alternative to RA or BPO.<sup>9,11,12,32,35</sup> AA has a mild comedolytic and anti-inflammatory action, so it is better suited for acne, which is predominantly a comedone. Several studies found that the efficacy of AA was comparable to that of RA or BPO monotherapy, but other studies reported better efficacy when paired with another first-line topical therapy.<sup>3,36</sup> A systematic review found that the effectiveness of AA was less than that of BPO and was indifferent to clindamycin based on the patient's self-assessment after 8 weeks.<sup>34</sup> However, AA was better tolerated and safer than RA and BPO.<sup>9</sup>

Adjuvant therapy helps in skin repair during the treatment course and mitigates the side effects of the main therapy.<sup>3,8</sup> Education about AV and gentle facial cleansers. Good patient education may improve patient adherence to planned regimens, which enhances the success of therapy.<sup>8</sup> Gentle facial cleansers are advised to be used twice daily to clean dirt, dead skin, sebum, and cosmetics, while maintaining the skin barrier and moisture. Excessive use is avoided to prevent skin damage and irritation that can worsen AV.<sup>37,38</sup> Patient education and gentle facial cleansers play an important role in supporting successful therapy; therefore, these approaches must be integrated into acne treatment.



Other adjuvant therapies received by the subjects included chemical peels, corticosteroid injection, comedone extraction, light/laser therapy, and other dermocosmetics. Chemical peels are usually prepared with glycolic acid and trichloroacetic acid and are beneficial for mild-to-moderate acne by accelerating exfoliation and tissue repair and triggering collagen synthesis. The procedure is well tolerated in Asians.<sup>11</sup> A randomized trial found that comedone extraction every two weeks was more effective in reducing the total lesion count compared to doxycycline at week 6 for moderate acne. The combination of comedone extraction and RA may minimize scar tissue formation due to blackhead extraction.<sup>39</sup> Laser therapy when administered as a part of holistic skin care or with other dermocosmetics may reduce the lesion count and improve the skin condition.<sup>37</sup>

Other dermocosmetics, such as comedolytics, sebum controllers, and sunscreens, have various actions depending on the nature of the drug.<sup>3,40</sup> A recent study showed that nicotinamide as a sebum controller is effective in reducing non-inflammatory lesions after 2 weeks in combination with zinc and antibacterial adhesive (ABA).<sup>41</sup> Dermocosmetics are beneficial as adjuncts and well-tolerated by Asians, however.<sup>40</sup> No studies have profiled the use of these adjuvant therapies for acne in general.

This study found that standard therapy based on Dr. Cipto Mangunkusumo Hospital's CPG, in accordance with acne severity, was effective within three months. Standard therapy significantly decreased the number of noninflammatory, inflammatory, and total lesions, with a median lesion count reduction of >70%. Treatment was deemed to be effective if there was a reduction of at least 50% in the acne lesion count based on Sitohang's cut-off.<sup>39</sup> In addition, there was a significant improvement in severity, as indicated by the increase in the proportion of mild acne and a decrease in moderate and severe acne within the same subjects observed at week 12. The results of this study are supported by the analysis of the effectiveness of each therapy and its combination in previous studies adjusted to the degree of severity.<sup>32,35,42</sup>

RA is the backbone therapy for all acne severities owing to its broad actions of comedolytic and mild anti-inflammatory.<sup>10</sup> RA significantly ameliorated acne severity in 12 weeks, and there was no significant difference between tretinoin concentrations of 0.04% and 1%. Tretinoin 0.5% was more effective at reducing the total lesion count than 0.1% or 0.3% at week 12. The side effects of dry skin, erythema, and irritation are more common with tretinoin use than with adapalene.<sup>35</sup> Tolerability to adapalene was highest in Caucasians, followed by Malays, and lowest in Chinese.<sup>12</sup>

BPO reduced the total, inflammatory, and non-inflammatory lesion counts with a regimen duration of more than eight weeks, and improvement in non-inflammatory lesions was evident at week 5. The risk of BPO side effects, which are similar to the side effects of RA, did not differ between most concentrations, but it was significantly higher in 10% BPO than in 2.5% BPO. There is conflicting evidence on the effectiveness of BPO compared to RA.<sup>42</sup> Systemic antibiotics must be administered for severe and moderate acne, especially if inflammatory lesions predominate.<sup>3,6</sup> Tetracyclines have anti-inflammatory and antibacterial effects and are relatively inexpensive, with good tolerability compared to other systemic antibiotics, but often cause side effects such as nausea, stomach discomfort, and photosensitivity.<sup>3,30</sup> The choice of oral antibiotics should be tailored to the patient's condition and contraindications because they are similarly effective.<sup>9,12</sup>

In general, effectiveness did not differ between the first-line monotherapy choices and paired first-line therapy choices, but a combination therapy was superior to monotherapy.<sup>9,32,35</sup> Compared with placebo, tretinoin, and clindamycin monotherapy, there was a significantly higher reduction in the total lesion count with a combination of RA 0.025% or 0.04% and BPO 5%, and a reduction in non-inflammatory and inflammatory lesions and acne severity with a combination of topical RA and clindamycin.<sup>42</sup> The combination of three topical drugs, RA, BPO, and antibiotics, significantly decreased inflammatory, non-inflammatory, and total lesions after 12 weeks. In moderate to severe acne, the addition of systemic antibiotics is more effective and give a quicker improvement than topical therapy alone.<sup>3,32</sup> In combination with RA and BPO, oral tetracycline has a higher effectiveness than topical antibiotics.<sup>32</sup> The combination regimen allows higher effectiveness due to the multiple drug actions on different acne pathogenesis.<sup>12</sup>

## Limitation

This study used medical records; therefore, the collected data depended on the availability of patient details, diagnosis, and treatment information. Drug side effects were not explored, which might have contributed to the loss to follow-up, thus introducing a bias. Additionally, the analysis of the effectiveness of standard therapy did not consider the effect of adjuvant therapy because of the numerous variations in adjuvant treatment, resulting in statistical difficulties. Further research is needed on this matter.



## Conclusion

Standard therapy based on the clinical practice guidelines of Dr. Cipto Mangunkusumo Hospital is effective in treating acne vulgaris. Standard treatment adjusted for acne severity significantly reduced non-inflammatory, inflammatory, and total lesion counts and acne severity after a 12-week regimen. Therefore, this guideline can be used as a recommendation for acne vulgaris management in Indonesia.

## Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

## Ethics Approval

This study was approved by the Health Research Ethics Committee of Faculty of Medicine Universitas Indonesia-Cipto Mangunkusumo Hospital with the code of #KET-344/UN2.F1/ETIK/PPM.00.02/2023. Researchers have signed a letter of agreement regarding confidentiality of retrospective research data with Faculty of Medicine Universitas Indonesia-Cipto Mangunkusumo Hospital as a condition for ethical approval, therefore review of patients and parental patients' medical records was not required. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 helsinki declaration and its later amendments or comparable ethical standards.

## Informed Consent

Does not apply to this study.

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## Disclosure

This manuscript is part of the author's thesis. The part that appears online is an archive conducted by the Universitas Indonesia as a thesis requirement and is not a publication. This research has never been published elsewhere. The authors report no conflicts of interest in this work.

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