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Comparison of direct medical cost between ramipril and candesartan in hospitalized acute decompensated heart failure at West Nusa Tenggara Regional Hospital

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Abstract

Introduction: Pharmacoeconomy is the field of study regarding costs analysis associated with the use of drugs in health care. The purpose of pharmacoeconomics is to compare a different drug used in the treatment with the same and different creaments in different circumstances. The purpose of this study is to determine and compare the average efficiency of direct medical costs between ramipril and candesartan combination drug in hospitalized heart failure patients with a payer perspective at the West Nusa Tenggara Regional General Hospital, Mataram, Indonesia.

Method: This study is part of an economic evaluation of direct medical cost analysis research in hospitalized heart failure patients with a payer perspective. Study design using a retrospective approach involving 45 patients 23 ith heart failure who met the study inclusion criteria and exclusion criteria. Independent t-test was used to compare the direct medical cost between ramipril and cand artan.

Results: The average gross total cost of using ramipril combination was Rp. 4,197,011 while the average total cost of using candesartan combination was Rp. 3,099,088. These results indicate there are savings in the average total cost of treatment for heart failure using candesartan that is Rp. 1,097,923. Candesartan combination provides the lowest value and is a more efficient choice compared to ramipril combination. Meanwhile, after t-test comparison reveal no significant different average direct medical costs in patients using the ramipril combination compared with the candesartan combination (p>0.05).

Conclusion: The results of this study indicate that there is no significant difference between the average direct medical costs in patients using ramipril compared with candesartan combination.

Keywords: heart failure, ramipril, candesartan, cost analysis, direct medical costs.

Introduction

The heart is the most important organ in circulation. The heart works to pump blood throughout the body to meet the body's metabolic needs at all times, bogg at rest and work. Most sufferers live after having a heart attack but then suffer heart frigure.^{1,2} Heart failure is a clinical syndrome caused by structural and/or functional abnormalities. Heart failure is a growing problem

throughout the world, with more than 20 million people affected by heart failure.³⁻⁵ In developed countries the prevalence of heart failure in the adult age group reaches 2% of the population.⁶ The prevalence of heart failure increases with age and affects 6-10% of people over 65 years.⁷⁻⁹

The World Health Organization (WHO) notes that 17.9 million people and all ridwide die from cardiovascular disorders with a percentage of 31% of deaths worldwide. More than 75% of cardiovascular sufferers occur in low and middle-income countries, and 80% of cardiovascular deaths are caused by heart attacks and strokes. In Indonesia, as many as 13,395 people with heart failure undergoing hospitalization, while as many as 16,431 people were undergoing outpatient treatment in all hospitals around Indonesia. In 2018 the results of Basic Health Research showed that the incidence of heart failure increased by 1.5% in Indonesia. While in the West Nusa Tenggara region the prevalence is 0.8%.

The additional cost-effectiveness ratio to expand the coverage of all heart failure patients is \$9,700 per life-year gained obtained in the base case. An analysis of the worst capped heart failure assuming simultaneous conservative results in an additional cost-effective ratio of \$110,000 per life-year gained. In a probabilistic sensitivity applysis, 99.74% of the possible additional ratios of cost-effective heart failure that were <\$50,000 per life-year gained. The cost of treatment is a very important issue for developing countries like Indonesia. One that affects the amount of the cost of handling heart failure is the type of drug used. Therefore in the treatment of heart failure a rational and comprehensive treatment is needed to achieve optimal medical service. 14-16

Pharmacoeconomics is the field of study regarding costs analysis associated with the use of drugs in health care. The purpose of pharmacoeconomics is to compare a different drug used in the treatment with the same condition or can be the opposite, ie comparing different treatments in different conditions.¹⁷ The results of the pharmacoeconomics can be used as a reference or assist policymakers in determining choices for available treatment alternatives so that health services become more efficient and economical. The study aims to determine and compare the average efficiency of direct medical costs between ramipril and candesartan combination drug in hospitalized heart failure patients with a payer perspective at the West Nusa Tenggara Regional General Hospital, Mataram, Indonesia.

Method

This study is part of a hospital economic evaluation of direct medical cost analysis in acute decompensated heart failure hospitalization. Study design using a retrospective approach with a payer's perspective.¹⁸ The inclusion criteria in this study were patients with main diagnoses of acute decompensated heart failure who were hospitalized in West Nusa Tenggara Regional Hospital who were seeking treatment in the period 2018.

The type of data in this study is secondary data from hospital information system (SIRS), where the data obtained was the primary diagnosed heart failure patient data that met the patient criteria in the study which included age, sex, concomitant diseases and use of combination of

ramipril (furosemide 40 mg, spinolactone 25 mg, bisoprolol 5 mg, ramipril 5 mg) or using a combination of candesartan (furosemide 40 mg, spironolactone 25 mg, bisoprolol 5 mg, candesartan 16 mg) West Nusa Tenggara Regional Hospital 2018. The criteria used in assessing costs is the comparison between heart failure patients using the combination of ramipril compared to candesartan combination. A total of 240 patients diagnosed with heart failure who received treatment at West Nusa Tenggara Regional Hospital in2018, 45 samples were obtained that met the inclusion criteria, 33 patients were using the Ramipril combination and 12 patients using the candesartan combination.

Statistical analysis in this study using SPSS version 21.0 (IBM Corporation, Armonk, NY, USA). Independent t-tes was used to compare direct medical cost between ramipril and candesartan combination. All value considered significant if p<0.05.

Result Characteristics of the study

Table 1. Clinical characteristics

Characteristics	racteristics Drugs combin		mbination Total (n=45)		Percentage (%)	
	Ramipril	Candesartan	Ramipril n=33	Candesartan n= 12	Ramipril	Candesartan
Sex	Male	Male	17	8	51.51%	66.66%
	Female	Perempuan	16	4	48.48%	33.33%
Age	18-65 years	36-65 tahun	27	7	81.81%	58.33%
	≥65 years	≥65 tahun	6	5	18.18%	41.66%
Comorbidities	With comorbidities	With comorbidities	3	0	90.9%	100%
	Without comorbidities	Without comorbidities	30	12	9.1%	0%
Status	Alive	Alive	14	4	42.42%	33.33%
	Death	Death	19	8	57.57%	66.66%

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Based on the results of this study indicate that inpatient heart failure patients in RSUDP NTB who received therapy with the combination of ramipril were 17 people (51.52%) were male and 16 people (48.48%) were female. While those who received candesartan therapy were 8 people (66.67%) who were male and 4 people (33.33%) were female. These results indicate that more heart failure patients are male than female. Meanwhile, in age characteristics shows, 18-65 years of age most diagnosed with heart failure by 81.82% and age \geq 65 years by 18.18%. While the characteristics of age at Candesartan are age 35-65 years as much as 58.34% and age \geq 65 years as much as 41.66%. Based on characteristics of concomitant diseases in the ramipril combination group of 90.9% had concomitant diseases and as many as 9.1% who did not have concomitant diseases. Whereas in the candesartan combination group all patients had concomitant disease (100%). In both groups it was seen that the majority of heart failure patients in the were mostly

accompanied by concomitant diseases. Life status characteristics shows in the ramipril group patients mostly died (57.58%) compared to the number of living patients by 42.42%. Whereas in the candesartan group it was known that heart failure patients who died by 66.67% and patients living by 33.33% (**Table 1**).

Direct Medical Cost

The description of medical expenses at the hospital can be used as input in determining the planning and control of hospital services. Costs that will be calculated in this study are direct medical costs including ramipril and candesartan drugs, other drugs, medical equipment costs, doctor's fees, nurse fees, laboratory fees and accommodation costs.

Tabel 2. Medication cost between ramipril and candesartan combination

Medication	Inpatient class	Number of patient	Item total cost (IDR)	Average medication cost (IDR)
Ramipril	VIP	5	71,773	14,355
	1	2	44,213	22,106
	2	7	77,017	11,002
	3	19	242,055	12,739
Candesartan	VIP	3	74,948	24,983
	1	1	26,964	26,964
	2	2	24,771	12,385
	3	6	123,401	20,566

Based on **table 2**, the average cost of drugs for heart failure patients using a combination of ramipril and candesartan combination has a different amount of costs. The difference in costs in each class is influenced by differences in length of stay, the number of drugs used and comorbidities besides heart failure and the types of drugs consumed so that it affects the costs that must be paid by the payer. The payer in this case is the Indonesian National Health Insurance Administering Agency (BPJS).

Table 3. Others medication cost comparison between ramipril and candesartan combination

Medication	Inpatient class	Number of patient	Item total cost (IDR)	Average medication cost (IDR)
Ramipril	VIP	5	1,918,688	383.738
	1	2	5,497,997	2,748,998
	2	7	766,951	110,993
	3	19	19,897,806	1,047,252
Candesartan	VIP	3	1,849,651	616,550
	1	1	318,754	318,754
	2	2	148,499	74,249
	3	6	1,991,553	331,925

Based on **table 3**, the average cost of other drugs for heart failure patients using the combination of ramipril and candesartan combination has a different amount of costs. Costs for drugs other than heart failure include medications used to treat comorbidities in addition to heart failure. Common comorbidities in heart failure patients are hypertension, diabetes mellitus, and myocardial infarction. Non-cardiovascular drugs used include ranitidine, lansoprazole, metformin, simvastatin, clopidogrel, and ceftriaxone.

Tabel 4. Medical equipment cost comparison between ramipril and candesartan combination

Medication	Inpatient class	Number of patient	Item total cost (IDR)	Average equipment cost (IDR)
Ramipril	VIP	5	573,594	114,719
	1	2	643,676	321,838
	2	7	620,930	88,704
	3	19	26,330,366	1,385,808
Candesartan	VIP	3	845,265	281,755
	1	1	219,409	219,409
	2	2	54,062	27,031
	3	6	1,140,748	190,124

Based on table 4, the average cost of medical devices for heart failure patients using a combination of ramipril and candesartan has a different amount of costs. The difference in the cost

of medical equipment in each class is influenced by differences in length of stay and the number of equipment used, so that it affects the cost that must be paid by the payer.

Tabel 5. Average doctor visit and hospitalization cost comparison between ramipril and candesartan combination

Medication	Inpatient class	Number of patient	Item total cost (IDR)	Average fee cost (IDR)
Doctor visit fee				
Ramipril	VIP	5	2,625,000	525,000
	1	2	1,020,000	510,000
	2	7	1,000,000	142,857
	3	19	3,620,000	190,526
Candesartan	VIP	3	3,875,000	1,291,667
	1	1	180,000	180,000
	2	2	220,000	110,000
	3	6	1,200,000	200,000
Hospitalization cost				
Ramipril	VIP	5	5,695,350	1,139,070
_	1	2	5,898,600	2,949,300
	2	7	3,579,200	511,314
	3	19	17,974,973	946,051
Candesartan	VIP	3	3,647,133	1,215,711
	1	1	394,600	394,600
	2	2	741,223	370,616
	3	6	5,030,075	838,345

Based on table 5, the average cost of doctors fee and hospitalization cost using a combination of ramipril and candesartan combination has a different amount of costs. The difference in costs in each class is influenced by differences in length of stay, number of drugs, medical equipment and service (oxygen installation, blood sampling, adult infusion set), and comorbidities in addition to heart failure and types of drugs used, so that influenced the costs to be paid by the National Health Insurance (BPJS).

Tabel 6. Average laboratory cost comparison between ramipril and candesartan combination

Medication	Inpatient class	Number of patient	Item total cost (IDR)	Average cost (IDR)
Laboratory cost				
Kombinasi	VIP	5	4.707.050	941.410
Ramipril	1	2	1,645,000	822,500
	2	7	2,389,783	341,397
	3	19	8,306,340	422,965
Kombinasi	VIP	3	1.749.000	583.000
Candesartan	1	1	205,000	205,000
	2	2	389,000	194,500
	3	6	1,690,000	281,666
Accommodation				
Ramipril	VIP	5	6.500.000	1.300.000
1	1	2	2,550,000	1,275,000
	2	7	1,875,000	267,857
	3	19	6,300,000	331,578
Candesartan	VIP	3	8.150.000	2.716.667
	1	1	300,000	300,000
	2	2	450,000	225,000
	3	6	1,450,000	241,666

Based on table 6, there is a difference in the cost of the laboratory and accommodation between ramipril and candesartan combination. Laboratory examination costs are preoperative and postoperative preparations, for patients who will undergo surgery required an individual examination based on the patient's condition. Differences in patient conditions cause different types, amounts and laboratory costs that must be incurred during treatment. Meanwhile, difference in accommodation cost due to class difference that affects the costs borne by patients. The cost for each class is different because the facilities of each room class are different. The cost of the VIP class is greater because the number of beds in the room has complete facilities compared to other treatment classes.

Table 7. Average emergency and intensive cardiac care unit cost comparison between ramipril and candesartan combination

Medication	Item total cost (IDR)	Average cost (IDR)
Emergency		
department cost		
Kombinasi	2,900,000	241,667
Ramipril	2,900,000	241,007
Kombinasi	1,000,000	142,857
Candesartan	1,000,000	142,837
Intensive cardiac		
care unit cost		
Kombinasi	3,500,000	700,000
Ramipril	3,300,000	700,000
Kombinasi	0	
Candesartan	U	0

Based on table 7, the average cost of emergency room much higher in the ramipril combination Rp. 241,667 compared to the candesartan combination of Rp. 142,857. This is because the actual number of patients who get the ramipril combination more than patients who get the candesartan combination. Meanwhile, the average cost of the intensive cardiac care unit on the ramipril combination is Rp. 700,000, while for candesartan combinations Rp. 0. This happens due to samples in studies that received candesartan combination therapy none were treated in the intensive ward.

Direct medical cost analysis

Table 8. Direct medical cost comparison between ramipril and candesartan

			Total direct	Average direct	
Medication	Inpatient	Number of	medical cost (IDR	medical cost (p
Wiedication	class	patient)	IDR)	
Ramipril	VIP	5	22.591.455	4.518.291	
	1	2	19,049,486	9,524,743]
	2	7	11,908,881	1,701,269	1
	3	19	84,951,540	4,471,134	0.570
Total			138,501,362	4,197,011	1
Candesartan	VIP	3	20,290,997	6,763,666]
	1	1	1,744,727	1,744,727	

Total	3	6	13,125,777 37,189,056	2,187,630 3,099,088	
Mean difference of direct medical cost		IDR 1,0	97,923		

Based on table 8, the average direct medical costs of patients using the Ramipril combination amounted to IDR 4,197,011 while the average direct medical costs of patients using the candesartan combination amounted to IDR 3,099,088. The difference between the average direct medical costs between a combination of ramipril and candesartan is Rp. 1,097,088. These results can illustrate that candesartan drugs are more cost-effective than ramipril drugs. Candesartan can provide lower economic value in the treatment of heart failure compared with ramipril. Meanwhile, after t-test comparison we found p=0.570 (p<0.05) which means there is no significant difference between the average direct medical costs in patients using the ramipril combination compared with the candesartan combination. However, mathematically the cost of candesartan is more efficient compared to ramipril. Graph comparison between all cost parameter can be seen in figure 1.

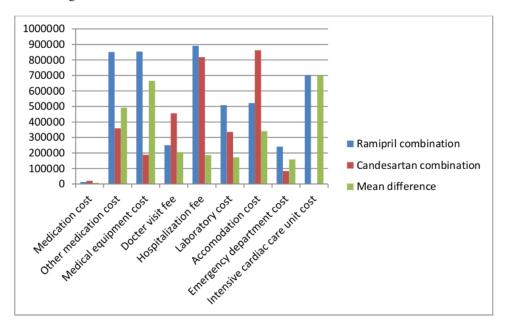


Figure 1. Comparison graph between all study parameter between ramipril and candesartan combination.

Discussion

According to Choi et al. the incidence of heart failure is more common in men than women, this is related to lifestyle and other risk factor such as smoking and alcohol consumption. 19 Study

by Mosterd et al. age is one of the factors that influence the incidence of heart failure, older age contribute as a factor for developing heart failure by 10% if it is not matched by a healthy lifest to a Lawson et al. study >85% of patients with heart failure have comorbidities or comorbidities. The World Health Organization (WHO) notes that 17.9 million people worldwide die from cardiovascular disorders with a percentage of 31% of deaths worldwide.

The cost of each patient varies due to the length of time the patient has been inpatient and treatment. The results obtained are similar to Rahmawati et al. research which states that the use of candesartan drugs is more efficient than the use of other medications for treatment in patients with heart failure.²¹

Another study conducted by Schadlich et al. Regarding coss effectiveness of ramipril in patients with heart failure in myocardial infarction in Germany, there is a variation in the value of ramipril that is 2500 to 8300 deutschmarks (DM) per life-year gained and ramipril shows a favourable cost incremental cost-effectiveness ratio in heart failure treatment compared to placebo.²²

Another study conducted in Indonesia by Baroroh et al. Regarding the cost-effectiveness of candesartan compared to the combination of candesartan amlodipine in patients with hypertension in the setting of an outpatient clinic, it shows that candesartan alone has a better cost-effectiveness of IDR 580,993 in one month of treatment.²³

Conclusion

We concluded there was no significant difference between the average direct medical costs in patients using the ramipril combination compared with the candesartan combination. Economically the candesartan combination drug saves more costs (IDR 3,099,088) compared to the ramipril combination (IDR 4,197,011) with an average difference in cost of Rp. 1,097,923.

Conflict of interest

The authors declare there is no conflict of interest regarding publication of current study.

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The current study doesn't receive any specific grant from government or any private sectors.

Ethical statement

This study was conducted after obtaining ethical clearance from director of West Nusa Tenggara Regional Hospital, with ethical clearance reference number number 070/2037/RSUDP NTB.

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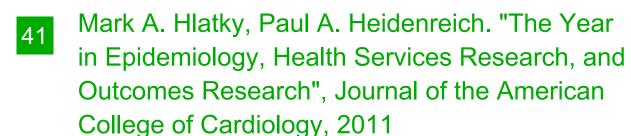
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outpatient at Karanganyar public hospital", IOP Conference Series: Materials Science and Engineering, 2017

Publication



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Publication

Mi-Hyang Jung, Hack-Lyoung Kim, Jae Hyuk Choi, Sunki Lee et al. "Heart failure awareness in the Korean general population: Results from the nationwide survey", PLOS ONE, 2019

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Publication

Submitted to University of Technology, Sydney Student Paper

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Torbjørn Omland. "Advances in congestive heart failure management in the intensive care unit: B-type natriuretic peptides in evaluation of acute heart failure", Critical Care Medicine, 2008

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Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com>

revision required (Bali Med J 1871)

6 messages

Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com> To: nuqi.gra@gmail.com

Sat, May 23, 2020 at 8:41 AM

Dear Authors,

Thank you for submitting your article entitled: "Comparison of direct medical cost between ramipril and candesartan in hospitalized acute decompensated heart failure at West Nusa Tenggara Regional Hospital"

Based on our author guidelines, Your article fulfilled the minimal required structure, https://www.balimedicaljournal.org/index.php/bmj/pages/view/authorguidlines In order to have a better-structured article, we suggest you edit based on a checklist and the collection in our archive (https://www.balimedicaljournal.org/index.php/bmj/issue/archive_).

According to the new International regulation, please fulfill the requirements below:

- 1. Please include Ethical clearance number/statement at the end of the manuscript if the bacteria were collected from clinical isolates (confirmed).
- 2. Please state your conflict of interest in the paper. (unconfirmed)
- 3. Please state the funding (if any) in your paper. (unconfirmed)
- 4. Please state each author's contribution. (unconfirmed)
- 5. Based on our proofreading application, we detected 184 critical grammatical errors.

According to our initial review, your article needs Minor Revision. Please revise your article and send it back to us in 7 days

Please find the attached revision note for your manuscript and do not forget to full fill the icime author list and contributor list

Thank you for trusting us with your hard work and we are looking forward to your response.

Warm regards,

Executive Editor BaliMedJ

Bali Medical Journal (BaliMedJ) P-ISSN: 2089-1180 **E-ISSN** 2302-2914 Indexed at: Web of Science (WOS) Clarivate Analytics **SCOPUS Elsevier All Indexing Organisation**



3 attachments



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ICJME author ship criteria.pdf 658K

nurul qiyaam <nuqi.gra@gmail.com>

Mon, May 25, 2020 at 2.32 PM

To: Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com>

Dear Editoria Team of Bali Med J

Thank you for your advice revision, soon I will sent the revision along with ICJME author list and contributor list

Best regards

Nurul Qiyaam

[Quoted text hidden]

nurul qiyaam <nuqi.gra@gmail.com>

Mon, Jun 8, 2020 at 11:02 AM

To: Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com>

Dear Editoria Team of Bali Med J

I have sent the revision trough out the system, I also attached the revised manuscript along with the ICJME author list and contributor list in the attached ment below

Warm and regards

Nurul Qiyaam

[Quoted text hidden]

3 attachments



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Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com>

Tue, Jun 9, 2020 at 10:33 AM

To: nurul qiyaam <nuqi.gra@gmail.com>

Dear Author

We had received your full revision

Soon we will come back for final decision

Best and regards Managing Editor Bali Med J [Quoted text hidden]

Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com>

Wed, Jun 24, 2020 at 2:12 PM

To: nurul qiyaam <nuqi.gra@gmail.com>

Dear author: please find the attached acceptance letter and invoice billing for your manuscript

Letter of Acceptance

24 June 2020

Dear: Nurul Qiyaam*, Baiq Leny Nopitasari, Cyntiya Rahmawati, Baiq Nurbaety, Emasiska Ajeng Pratiwi

Pharmachy Department, Faculty of Medicine, Universitas Muhammadiyah Mataram, Indonesia *Corresponding email author: nuqi.gra@gmail.com

I am very excited to accept your paper entitled:

"Comparison of direct medical cost between ramipril and candesartan in hospitalized acute decompensated heart failure at West Nusa Tenggara Regional Hospital."

Your paper will be published in the issue of Vol. 9 Number 2, 2020.

http://dx.doi.org/10.15562/bmj.v9i2.1871

(Online Link: http://balimedicaljournal.org/index.php/bmj/article/view/1871).

And it usually takes 2 to 4 months for your journal to show up at Google Scholar, but if you need it fast, you may add it up manually using your google scholar account. The CrossRef and DOI number usually activate in 3 until 6 months.

Bali Medical Journal is indexed in Web of Sciences (Thomson Reuters) and many other indexing organization: http://balimedicaljournal.org/index.php/bmj/pages/view/indexing

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(Pubmed)

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Journal Editors

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23. Genamics

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25. UDL-Edge (Malaysia)

Please do not hesitate to contact us if you need anything. It has been a pleasure for us to proofread and edit your work, and we are looking forward to your colleagues and your other papers in the near future

2 attachments



38947_612 Letter of Acceptance 1871 Nurul Qiyaam.pdf



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nurul qiyaam <nuqi.gra@gmail.com>

To: Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com>

Dear Editorial Board Member of Bali Med J

Thank you for the acceptance letter, its an honor to be published in your journal

Please find the attached payment proof for my manuscript

Warm regards Nurul Qiyaam

Pada tanggal Rab, 28 Sep 2022 pukul 22.47 Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com> menulis:

[Quoted text hidden]



1871-bmj-payment.jpeg 157K

Sat, Jun 27, 2020 at 12:20 AM

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation	Reported on page No
Title and abstract	1	(a) Indicate the study's design with a commonly	The study design has already
		used term in the title or the abstract	indicated in the abstract
		(b) Provide in the abstract an informative and	The abstract has presented
		balanced summary of what was done and what was	informative and balanced
		found	summary of the study
Introduction			·
Background/rationale	2	Explain the scientific background and rationale for	The background of the study
_		the investigation being reported	has been clearly explained.
Objectives	3	State specific objectives, including any	The objective(s) of the study
·		prespecified hypotheses	clearly stated in the
			introduction section
Methods			
Study design	4	Present key elements of study design early in the paper	Clearly presented in the paper
Setting	5	Describe the setting, locations, and relevant dates,	The setting, location, and
		including periods of recruitment, exposure, follow-	relevant dates has been
		up, and data collection	described
Participants	6	(a) Give the eligibility criteria, and the sources and	The inclusion and exclusion
•		methods of selection of participants	criteria not clearly described.
Variables	7	Clearly define all outcomes, exposures, predictors,	The outcome of the study has
		potential confounders, and effect modifiers. Give	been stated in the paper
		diagnostic criteria, if applicable	1 1
Data sources/	8*	For each variable of interest, give sources of data	Clearly described in the paper
measurement		and details of methods of assessment	
		(measurement). Describe comparability of	
		assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of	Not described
		bias	
Study size	10	Explain how the study size was arrived at	Not described in the paper
Quantitative variables	11	Explain how quantitative variables were handled in	Data analysis has been clearly
Quantum variables		the analyses. If applicable, describe which	described using descriptive,
		groupings were chosen and why	independent t-test or mann
		groupings were enosen and why	whitney test
Statistical methods	12	(a) Describe all statistical methods, including those	The statistical method has been
		used to control for confounding	described
		(b) Describe any methods used to examine	N/A
		subgroups and interactions	
		(c) Explain how missing data were addressed	Not explained in the paper
		(d) If applicable, describe analytical methods	N/A
		taking account of sampling strategy	
		(<u>e</u>) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of	Described well in the result
		study—eg numbers potentially eligible, examined	section

		for eligibility, confirmed eligible, included in the	
		study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	Not described
		(c) Consider use of a flow diagram	Not described
Descriptive data	14*	(a) Give characteristics of study participants (eg	The characteristics has been
		demographic, clinical, social) and information on	described in table 1
		exposures and potential confounders	
		(b) Indicate number of participants with missing	Not explicitly stated, but can be
		data for each variable of interest	inferred
Outcome data	15*	Report numbers of outcome events or summary	N/A
		measures	
Main results	16	(a) Give unadjusted estimates and, if applicable,	Descriptive method with
		confounder-adjusted estimates and their precision	spearman test, and chi-square
		(eg, 95% confidence interval). Make clear which	test.
		confounders were adjusted for and why they were	
		included	
		(b) Report category boundaries when continuous	N/A
		variables were categorized	
		(c) If relevant, consider translating estimates of	N/A
		relative risk into absolute risk for a meaningful	
		time period	
Other analyses	17	Report other analyses done—eg analyses of	All analysis performed has
		subgroups and interactions, and sensitivity analyses	been well presented
Discussion			
Key results	18	Summarise key results with reference to study	Well described
		objectives	
Limitations	19	Discuss limitations of the study, taking into	The limitation not stated at the
		account sources of potential bias or imprecision.	discussion section
		Discuss both direction and magnitude of any	
		potential bias	
Interpretation	20	Give a cautious overall interpretation of results	The interpretation of the results
•		considering objectives, limitations, multiplicity of	obtained has been carefully
		analyses, results from similar studies, and other	interpreted with comparison of
		relevant evidence	results of similar studies
Generalisability	21	Discuss the generalisability (external validity) of	Not clearly described
·		the study results	•
Other information			
Funding	22	Give the source of funding and the role of the	Not described
<i>O</i>		funders for the present study and, if applicable, for	
		the original study on which the present article is	
		based	
		ouoca	

^{*}Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at

http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

In order to make current manuscript better we advice the following revision

- 1. Please not use all capital in Running title
- 2. Please divide the abstract into intro, method, result, and conclusion.
- 3. Kindly describe the aim of the study at the introduction section
- 4. Kindly describe the rationale of the study at the introduction section (why we have to evaluate cost effectiveness between Ramipril and candesartan since bot are very similliar medication belong to ACE-I and ARB group)
- 5. Describe the inclusion and exclusion criteria at the method section.
- 6. Make sure to add limitation of the study at the end of discussion section.
- 7. Kindly double check your manuscript all the reference must be cited in the text or vice versa.
- 8. Any comparison regarding simmiliar study must be added at the discussion section, may be any comparison from Indonesia regarding cost effectiveness of cadesartan and ramipril
- 9. Make sure to add conflict of interest, funding, acknowledgement, and ethical aspect of the study. Since those kind of thing are very important in journal article.

Journal:

- 1. Thomas MC. Diuretics, ACE inhibitors and NSAIDs the triple whammy. Med J Aust. 2000;172:184–185.
- 2. Guilbert TW, Morgan WJ, Zeiger RS, Mauger DT, Boehmer SJ, Szefler SJ, et al. Long-term inhaled corticosteroids in preschool children at high risk for asthma. N Engl J Med. 2006;354:1985–97.

Sitasi WEB:

1. Thomas ABC. Vancouver reference style [Internet]. Oaktown (ON): University of Oaktown, Department of Science; 2007 Nov 1 [updated 2008 Jan 11; cited 2008 Feb 19]. Available from: http://www.org-name.org

Chapter di dalam buku:

1. Bjork CE Jr, McLeod RD. Formatting citations. In: Laurent B 3rd, Cool JR, editors. A history of citations and references. 5th ed. Geneva (Switzerland): Tangelo Press; 2006. p. 93-7.

Buku utuh:

1. Thomas ABC, editor. Vancouver reference style: a history. New York: Z&E Publishers; 2007. 582 p.