Health Economics & Outcome Research: Open Access

Asamani, Health Econ Outcome Res Open Access 2017, 3:4
DOI: 10.4172/2471-268X.1000145

Research Article Open Access

The Cost-Effectiveness of Entresto™ (Sacubitril and Valsartan) Compared with Enalapril in Managing Chronic Heart Failure in Ghana: Decision Analytic Modelling

James Avoka Asamani*

Head, Policy, Planning and Budgeting, Planning and Monitoring Department, Human Resources Directorate, Ghana Health Service, PMB, Ministries, Accra, Ghana

Abstract

Background: Over the years, Angiotensin-converting enzyme inhibitors (ACEis) and Angiotensin Receptor Blockers (ARBs) have been the groups of medications of choice for managing Chronic Heart Failure (CHF). However, Entresto™, a formulation of Sacubitril and Valsartan has shown to be of superior effectiveness and thus, approved for use in many countries. Nonetheless, there is a limited economic evaluation of Entresto™ in Low-and-Middle Income Countries (LMICs), leaving significant gaps in the body of evidence supporting its cost-effectiveness.

Objective: To model the lifetime cost-effectiveness of Entresto™ as compared to Enalapril in the treatment of a cohort of 42-year old patients with stage II-IV CHF with reduced ejection fraction, from the health system perspective.

Methods: A three-state Markov model was developed to simulate the long-term outcomes and costs of care for a hypothetical cohort of 42-year-old patients with CHF who were assumed to receive either Entresto™ plus recommended therapy or Enalapril plus recommended therapy (standard care). One-way sensitivity analysis was conducted using a best and worst case scenario analysis while probabilistic sensitivity analysis was done using beta distribution around the input parameters.

Results: The results show that after 30 years, more patients taking Enalapril died as compared with those taking Entresto™ (85.3% *vs.* 96.5%) but the lifetime cost of Entresto™ treatment was higher than Enalapril [US$44,656.13 (GH¢192,021.35) *vs.* US$922.99 (GH¢3,968.86)]. Also, Entresto™ as compared with Enalapril, yielded higher QALYs (7.59 *vs.* 5.33) culminating in an Incremental Cost Effectiveness Ratio (ICER) of US$19,343 (GH¢83,175.08) per QALY which may be deemed not cost-effective based on an assumed Willingness to Pay (WTP) threshold of US$5,121 (three times Gross Domestic Product Per Capita).

Conclusion: In the context of Ghana, with maximum WTP threshold of US$5,121 per QALY (threefold per capita GDP), Entresto™ is not deemed a cost-effective alternative to Enalapril unless its US market price of US$380 per monthly pack is reduced by at least 73% or the WTP threshold is raised above US$10,000 per QALY. The National Health Insurance Authority (NHIA) and the Ghana National Drugs Programme (GNDP) should consider engaging the manufacturers of Entresto™ for a possible price reduction or secure a subsidy from the government or both to make the drug available for Ghanaian CHF patients.

Keywords: Entresto; Sacubitril and valsartan; Chronic health failure; Decision analytic modelling; Economic evaluation

Introduction

Chronic Heart Failure (CHF) is a complicated clinical syndrome resulting from cardiac disorders that weaken the capacity of the ventricles to pump blood to meet essential metabolic demands of the body [1]. CHF is essentially characterised by dyspnoea and fatigue, and patients often get hospitalised for these symptoms.

CHF has become a disease of significant public health concern, affecting almost 20 million people globally and its prevalence is projected to rise by about 25% by 2030 [1]. Besides the devastating morbidity and mortality associated with the disease, its economic burden on individuals and payers of health care is equally enormous. For instance, the United States of America is reportedly spending US$30 billion annually while it also cost the British National Health Service £2.3 billion annually [1,2]. In Ghana, it is estimated that the direct cost of CHF for the health system of Ghana is about US$2 million with additional US$24 million indirect cost to the economy in the form of productivity losses [3].

Hospital-based studies have shown that the prevalence of heart failure amongst patients seeking treatment at cardiology clinics in Ghana is as high as 76%, affecting mostly the young and productive population [4]. The mean age of heart failure patients at the time of diagnosis in Ghana has been reported to be between 42 and 57 years [4,5]. Besides the debilitating symptoms, CHF has a poor prognosis of up to 50% and 90% for 5-year and 10-year mortality rates respectively [2,6]. The goals of treatment in most CHF patients includes slowing the progression of deterioration of cardiac function, improve symptoms and quality of life, avert hospitalizations and ultimately decrease mortality [7].

Over the years, the mainstay of treatment has been the Angiotensin-converting enzyme inhibitors (ACEis) or when contraindicated, angiotensin receptor blockers (ARBs) as first-line medications.

***Corresponding author:** James Avoka Asamani, Health Economics, Planning and Policy Specialist, Head, Policy, Planning and Budgeting, Planning and Monitoring Department, Human Resources Directorate, Ghana Health Service, PMB, Ministries, Accra, Ghana, Tel: +2330209409458; E-mail: jamesavoka@gmail.com

Received December 12, 2017; **Accepted** December 26, 2017; **Published** December 29, 2017

Citation: Asamani JA (2017) The Cost-Effectiveness of Entresto™ (Sacubitril and Valsartan) Compared with Enalapril in Managing Chronic Heart Failure in Ghana: Decision Analytic Modelling. Health Econ Outcome Res Open Access 3: 145. doi: 10.4172/2471-268x.1000145

Enalapril, one of the ACEs has particularly proven to be most useful in reducing CHF-related mortalities and hospitalisation [8]. However, a new drug, Entresto™ (a formulation of Sacubitril and Valsartan) has shown superior reduction in rates of hospitalisations and mortalities in CHF patients as compared to Enalapril [7,9-11].

The pivotal trial showed that as compared with enalapril, Entresto provided significant reductions in the composite endpoint of cardiovascular death or hospitalization for heart failure (21.8% *vs.* 26.5%); cardiovascular death (13.3% *vs.* 16.5%); hospitalization for worsening heart failure (incidence 12.8% *vs.* 15.6%); and all-cause mortality (17.0% *vs.* 19.8%) [9,10]. The superior benefits of Entresto™ were seen across various population sub-groups based on age, sex, weight, race, NYHA class, presence or absence of reduced kidney function, diabetes mellitus, atrial fibrillation, hypertension, and prior hospitalization. Consequently, Entresto™ has been approved in various jurisdictions [11,12] for use in conjunction with other standard recommended treatments.

In the context of developed countries with very high Willingness To Pay (WTP) thresholds, a number of studies have found Entresto™ to be cost-effective as compared to Enalapril [13-15]. Nonetheless, some of the models have attracted criticism on the basis of transparency and transferability of the findings [16]. Additionally, there appears to be limited evidence of the cost-effectiveness of Entresto™ in Low-and-Middle Income Countries (LMICs) such as Ghana. The foregoing leaves significant gaps in the body of evidence supporting Entresto™ and thereby giving rise to the need for context-specific economic evaluation in different countries.

Entresto™ at the time of writing this paper was not commercially available in the Ghanaian market for use in CHF management, and for that matter is also not yet part of the Essential Medicines List (EML) and the National Health Insurance Scheme Medicines List (NHIS ML) in Ghana [17]. To add to the available evidence especially from the perspective of resource-constrained countries, we sought to assess the cost-effectiveness of Entresto™ (formulated as 97 mg of sacubitril plus 103 mg of valsartan given twice daily) as compared with Enalapril (given 10 mg twice daily, as an example of commonly used ACEs) in addition to recommended therapy in the Ghanaian context. These dosage forms were chosen for the modelling to reflect the pivotal trial data [9,10]. Therefore, the objective of the paper is to report a model-based lifetime cost-effectiveness of Entresto™ as compared to Enalapril in the treatment of a cohort of 42-year old patients with stage II-IV CHF with reduced ejection fraction, from the health system (in the case of Ghana, the National Health Insurance Authority's [NHIA]) perspective.

Methods

Overview

A Markov model was developed to simulate the long-term outcomes and costs of care for a hypothetical cohort of 42-year-old patients with CHF who were assumed to receive either Entresto™ plus recommended therapy or Enalapril plus recommended therapy (standard care). Estimation of the model parameters was based largely on findings reported from a pivotal trial, PARADIGM-HF trial [9,10] and previous economic evaluations involving CHF patients [2,18,19]. A cohort of 42 years old was used to reflect the reported mean age at diagnosis for CHF patients in Ghana [5].

Model type and structure

Even though CHF is often classified using the New York Heart Association (NYHA) criteria which is solely based on the severity of symptoms, various treatment guidelines rather focus on not only ameliorating the symptoms to improve quality of life (QoL), but also the prevention of hospitalisation and prolongation of survival [7]. Based on the European Society of Cardiology guidelines for managing CHF [8], Markov transition states were identified and represented in the schematic diagram shown in Figure 1. Given the long-term nature of the disease condition and the recurrent tendency of hospitalisation, a Markov model was deemed appropriate for the evaluation [20].

Patients enter the model following a diagnosis of CHF and are either hospitalised if in advanced stage (worsening symptoms) or may not be hospitalised if their symptoms are stable (not severe). The patients then have a probability of transitioning from one of these states to the other (i.e. hospitalised to not-hospitalised or vice versa). In each state of hospitalised or not-hospitalised, patients also have a probability of dying from cardiovascular-related causes.

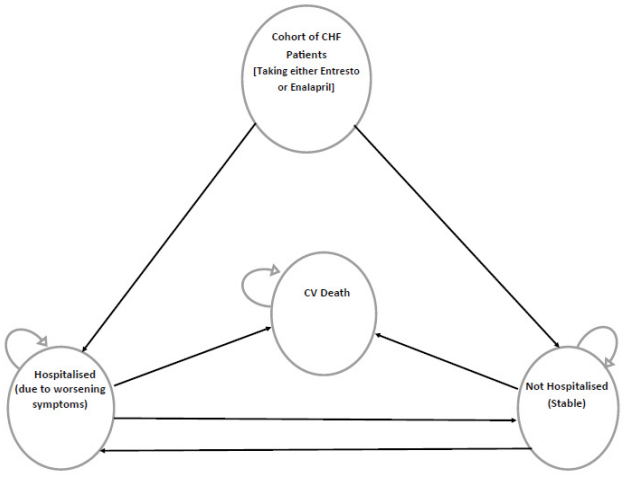
Given the high mortality rate among patients with CHF, only cardiovascular-related deaths are accounted for. The model also assumes that the transition probability from one state to another is constant throughout the patients' lifetime. Given that CHF is a long-term condition, the model tracks a cohort of 42-year-old patients diagnosed with CHF for 30 years or until they die (above the life expectancy of 62 years in Ghana).

Cycle length, discounting and half-cycle correction

Given that the natural course of CHF is associated with frequent exacerbation of symptoms requiring hospitalisation, and also with high monthly mortality following hospitalisation [21], this model was designed to have a one-month cycle length. Both costs and benefits were discounted at 3.5%. A half-cycle correction was also applied to discounted cost and benefits.

Health state utilities

A generic health measure, quality-adjusted-life-years (QALYs) which incorporate both the quality and length of life lived by CHF patients were used as the outcome of interest. The QALYs experienced in each state (hospitalised or not) were derived from the recent literature [2].



Source: Authors' construction

Figure 1: Model structure (Markov Model for CHF).

Cost data

Healthcare resource use and cost data were obtained from recent economic evaluations reports [2,22,23]and the NHIA price list in Ghana [17]. These include the monthly cost of Entresto™ and Enalapril as well as the cost associated with other recommended therapy, follow-up visits, hospitalisations and diagnostic tests. All other costs were considered similar in both patient groups treated with either Enalapril or Entresto™ and hence have not been reported [24]. All costs were converted to 2017 United States Dollars (USD).

Transition probabilities

Transition probabilities were derived in large part from the PARADIGM-HF trial (Prospective Comparison of ARNI With ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure) [9,10] and other published economi evaluations (Table 1) [13-15,25,26].

Unless otherwise stated, where the published data from PARADIGM-HF trial was used for extrapolation, patients who died from non-cardiovascular causes were excluded. Where data from epidemiological studies was incorporated [6,26], it was assumed to be for standard care (Enalapril) which was then adjusted based on the reported risk difference in the PARADIGM-HF trial for Entresto™. Conversion of proportions to rates and transition probabilities was done using standard formulae with the aid of Microsoft Excel [27,28].

Sensitivity analysis

One-way sensitivity analysis was done and presented as best and worst case scenarios. One-way sensitivity analysis was conducted on the assumption of health state utilities and costs (Table 2). Also, probabilistic sensitivity analysis (PSA) was conducted and the results presented in the form of a scatterplot on a cost-effectiveness plane and cost-effectiveness acceptability curve (Figures 2 and 3). In PSA, transition probabilities and health state utilities in both Enalapril and Entresto™ arms were randomly and simultaneously varied across their plausible ranges using beta distribution [27].

Parameter	Estimated Monthly Probability	Standard Error (SE)	Source of data/ Remarks
ENALAPRIL			
Diagnosed with CHF			
Hospitalised	0.0216	0.006	Extrapolated(9,10)
Not Hospitalised	0.9784	0.002	Extrapolated(9)
Cardiovascular-related death			
Hospitalised	0.0084	0.024	Extrapolated (9,18)
Not Hospitalised	0.0094	0.005	Extrapolated (9,18)
Hospitalised and discharged	0.0053	0.005	Delea et al. (1999)
Initially not Hospitalised but later Hospitalised	0.052	0.012	Extrapolated ((6)
ENTRESTOTM			
Diagnosed with CHF			
Hospitalised	0.0053	0.005	Extrapolated(9,10)
Not Hospitalised	0.9947	0.001	Extrapolated(9)
Cardiovascular-related death			
Hospitalised	0.0068	0.003	Extrapolated (9,18)
Not Hospitalised	0.0053	0.005	Extrapolated (9,18)
Hospitalised and discharged	0.8123	0.022	Delea et al. (1999)
Initially not Hospitalised but later Hospitalised	0.0364	0.01	Extrapolated ((6)

Notes: Conversions of proportion to rate and then to probability was done using standard formulae [27].

Table 1: Transition probabilities.

Parameter	Incremental		ICER (US$/ QALY)
	Cost (US$)	QALY	
Health State Utility (QALYs)			
Hospitalised			
Lower bound	39,501.21	1.8	21,979.69
Upper bound	39,501.21	1.79	22,008.02
Not Hospitalised			
Lower bound	39,501.21	1.63	24,247.88
Upper bound	39,501.21	1.96	20,123.23
Best Case (Health State Utilities)	39,501.21	1.63	20,123.23
Worst Case (Health State Utilities)	39,501.21	1.96	24,247.88
Cost of Entresto™			
Lower bound	32,313	2.26	14,292.10
Upper bound	54,479	2.26	24,096.16

Table 2: One-way sensitivity analysis varying Health State Utilities and Cost of Entresto™.

Results

Base case analysis

The base case results show that after 30 years, 96.5% of the simulated patients taking Enalapril are expected to die as compared with 85.3% of those taking Entresto™. Furthermore, Entresto™ as compared with Enalapril, yielded higher QALYs (7.59 *vs.* 5.33). However, Entresto™ also yielded higher lifetime cost of US$44,656.13 (GH¢192,021.35) compared with US$922.99 (GH¢3,968.86) for Enalapril. Therefore, Entresto™ accrued an incremental benefit of 2.26 QALYs with a corresponding incremental cost of US$43,733 (GH¢188,052.49) as compared with Enalapril (Table 3). Thus, while Entresto™ was relatively more effective, it was also relatively expensive when compared with Enalapril. The resulting Incremental Cost Effectiveness Ratio (ICER) is US$19,343 (GH¢83,175.08) per QALY for Entresto™ (using Enalapril as the standard comparator).

Ghana's Gross Domestic Product (GDP) per capita is estimated at US$1,707 (Bank of Ghana - BoG, 2017). Given that Ghana has no official cost-effectiveness threshold, we used the WHO-CHOICE criteria of a maximum of threefold GDP per capita [29] as the threshold for cost-effectiveness. This translates into a cost-effectiveness threshold of US$5,121 for new health technologies in Ghana. Based on this criterion, Entresto™ does not meet the cost-effectiveness threshold for Ghana. However, compared to high-income countries like the United States where the cost-effectiveness threshold is as high as US$50,000 per QALY or the United Kingdom where the National Institute for Health and Care Excellence (NICE) has set a threshold of £20,000 per QALY for new health technology in England and Wales, Entresto™ could have been deemed as a cost-effective alternative to Enalapril in the management of patients with CHF (Table 4).

Sensitivity analysis

One-way sensitivity analysis was conducted using the plausible ranges of health state utilities (QALYs) and costs (Table 2). By Ghana's threshold based on threefold of the GDP per capita (US$5,121), Entresto™ remained not cost-effective when both the best case and worst case utility values are assumed. Thus, the cost-effectiveness of Entresto™ was not sensitive to the plausible range of utilities reported in the literature [2,19].

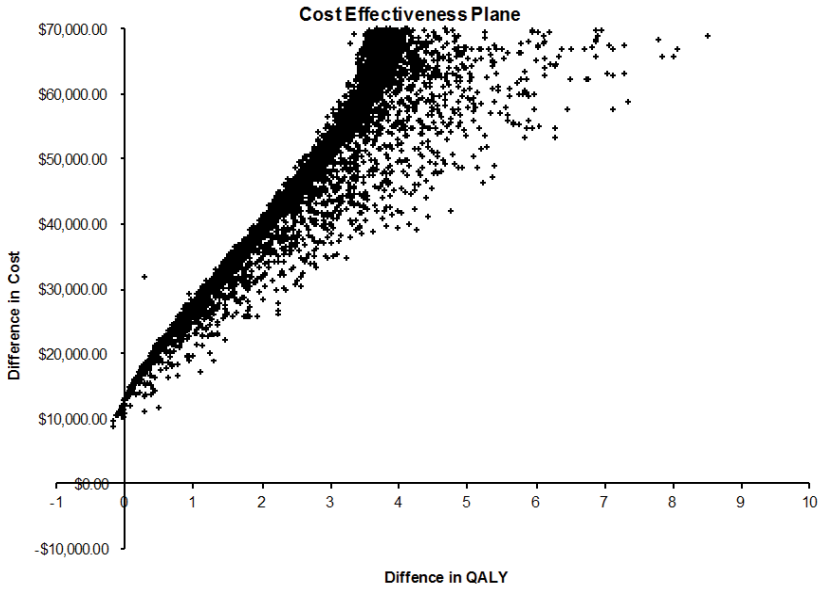


Figure 2: Cost-effectiveness Plane with Scatterplots of 10,000 iterations in PSA (Showing distribution in various quadrants).

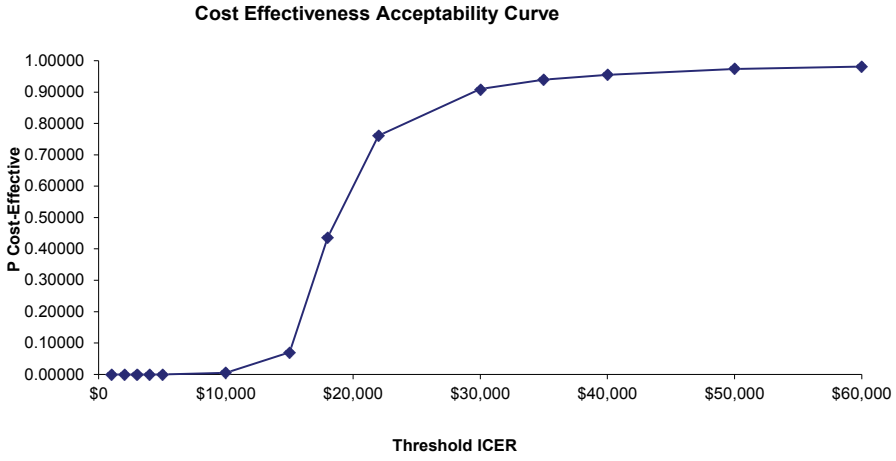


Figure 3: Cost-effectiveness Acceptability Curve (Probability of Entresto™ being cost-effective at various WTP thresholds).

Drug	Cost, US$ (GH¢)	QALYs	Incremental		ICER
			Cost	QALYs	
Enalapril	US$922.99 (GH¢3,968.86)	5.33			
EntrestoTM	US$44,656.13 (GH¢192,021.35)	7.59	US$43,733 (GH¢188,052.49)	2.26	US$19,343 (GH¢83,175.08)

Table 3: Base case cost-effectiveness results.

Also, when both the lower and upper price limits of Entresto™ were assumed in the model, the ICER remained insensitive (best case scenario of US$14,292.10 and worst case scenario of US$24,096.16 per QALY). However, a threshold analysis shows that Entresto™ could only become cost-effective in the Ghanaian context when it is sold at US$101.96 (GH¢438.43) or lower for a one-month pack. From the foregoing, the cost-effectiveness of Entresto™ as compared to Enalapril in the Ghanaian healthcare market will be dependent on the willingness of the manufacturer to reduce the price of Entresto™ by 73% of the US market price or the ability and willingness of the National Health Insurance Authority in Ghana to pay above the assumed cost-effectiveness threshold.

Probabilistic sensitivity analysis

Probabilistic sensitivity analysis was conducted to assess overall uncertainty around the input parameters. The transition probabilities for both Enalapril and Entresto™ and the health state utilities (QALYs) were simultaneously varied in a beta distribution. Following 10,000 iterations, 99.76% of the simulations were within the North East (NE) quadrant of the cost-effectiveness (CE) plane leaving only 0.24% in the

Parameter	Value	Lower	Upper	Data Source
Cost in US$ (GH¢)				
Hospitalisation only	75.24 (GH¢323.54)	54.72 (GH¢235.29)	114.65 (GH¢493.01)	NHIA ML, 2016
Outpatient care	3.07 (GH¢13.18)	2.37 (GH¢10.2)	6.06 (GH¢26.05)	NHIA ML, 2016
Enalapril cost per month	4.00 (GH¢17.2)	2.00 (GH¢8.6)	7.00 (GH¢30.1)	ICER, 2015
EntrestoTM cost per month	380.00 (GH¢1,634)	281.25 (GH¢1,209.36)	472.92 (GH¢2,033.54)	ICER, 2015
Utility Values (Quality-Adjusted Life Years - QALYs)				
Hospitalised	0.759	0.6806	0.8374	-19
Not Hospitalised	0.785	0.7125	0.8575	-19
CHF patients entering model	0.7675	0.6	0.9	-19
Exchange rate: GH¢4.3 to US$1(average 2017 rate); All costs were converted to 2017 values				

Table 4: Costs and utility values.

North West (NW) quadrant. No simulations fell within the other two quadrants (Figure 2).

This implies a 0.24% probability of Entresto™ being dominated by Enalapril. Also, based on 10,000 iterations of uncertainties, the 95% confidence interval of the ICER is estimated at US$9,905 (GH¢42,591.5) - US$38,466 (GH¢165,403.8) which are clearly above the WHO-CHOICE threshold for a country like Ghana with GDP per capita of only US$1,117. The PSA further demonstrated that the probability of Entresto™ being cost-effective in the Ghanaian context even if the WTP was raised to US$10,000 is only 5%. However, probability of cost-effectiveness of Entresto™ at higher WTP thresholds of US$18,000, US$22,000, US$30,000 and US$50,000 per QALY is about 43.7%, 76.15%, 91% and 97.4% respectively (Figure 3).

Discussion

Entresto™ showed significant clinical superiority compared to Enalapril in reducing the risk of death and hospitalisation within in a large multi-country clinical trial [9,10]. Based on the results of this landmark trial, we modelled the cost-effectiveness of Entresto™ compared with Enalapril in managing CHF over a lifetime horizon, from a Ghanaian National Health Insurance Authority's perspective. Based on the WHO-CHOICE criteria of using threefold GDP per capita at the cost-effectiveness threshold, and given Ghana's per capita GDP of US$1,707 our base case analysis demonstrates that Entresto™ may not be cost-effective alternative to Enalapril in Ghana's context [ICER = US$19,343 (GH¢83,175.08) per QALY]. The base case result was not sensitive to the extremes of health state utility scores and current price limits of Entresto™. Nonetheless, if the price of Entresto™ could be reduced or subsidized to US$101.96 or lower, it would become cost-effective. On the other hand, Entresto™ may become cost-effective if the cost-effectiveness threshold is adjusted above US$10,000 per QALY.

This study appears to be the first attempts to explore the cost-effectiveness of Entresto™ in the context of a Low-and-Middle-Income-Country (LMIC), particularly from Africa. However, a number of economic evaluations of Entresto™ has been done solely in the context of high-income countries [13-15,22]. The incremental cost-effectiveness ratio reported in the current study is largely consistent or even lower than reported in the earlier economic evaluations. For instance, based on a larger societal perspective, Sandhu et al. [15] reported a base-case ICER of US$47,053 per QALY while Gaziano and colleagues also reported US$45,017 per [13], both of which are well above the ICER of US$19,343 reported in this study. However, the previous studies concluded that Entresto™ represents a cost-effective use of healthcare resources as compared to the standard comparator whilst the current study concludes otherwise in Ghana's context. This contrast is mainly as a result of the varying perspectives adopted for the analysis and vast differences in WTP thresholds across countries. The WTP adopted in the current study is based on WHO-CHOICE's recommendation which has been criticised as not been realistic and may also harbour technical and ethical inconsistencies [30] which may be deemed as a limitation. Also, some of the previous studies implicitly assumed that anytime CHF patients are hospitalised, they would remain in that state until death [13]. The current study, however, made the alternative assumption leading to a possibly higher estimation of the benefits accrued from Entresto™.

Nonetheless, further studies are needed to fully understand the benefits and safety issues surrounding the use of Entresto™ since the simulations shown on the CE-plane show negligible probability (0.24%) where Entresto™ could be dominated by Enalapril. The circumstances under which Enalapril could dominate Entresto™ has not been well established in the literature except that the original trial reported a higher rate of a serious complication, angioedema in the Entresto™ group as compared to the Enalapril (0.5% *vs.* 0.2%) [9]. Even though this was not statistically significant in the trial (P=0.13), it could lead to some disutility in patients taking Entresto™ which could adversely impact the cost-effectiveness. Further studies and evaluations need to explore this to enrich the body of evidence for quality decision-making.

Limitations

It is important to highlight some limitations of this study. One of such limitations is fact that only cardiovascular-related deaths and hospitalisations occurring in CHF patients were accounted for in this model. This might have underestimated the overall benefit of Entresto™ since [10] reported significant reductions in the risk of all-cause mortality attributable to Entresto™.

Also, a Markovian assumption applied in this study is that patients have constant lifetime probabilities of transitioning from one state to the other [20]. However, it is plausible that, as CHF patients increase in age, their condition tends to progressively worsen and as such their chances of moving between states (say from Not Hospitalised to Hospitalised) tend to increase.

Finally, the cost of Entresto™ was based on US market prices reported in the literature since it was not available on the Ghanaian market. Thus, there might have been an overestimation of the cost of Entresto™ as our experience has shown that the prices of medicines tend to be lower in Ghana as compared to the US.

Conclusion

This study modelled the lifetime cost-effectiveness of Entresto™ compared with Enalapril in the management of patients with CHF. In a LMIC setting with maximum WTP threshold of US $5,121 per

QALY (threefold per capita GDP), Entresto™ is not deemed a cost-effective alternative to Enalapril (ICER = US$19,343). However, the circumstances under which Entresto™ could become cost-effective in Ghana includes reducing the price of the monthly pack of Entresto™ from the current market price of about US$380 to US$102 or raising the WTP threshold above US$10,000 per QALY. Thus, making Entresto™ available in the Ghanaian healthcare industry for all patients who may need it necessarily requires a price reduction from the manufacturer or a subsidy from the government or both.

On the balance of the clinical and economic evidence, the NHIA in Ghana in collaboration with the Ghana National Drugs Programme (GNDP) should consider a dialogue with the manufacturer of Entresto™ to explore the feasibility of introducing it in the Ghanaian healthcare market but in a manner as to avoid catastrophic health expenditures related to the new drug. Moreover, given the considerable uncertainty that lingers, it is recommended that the on-going trials involving Entresto™ addresses these concerns and also include economic analysis using the trial data for comparison.

References

1. Mazurek JA, Jessup M (2015) Understanding Heart Failure. Card Electrophysiol Clin 7: 557–575.
2. Griffiths A, Paracha N, Davies A, Branscombe N, Cowie MR, et al. (2013) The cost effectiveness of ivabradine in the treatment of chronic heart failure from the UK National Health Service perspective. Heart 100: 1031-1036.
3. Cook C, Cole G, Asaria P, Jabbour R, Francis DP (2014) The annual global economic burden of heart failure. Int J Cardiol 171: 368-376.
4. Owusu IK, Adu-Boakye Y (2013) Prevalence and aetiology of heart failure in patients seen at a teaching hospital in Ghana. J Cardiovasc Dis Diagn 1: 131.
5. Amoah AGB, Kallen C (2000) Aetiology of Heart Failure as Seen from a National Cardiac Referral Centre in Africa. Cardiology 93: 11-18.
6. Roger VL (2013) Epidemiology of heart failure. Circ Res 113: 646-659.
7. Ansara AJ, Kolanczyk DM, Koehler JM (2016) Neprilysin inhibition with sacubitril/valsartan in the treatment of heart failure: mortality bang for your buck. J Clin Pharm Ther 41: 119-127.
8. McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Böhm M, et al. (2012) ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012. Eur J Heart Fail 14: 803-869.
9. McMurray JJV, Packer M, Desai AS, Gong J, Lefkowitz MP, et al. (2016) Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure. N Engl J Med 371: 993–1004.
10. Packer M, McMurray JJ, Desai AS, Gong J, Lefkowitz MP, et al. (2016) Angiotensin receptor neprilysin inhibition compared with enalapril on the risk of clinical progression in surviving patients with heart failure. Circulation 131: 54–61.
11. Sible AM, Nawarskas JJ, Alajajian D, Anderson JR (2016) Sacubitril/Valsartan: A Novel Cardiovascular Combination Agent. Cardiol Rev 24: 41–47.
12. European Medicines Agency.
13. Gaziano TA, Fonarow GC, Claggett B, Chan WW, Deschaseaux-Voinet C, et al. (2017) Cost-effectiveness analysis of sacubitril/valsartan vs enalapril in patients with heart failure and reduced ejection fraction. JAMA Cardiol 1: 666–672.
14. King JB, Shah RU, Bress AP, Nelson RE, Bellows BK (2016) Cost-effectiveness of sacubitril-valsartan combination therapy compared with enalapril for the treatment of heart failure with reduced ejection fraction. JACC Heart Fail 4: 392–402.
15. Sandhu AT, Ollendorf DA, Chapman RH, Pearson SD, Heidenreich PA (2017) Cost-Effectiveness of Sacubitril–Valsartan in Patients With Heart Failure With Reduced Ejection FractionSacubitril–Valsartan in Heart Failure With Reduced Ejection Fraction. Ann Intern Med 165: 681–689.
16. Langley PC (2016) Cost-Effectiveness and Formulary Evaluation: Imaginary Worlds and Entresto Claims in Heart Failure. Innov Pharm 7: 6.
17. http://www.nhis.gov.gh/medlist.aspx
18. Delea TE, Vera-Llonch M, Richner RE, Fowler MB, Oster G (2016) Cost effectiveness of carvedilol for heart failure. Am J Cardiol 83: 890–896.
19. Göhler A, Geisler BP, Manne JM, Kosiborod M, Zhang Z, et al. (2009) Utility Estimates for Decision–Analytic Modeling in Chronic Heart Failure—Health States Based on New York Heart Association Classes and Number of Rehospitalizations. Value Health 12: 185–187.
20. Barton P, Bryan S, Robinson S (2004) Modelling in the economic evaluation of health care: selecting the appropriate approach. J Health Serv Res Policy 9: 110–118.
21. Lee D, Wilson K, Akehurst R, Cowie MR, Zannad F, et al. (2014) Cost-effectiveness of eplerenone in patients with systolic heart failure and mild symptoms. Heart 100: 1681–1687.
22. Institute of Clinical and Economic Review (ICER) (2016) CardioMEMSTM HF System (St. Jude Medical, Inc.) and Sacubitril/Valsartan (EntrestoTM, Novartis AG) for Management of Congestive Heart Failure: Effectiveness, Value, and Value-Based Price Benchmarks. California. Report No.: Final Report.
23. National Health Service (2016) Cost of Medicines- NHS Business Services Authority.
24. Morris S, Devlin N, Parkin D, Spencer A (2012) Principles of economic evaluation in health care. Econ Anal Health Care 2nd Edn Chichester John Wiley Sons 232–250.
25. Delea TE, Vera-Llonch M, Richner RE, Fowler MB, Oster G (2016) Cost effectiveness of carvedilol for heart failure. Am J Cardiol 83: 890–896.
26. Roger VL, Weston SA, Redfield MM (2016) TRends in heart failure incidence and survival in a community-based population. JAMA 292: 344–350.
27. Briggs A, Sculpher M, Claxton K (2006) Decision modelling for health economic evaluation. OUP Oxford.
28. Drummond MF, Sculpher MJ, Torrance GW, Stoddart GL (2015) Methods for the Economic Evaluation of Health Care Programmes. Fourth. Oxford: Oxford university press.
29. WHO WH. Choosing interventions that are cost-effective [WHO-CHOICE]. World Health Organization, Geneva, Switzerland.
30. Marseille E, Larson B, Kazi DS, Kahn JG, Rosen S, et al. (2017) Thresholds for the cost–effectiveness of interventions: alternative approaches. Bull World Health Organ 93: 118–124.