A cost of illness comparison between clinical judgement and molecular point-of-care testing for influenza-like-illness patients in primary care in Germany

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Abstract

Seasonal influenza poses a serious public health problem causing a high economic burden for the society (1). An early diagnosis supported by routine use of rapid influenza tests is likely to reduce overall costs in cases of suspected infection (2). It is associated with a constraint in the spread of the disease and a reduced risk of extra diagnostics and hospitalization (3,4,5). However, rapid diagnostic tests have not yet been integrated into a routine use in German primary care. Here we show that the point-of-care testing may produce lower costs of illness than relying on clinical judgement alone. We developed a decision tree model to simulate costs of illness for a hypothetical cohort of influenza like illness (ILI) patients in primary care with different diagnostic approaches: clinical judgement with no technical support and point of care testing. The cost calculating model includes direct costs of illness from a payor perspective and is calculated for age groups of elderly, adults and children. The costs of illness for ILI patients are lower by 7.05 € per patient when comparing the POCT pathway to clinical judgement alone. On a national level this could mean lower costs of 64,195,730 € when calculated for a peak influenza season. The costs of illness as well as their difference varies widely among the age groups. Using clinical judgement alone the costs of illness sum up to 155.99 € for the elderly (aged 60+) compared to 76.31 € for adults and 74.15 € for children. With POCT the costs of illness for the elderly amount 115,09 € which is 26% lower than the costs without diagnostic support. The costs for adults and children are 74.42 € and 75.66 € which means lower costs of illness of 2.5% for adults and higher costs of 2% for children. Our results demonstrate that the use of POC testing to support primary care physicians in detecting influenza in influenza-like-illness patients may reduce overall cost of illness in Germany. This is most significant when used for elderly patients. Provided data can help governments to make informed decisions about potential costs savings by integrating POCT into the reimbursement scheme.

Introduction

Influenza is a highly transmissible, acute infection of the respiratory tract, causing seasonal epidemics, especially during winter months. It can lead to numerous complications such as chronic cardiac, pulmonary or metabolic diseases[6]. Influenza is a significant contributor to global mortality and morbidity causing about 500,000 deaths per year worldwide[7]. In the 2017/2018 influenza season in Germany around 9 million patients were registered seeking medical care in primary healthcare settings due to influenza-related diseases. 60,000 patients were registered with influenza related hospitalizations. In 1,129 cases, the public health department reported that the person died of the influenza disease or its consequences[8]. This data indicates a serious public health problem causing a high economic burden for society.

According to WHO Manual (2016) the economic burden of a disease from a societal perspective is the sum of direct and indirect costs. Direct costs are associated with the use of medical resources (eg. ambulatory care, hospitalization, pharmaceuticals) usually covered by the health systems payers and to individual expenditures by the people or families affected (eg. transportation to the hospital, additional food costs and extra expenses for accommodation). Indirect costs are defined mainly as the value of lost productivity because of absenteeism from work or school, that applies to patients and their caregivers during the disease-related treatment and hospitalization[1]. Influenza-like-illnesses contribute to loss of productivity as an indirect cost which makes up 80–90% of total costs of illness[9]. The direct cost of illness together with the productivity loss in Germany sum up to 2.2 billion Euro per year in an average season and can even be higher in a peak seasons[10]. The corresponding cost per confirmed influenza case was 514 € from a societal perspective and 59 € from a health systems payer perspective in the year 2012[11].

It has already been shown, that the routine use of rapid influenza tests and early diagnosis is likely to reduce overall costs in cases of suspected influenza in German hospitals[2]. Detection of influenza during a patient's first visit in primary care allows immediate clinical decisions including targeted antiviral treatment and infection control measures[4]. Early antiviral therapy reduces the risk of complications, hospitalization or even death[12]. An early detection also reduces inappropriate use of antibiotics and decreases additional GP visits as well as additional diagnostics (eg. bloodwork or chest x-rays)[13,5]. Timely and accurate diagnosis is a key factor in prevention of virus spread[3]. However, distinguishing influenza from other respiratory viruses causing similar symptoms is a difficult task for physicians[14]. Up to date point-of-care testing (POCT) can help to overcome this problem. Therefore, countries such as Japan have established and integrated point-of-care testing (POCT) as a standard operation in their diagnostic pathway for influenza in primary care[15].

In the past rapid diagnostic tests for influenza were not very reliable because of their low sensitivity of antigen detection[16]. In recent years much more dependable new rapid nucleic acid amplification tests (NAAT) have been developed. They are self-contained, easy to use, and can detect viral RNA in 15 minutes. In Germany point-of-care testing for influenza is not yet part of the reimbursement scheme of the statutory health insurance and hence not part of standard diagnostics.

The objective of this study is to analyze differences in the cost of illness when using a diagnostic pathway supported by molecular POCT in comparison to clinical judgement in primary care in Germany. Estimates on this issue have not been published so far. Providing data on potential cost savings can help governments to make an informed decision about the potential benefits of integrating POCT into the reimbursement scheme of SHI funds.

Methodology

The study is a direct cost of illness calculation from a health care system perspective comparing NAAT POCT testing and clinical judgement to diagnose influenza. The definition of direct costs follows the WHO Manual for estimating the economic burden of seasonal influenza[1]. A decision tree model (Fig. 1.) was developed to simulate influenza-like-illness (ILI) patients in primary care with different diagnostic approaches. Patients directly presenting in an emergency department or an urgent care center were excluded.

Patients seeing a physician using rapid testing as diagnostic support are on the POCT arm of the model. The other patients are on the clinical judgement arm. Both arms have corresponding consequential costs depending on the different probabilities of resource utilization and the prescribed therapy. The sum of

costs of each arm represents the direct costs of illness for the diagnostic approach. The clinical judgement arm represents the status quo of influenza-like-illness treatment in Germany. To display the change in probability in resource utilization such as hospitalization or follow-up visits we used odds ratios taken from existing literature in which health care resource utilization with and without POC diagnostics was measured. The studies were found by a systematic literature search on MEDLINE in the period of 2010–2021 using the key words “influenza“, “cost of illness”, “hospitalization”, “point of care testing”, “early treatment”. The studies were selected based on the following criteria (1) publications were written in English and German, (2) rapid tests were done with NAAT (3) the study was performed in an OECD country. Since POCT influenza testing is not common in primary care as of yet, we opened the search to secondary care studies as well if there was no original data available from primary care. Whenever the studies used age as a discriminating factor we did so as well. All articles found were screened for relevance and applicability to our analysis. When variables were found in several publications we used the weighted average in the calculation.

Model inputs

Clinical parameters

Clinical parameters are shown in Table 2. A retrospective study that was conducted by analyzing database medical records of patients, diagnosed by German office-based physicians in two influenza seasons from May 2010 to April 2012. This estimated the probability of additional GP visits to be 20% for adults and 50% for children, the probability of antiviral treatment was 5.7% for adults and 6.6% for children, and probability of antibiotic treatment 33.1% for adults and 16.8% for children[11]. A paid transport to GP probability of 6.5% was calculated based on the number of total paid transports of non-emergency ambulance rides as well as paid taxi transports (46 million)[17] and the number of 709 million total visits in primary care[18]. The influenza-related-hospital admissions based on a data from German primary care practices from the 2017/18 season were reported for adults 0.31%, children 0.3% and elderly 1.5%[8]. The additional x-ray probability was reported 33% and of other diagnostics 52% in a randomized trial conducted in a pediatric emergency department and an acute care clinic[19].

Cost parameters

Cost parameters are shown in Table 3. The economic model calculation was conducted from the perspective of healthcare payers in Germany therefore pricing in local currency was used. Costs for different medical services found in reports or scientific literature, if obtained from different years than 2020, have been adjusted to the base year 2020 for inflation rate in Germanv based upon the consumer price index, CPI. Costs for the initial GP visit were taken from the reimbursement catalogue of the National Association of Statutory Health Insurance Physicians[20,21] and depend on the patients age group: 13.20 € for adults, 20.89 € for children and 19.92 € for elderly. Since that payment is a quarterly lump sum the costs for follow-up visits of patients can only be taken into account if that visit happens in the next quarter. Given a uniform distribution of patient visits in a quarter and a maximum interval of 7 days for the next visit only 4% of the follow-up visits are reimbursed and hence included in the follow-up costs. Testing costs for NAAT testing of influenza A and B are also provided in the said catalogue and listed with 16.50 €. As already mentioned GPs currently are not reimbursed for POC testing with ILI patients. Based on the database of The National Association of Statutory Health Insurance cost of transportation was taken from the year 2018 and inflation-adjusted estimated to 44.27 € in the year 2020[17,22]. The daily cost of antivirals of 7.66 € and 1.44 € for antibiotics for the year 2020 was used based on the pricing from ifap Service - Institute for Physicians and Pharmacists GmbH[23]. Costs per hospital stay were taken from an influenza specific German hospital cost calculation based on representative data of publicly insured patients including ICD-10 diagnosis and hospitalization costs data in the period of 2013–2019. The data distinguishes patients with and without ventilation on ICU during their hospital stay. The costs add up to 36,000.00 € for patients ventilated on ICU and 3,400.00 € for patients treated on the normal wards[24]. We also included reimbursable transportation costs of 452.77 € for patients coming to the hospital with an ambulance[17,22]. Chest x-ray costs of 16.24 € were complemented by an age specific lump sum for each patient, both of which are taken from the German reimbursement catalogue[20]. Costs for other diagnostics of 56.85 € were taken from a Spanish POCT study[25].

Different parameters for compared diagnostic approaches

The distinction in costs of illness mainly stems from different probabilities in follow up treatment of ILI patients. As described above those probabilities were taken from the existing literature in which the effect of POC testing on follow-up resource utilization was examined. With influenza POC testing in ILI patients the probability for receiving antiviral medication is more than twice as high as for clinical judgement. It is on the other hand lower (0.6) for antibiotic prescription. Since early testing provides first diagnostic guidance the odd ratios for additional diagnostics as well as follow-up visits are also lower than 1. The most cost-intensive resource in health care, a hospitalization, is also strongly influenced by the adoption of rapid testing. The odds ratio of hospitalization rate is 0.5 when comparing POC testing with clinical judgment. When physicians rely on clinical judgement alone to diagnose a patient it is twice as likely that the patient gets hospitalized. The described ratios are summarized in Table 1. They are used for calculating the changes in probability of resource utilization for the POCT approach compared to clinical judgement and are reflected in the clinical parameters shown in Table 2.

Table 1
Differences in probabilities for resource utilization comparing clinical judgement and POCT

	Odds ratios Clinical judgment and POCT	Sources
Antiviral prescription	2.1	26
Antibiotic prescription	0.6	5,26
X-rays	0.7	19
Other diagnostic tests	0.8	19
Additional GP visit	0.4	5
Hospitalization	0.5	27

Table 2
Clinical parameters

	Adults		**Children**		**Elderly**		**References**
Pathway	**Clinical judgement**	**POCT**	**Clinical judgement**	**POCT**	**Clinical judgement**	**POCT**	
Clinical parameters							
P additional GP visit	20%	8%	50%	20%	20%	8%	11
P paid transport to GP	6.5%	6.5%	6.5%	6.5%	6.5%	6.5%	17,18
P paid transport to the hospital	58%	58%	58%	58%	58%	58%	28
P antiviral treatment	5.70%	11.97%	6.60%	13.86%	5.70%	11.97%	11
P antibiotic treatment	33.10%	19.86%	16.80%	10.08%	33.10%	19.86%	11
P hospitalization *(p_hosp)*	0.31%	0.16%	0.30%	0.15%	1.50%	0.75%	8
P ventilation on ICU when hospitalized *(p_vent)*	7%	7%	7%	7%	7%	7%	24
P x-ray	33%	20%	0%	0%	33%	23%	19
P other diagnostics	52%	39%	52%	39%	52%	39%	19

Table 3
Cost inputs

Cost inputs (EUR)	Adults	Children	Elderly	References
Costs per GP visit	13.20	20.89	19.92	20
Costs per GP follow-up visit	0.5	0.79	0.76	Calculation based on KBV[20] and probability of 3,8% to see physician in the following quarter
Testing costs	16.5	16.5	16.5	20
Transport costs to GP	44.27	44.27	44.27	17,22
Costs of antivirals/day	7.66	7.66	7.66	23
Costs of antibiotics/day	1.44	1.44	1.44	23
Costs per hospital stay (patients ventilated on ICU) *(c_vent)*	36,000	36,000	36,000	24
Costs per hospital stay (patients non-ventilated on ICU) *(c_hosp)*	3,400	3,400	3,400	24
Reimbursable transport costs to the hospital	452.77	452.77	452.77	Own calculation based on number of missions[17] and total mission costs[22]
Costs per x-ray	24.36	23.03	24.36	20
Costs for other diagnostics	56.85	56.85	56.85	25

Results

The cost of illness for ILI patients presenting in primary care in Germany without POCT assisted diagnosis is 87.87 €. The three largest cost factors are additional diagnostics, the first GP visit as well as costs for hospitalization. They add up to 86% of the total costs of illness. This lies within the scope of a prior study calculating the economic burden of influenza in which direct costs added up to inflation-adjusted 63.03 €[29]. The study is from 1999 and does not include transport costs or antiviral medication. Using molecular POC testing to detect influenza in ILI patients the direct costs add up to 80.83 €. The first two largest cost factors are the same as in the clinical judgement approach but the third one is unique to the POCT pathway: testing costs. The three together sum up to 67% of the total costs. Comparing both pathways, we find 8% or 7.05 € lower costs for patients diagnosed with POCT.

When comparing costs of illness in detail we saw a rise in antiviral medication costs of 2.48 € when using molecular POCT. This result is not surprising since precise prescription of antivirals is one of the main advantages of using POC testing for detecting influenza infection. The opposite effect can be observed with antibiotic prescription: The costs drop by 1.69 € when POCT is implemented. In relative savings in the number of prescriptions the additional antivirals are nearly offset by the reduction in antibiotics. In absolute monetary terms, however, antiviral medication is more costly than widely available antibiotics. In addition, targeted use of medication and prevention of unnecessary antibiotic prescriptions may have even a greater benefit than only decreasing health care cost directly, as it helps in reducing the problem of antimicrobial resistance. Other aspects with lower costs on the POCT diagnostic pathway are hospitalizations as well as a reduced volume of additional diagnostics.

The costs of illness differ widely among the age groups. Using clinical judgement alone the costs of illness sum up to 155.99 € for the elderly (aged 60+) compared to 76.31 € for adults and 74.15 € for children. With POCT the costs of illness for the elderly amount 115,09 € which is 26% lower than the costs without diagnostic support. The costs for adults and children are 74.42 € and 75.66 € which means lower costs of illness of 2.5% for adults and higher costs of 2% for children. While for the elderly the biggest cost factor is hospitalizations the main cost driver for adults and children is the GP visit. Since this visit cannot be reduced with POC diagnostics the hospitalization rate is lowered for ILI patients when not only using clinical judgement.

Looking on a national level the costs of illness for ILI patients are 800,339,641 € with clinical judgement and 736,143,912 € with POCT assistance based on the patient numbers of the influenza season 2017/18. Taking age into account the numbers are 145,108,274 € and 148,066,319 € for children, 440,802,489 € and 429,870,865 for adults, and 214,428,877 € and 158,206,728 € for the elderly. In total there are lower costs of 64,195,730 € when using POCT for diagnosing influenza in ILI patients. The biggest cost difference lies with the elderly patients with lower costs of 56,222,149 € with diagnostic support.

Table 4
Calculation general

Cost item	POCT	Clinical judgement	Delta	Delta p.p.
Antivirals	43,066,197.34 €	20,458,870.96 €	- 22,607,326.38 €	- 2.48 €
Antibiotics	23,230,593.64 €	38,620,117.79 €	15,389,524.15 €	1.69 €
Hospitalizations	137,952,124.19 €	272,360,682.54 €	134,408,558.35 €	14.76 €
GP 1st visit	144,509,610.37 €	144,509,610.37 €	- €	- €
GP follow up visits	726,132.24 €	1,811,177.87 €	1,085,045.63 €	0.12 €
X-ray	38,190,847.07 €	54,646,839.36 €	16,455,992.29 €	1.81 €
Additional diagnostics	198,189,706.91 €	267,932,342.54 €	69,742,635.63 €	7.66 €
Testing costs	150,278,700.00 €	- €	- 150,278,700.00 €	- 16.50 €
Sum	**736,143,911.76 €**	**800,339,641.43 €**	**64,195,729.67 €**	**7.05 €**
Cost of illness p.p.	**80.83 €**	**87.87 €**		

Table 5
Calculation age group specific: children

Cost item	POCT	Clinical judgement	Delta	Delta p.p.
Antivirals	10,372,916.91 €	4,932,063.89 €	- 5,440,853.02 €	- 2.78 €
Antibiotics	2,836,363.70 €	4,720,171.28 €	1,883,807.57 €	0.96 €
Hospitalizations	18,008,617.34 €	36,017,234.67 €	18,008,617.34 €	9.20 €
GP 1st visit	40,881,732.79 €	40,881,732.79 €	- €	- €
GP follow up visits	351,646.80 €	877,796.35 €	526,149.55 €	0.27 €
X-ray	- €	- €	- €	- €
Additional diagnostics	43,324,541.06 €	57,679,275.50 €	14,354,734.44 €	7.34 €
Testing costs	32,290,500.00 €	- €	- 32,290,500.00 €	- 16.50 €
Sum	**148,066,318.60 €**	**145,108,274.47 €**	**- 2,958,044.13 €**	**- 1.51 €**
Cost of illness p.p.	**75.66 €**	**74.15 €**		

Table 6
Calculation age group specific: adults

Cost item	POCT	Clinical judgement	Delta	Delta p.p.
Antivirals	26,438,676.99 €	12,570,931.15 €	- 13,867,745.84 €	- 2.40 €
Antibiotics	16,492,577.40 €	27,446,331.47 €	10,953,754.08 €	1.90 €
Hospitalizations	56,697,053.56 €	109,850,541.27 €	53,153,487.71 €	9.20 €
GP 1st visit	76,245,842.79 €	76,245,842.79 €	- €	- €
GP follow up visits	280,303.23 €	699,705.25 €	419,402.02 €	0.07 €
X-ray	30,547,000.25 €	43,762,456.90 €	13,215,456.64 €	2.29 €
Additional diagnostics	127,862,111.07 €	170,226,680.72 €	42,364,569.65 €	7.33 €
Testing costs	95,307,300.00 €	- €	- 95,307,300.00 €	- 16.50 €
Sum	**429,870,865.28 €**	**440,802,489.55 €**	**10,931,624.27 €**	**1.89 €**
Cost of illness p.p.	**74.42 €**	**76.31 €**		

Table 7
Calculation age group specific: elderly

Cost item	POCT	Clinical judgement	Delta	Delta p.p.
Antivirals	6,254,603.44 €	2,955,875.92 €	- 3,298,727.52 €	- 2.40 €
Antibiotics	3,901,652.54 €	6,453,615.04 €	2,551,962.49 €	1.86 €
Hospitalizations	63,246,453.30 €	126,492,906.60 €	63,246,453.30 €	46.01 €
GP 1st visit	27,382,034.79 €	27,382,034.79 €	- €	- €
GP follow up visits	94,182.21 €	233,676.27 €	139,494.06 €	0.10 €
X-ray	7,643,846.81 €	10,884,382.46 €	3,240,535.65 €	2.36 €
Additional diagnostics	27,003,054.78 €	40,026,386.32 €	13,023,331.54 €	9.47 €
Testing costs	22,680,900.00 €	- €	- 22,680,900.00 €	- 16.50 €
Sum	158,206,727.88 €	214,428,877.40 €	56,222,149.52 €	40.90 €
Cost of illness p.p.	115.09 €	155.99 €		

Discussion

Cost-of-illness studies are considered an important evaluation technique in healthcare. They itemize, value, and sum the costs to provide detailed information about the economic burden of an illness. Analyzing and comparing these costs can be beneficial, especially for health care decision-makers by providing important information to support the political process management functions in defining and prioritizing health policies and interventions that they plan to implement. This study demonstrates that POCT in primary care in Germany produces lower costs of illness than relying on clinical judgement alone. The savings amount up to 64,195,730 € for a season with 9,107,800 ILI patients or 7.05 € per patient. In the subgroups of patients with a higher risk of hospitalization such as the elderly, early testing at the point of care has a more significant impact on reducing health care spending und resource utilization.

The present study was limited by the fact that within the few studies looking at the consequences of introducing POC testing in primary care many are neglecting diagnostic accuracy and do not distinguish between test result and true infection status as confirmed by a real-time PCR in the case of influenza. This limitation becomes especially relevant when discussing the cost effects of POC testing in general without considering the testing technology (lateral flow or NAAT) which in return has a high impact on the accuracy of the diagnosis. Another limitation was that most studies from which we took performance data where not conducted in Germany. As described in the methods section studies were checked for applicability to the model. However, the German health care system has some peculiarities especially in the primary care sector. Many specialized doctors such as cardiologists or pulmonologists have their own offices independent from a hospital. Patients can go directly to these specialists without seeing their GP first. They will receive specialist level care without going to a hospital. This could mean that hospitalization rates in other countries do not necessarily reflect the hospital admission frequency in Germany as well. On the other hand there is a financial incentive for German hospitals to admit patients to the wards when they are seen at an emergency department. Other countries have higher discharge rates from emergency care[30,31]. The effects run contrary and might cancel each other out. This, however, is uncertain and remains a limitation on the results. A possible expansion of the model is to also look at other respiratory viruses such as RSV or SARS-CoV-2. Next to the medical benefits there could also be an additional economic upside: since the underlying technology of detecting the viruses is the same as for detecting influenza there could be synergies in device usage and hence testing costs.

In conclusion, using rapid molecular POC testing to support primary care physicians in detecting influenza in ILI patients reduces overall cost of illness in Germany. This is most significant when used for elderly patients. Fewer follow up GP visits, less additional diagnostics and reduction in hospitalizations contribute to the lower costs. Decision makers should also consider other potential benefits that result from POC testing, including a positive effect on antibiotic resistance due to less prescriptions as well as positive effects on labor productivity due to shorter period of symptoms with early antiviral treatment. Correct diagnosis using early POC testing may also result in more patients receiving correct treatment. So, from a societal perspective the benefits of POC testing are probably much higher than our estimations suggest.

Declarations

Data availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Author Contribution Statement

Study design: M. Brachmann, D. Sauerland

Data collection: M. Brachmann, P. Serwa

Data analysis: M. Brachmann, P. Serwa

Manuscript writing: M. Brachmann, P. Serwa

Commenting on manuscript, corrections and approval manuscript: all authors

Competing Interests

Matthias Brachmann is majority owner of bcmed GmbH which received a grant from Abbott Rapid Diagnostics International, Galway, Ireland, for researching the economic effects of point of care testing. Paulina Serwa is a project manager at bcmed GmbH.

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Figures

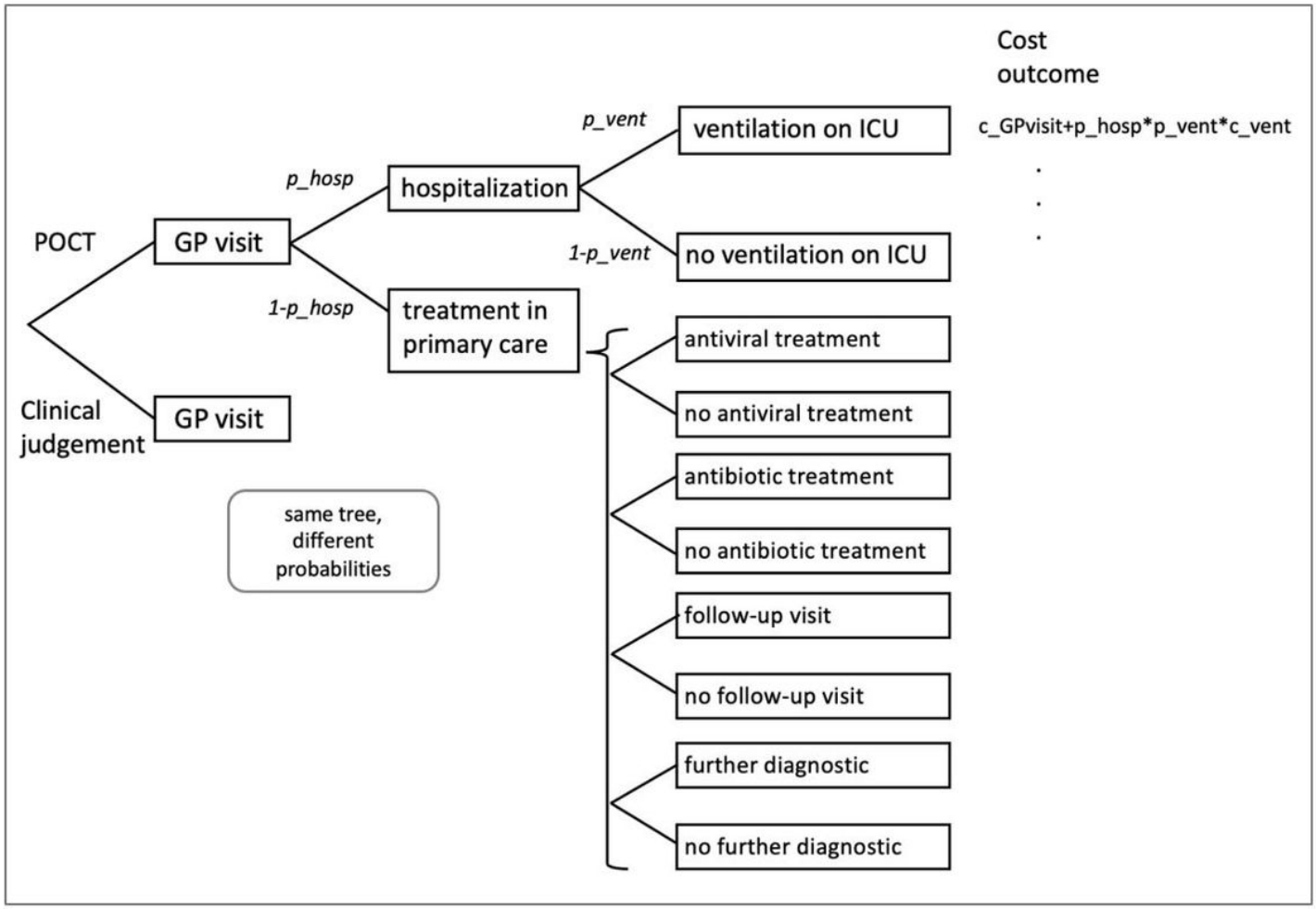

Figure 1

Simplified cost of illness calculation model