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The Economic Impact of the Introduction of Biosimilars in Inflammatory Bowel Disease

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Abstract

Objective: Inflammatory bowel disease [IBD] entails a high economic burden to society. We aimed to estimate the current and future impact of the introduction of biosimilars for infliximab on IBD-related health care costs.

Methods: We designed a stochastic economic model to simulate the introduction of biosimilars in IBD, using a 5-year time horizon, based on the Dutch situation. Prevalence data on ulcerative colitis [UC] and Crohn's disease [CD] and IBD-related health care costs data were used as input. Assumptions were made on price reductions of anti-tumour necrosis factor [TNF] therapy, increase of anti-TNF prescription rate, and development of hospitalization costs. The base case scenario included a gradual decrease in prices of biosimilars up to 60%, a gradual decrease in prices of original anti-TNF compounds up to 50%, and an annual increase of anti-TNF prescription rate of 1%, and this was compared with no introduction of biosimilars. Sensitivity analyses were performed.

Results: For the base case, cost savings over the total of 5 years were on average €9,850 per CD patient and €2,250 per UC patient, yielding in €493 million total cost savings [a reduction of 28%] for The Netherlands. Results were predominantly determined by price reduction of anti-TNF therapy, threshold price reduction at which physicians switch patients towards biosimilars and the extent to which switching will take place.

Conclusions: The introduction of biosimilars for infliximab can be expected to have a major impact on the cost profile of IBD. The economic impact will depend on local pricing, procurement policies and the physician's willingness to switch patients to biosimilars.

Key Words: Crohn's disease; ulcerative colitis; health care costs; biosimilars; anti-TNF; economics

1. Introduction

Inflammatory bowel diseases [IBD] are chronic intestinal disorders comprising Crohn's disease [CD] and ulcerative colitis [UC]. In Europe, the incidence rates are currently estimated to be 6.3 per 100 000 person-years for CD and 9.8 per 100 000 person-years for UC.[1,2] IBD is associated with a high economic burden to society;[3] the

mean annual IBD-related health care costs in CD and UC in 2011 were estimated at €6,500 and €2,400, respectively.[4] The anti-tumour necrosis factor [TNF] compounds infliximab and adalimumab were identified as the main cost drivers in IBD, accounting for 61% of annual IBD-related health care costs.[4–6] The proportion of costs for anti-TNF prescriptions is still increasing, but this is compensated by a decrease in costs for hospitalizations.[5,7]

Infliximab biosimilars, which are copy versions of currently licensed anti-TNF therapy, have been approved by the European Medicines Agency for the treatment of CD and UC, and have now entered the market. The patent on Remicade® has expired.[8] The anticipated price reduction of biosimilars relative to the prices of the originators is expected to have a major impact on the cost profile of IBD in the next few years.[9,10] In addition to the lower prices of biosimilars, the price of the originator can be expected to respond, although to a lesser extent, to the advent of these competing agents as well, which might consequently result in a change in prescription behaviour of anti-TNF therapy.

The aim of the present study was to estimate the current and future impact of the introduction of anti-TNF biosimilars on IBD-related direct health care costs in The Netherlands.

2. Methods

2.1. Model design

We designed a stochastic economic probabilistic model to simulate the impact of the introduction of anti-TNF biosimilars on annual IBD-specific health care costs in The Netherlands, compared with no biosimilar introduction [the reference case]. The model was built in Microsoft Excel 2010, using @Risk, an add-in [Pallisade Corporation @Risk v5.5, Ithaca, NY, USA] to perform analyses using Monte Carlo simulation techniques. Simulations were based on the Dutch situation, including Dutch prevalence data on UC and CD and Dutch IBD-related health care costs data. Assumptions had to be made on: 1] price reductions of anti-TNF therapy; 2] future development of increasing anti-TNF therapy prescription rates; and 3] development of hospitalization costs over time. The starting year was 2014. The time horizon modelled was 5 years. Health care costs for the years 2015 up to 2019 were simulated assuming: 1] no introduction of biosimilars [i.e. reference case]; and 2] introduction of biosimilars. For each simulation, 50 000 runs were conducted.

2.2. Model assumptions

2.2.1. Prevalence of IBD

Based on the Vektis database[8] [centre for information and standardization for insurance companies], which consisted of patients with at least one 'Diagnosis Treatment Combination' of IBD between 2008 and 2012 and alive on December 31, 2012,[9] we estimated the number of Dutch adult IBD patients in 2014 to be 85 400 [equalling 507 patients per 100 000 inhabitants, 55% UC and 45% CD patients], see Table 1. These estimations were assumed to remain stable over the next 5 years.[1]

2.2.2. B] Health care costs

Health care costs and prescription rates of anti-TNF therapy were extracted from the COIN study.[4] In short, the COIN-study enrolled more than 3000 Dutch IBD patients who were prospectively followed by means of 3-monthly detailed questionnaires on health care utilization [for full details see reference [4]]. For the current study, the most recently published 2-year follow-up data were used[5] and costs were updated to euros for the year 2014 [the starting year of the simulation] using Dutch consumer price indexes [CPI].[11] Health care costs were modelled as: 1] costs for Remicade® use [price based on average weight of 75 kg and 1.8 infusions per 3 months]; 2] costs for Humira® use (prices based on 6.5 injections per 3 months [81% administered adalimumab 40 mg per 2 weeks] or 13 injections per 3 months [19% of patients administered adalimumab 80 mg per 2 weeks]); 3] costs for biosimilar use; 4] hospitalization costs [including cost price per day spent on the medical ward of either a general hospital, an academic hospital or an intensive care unit, multiplied by the number of days admitted]; and 5] remaining health care costs [including costs for medications others than anti-TNF compounds, diagnostic procedures, outpatient clinic visits and IBD-specific surgery] [see Table 1, and details on unit prices of resource use in the COIN study [see Supplementary Table 1, available as Supplementary data at *ECCO-JCC* online]].[12,13] Annual costs for Remicade® use, Humira® use and biosimilar use were calculated by multiplying

Table 1. Assumptions regarding prevalence, health care costs and use of anti-TNF compounds in IBD patients in 2014.

Variable	Model input	Source/assumption/explanation
Prevalence		
Dutch prevalence of IBD; adult patients	IBD cases: 85,400 55% UC and 45% CD	Based on Vektis database[31]: number of patients with at least one 'Diagnosis Treatment Combination' of IBD between 2008 and 2012, and alive on December 31, 2012[32]; assumed to remain stable over time[1+22]
Anti-TNF use		
Percentage of IBD patients using anti-TNF compounds in 2014	CD: Remicade® 10%, Humira® 13% UC: Remicade® 3%, Humira® 2%	[5]
Annual costs		
Annual average health care costs/ patient, in euros for the year 2014, whereof	€/CD patient €/UC patient	Extracted from the COIN study[4,5] and updated for the year 2014 using Dutch consumer price indexes[33]
costs for Remicade® use	€ 2,025 € 633	
costs for Humira® use	€ 2,258 € 285	
costs for biosimilar use	€ 0 € 0	
hospitalization costs	€ 802 € 340	
costs of remaining health care utilization	€867 € 1,069	Including diagnostic procedures, outpatient clinic visits, surgeries and medication use other than anti-TNF compounds

IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis; TNF, tumour necrosis factor.

simulated annual prescription rates with simulated annual unit prices. Hospitalization costs were assumed to decrease over time.[5,7] Other health care consumptions were assumed to remain stable over time. Health care unit prices for the years 2015–2019 were simulated as real-time prices and were corrected for inflation, using the average annual observed consumer price index [CPI] of health care for the years 2005–2015.[11] Only medication prices were assumed to remain stable [i.e. no inflation], according to the findings of recent years.[11]

2.3. Reference case

The reference case represented the situation with no introduction of biosimilars for infliximab. In this simulation, the 2014 situation was maintained. Thus, neither anti-TNF prescription rates, nor hospitalization consumptions nor other health care consumptions were assumed to change over time. Correction was only applied for price inflation for the years 2015 up to 2019.

2.4. Base case scenario

When simulating the introduction of biosimilars, additional assumptions had to be made. In order to substantiate these assumptions, we presented different future scenarios to an expert panel of 15 gastroenterologists with expertise on IBD, employed in seven academic and six general Dutch hospitals. Based on the combined responses of this expert panel, the base case scenario was defined [Table 2]. [For full details see Supplementary Table 2, available as Supplementary data at *ECCO-JCC* online.] The assumptions in the base case scenario included:

1. The use of anti-TNF compounds will continue to increase annually by 1% (with a minimum of 1% and a maximum of 2% [modelled with Pert distribution[14]]), which is in line with the observed increase in the use of anti-TNF compounds in the COIN study[5] and the steady increase of anti-TNF volume over the years 2006–2014.[15]
2. Since biosimilars will be cheaper than the originators, we assumed that biosimilars will preferentially be prescribed in anti-TNF naïve patients, although a subset of patients can be expected to be initiated on a subcutaneous alternative, such as Humira®. We therefore assumed that 20% of new anti-TNF users will start on Humira® and 80% on infliximab [80% biosimilars and 20% Remicade®].
3. The expert panel expected that, due to price competition, the price of biosimilars will be considerably lower than the 2014 price of Remicade®, with a plateau of 40% of the original price reached after 5 years and with a minimum of 30% and a maximum of 60%, modelled as an exponential decrease [see Figure 1]. This estimate seems to be a reliable prediction based on recent pricing of biosimilars in The Netherlands.

Table 2. Model input for the base case scenario, in addition to the general assumptions.

Variable	Model input	Source/assumption/explanation
Anti-TNF [use and prices]		
Use of anti-TNF compounds 2015–2019	Linear increase of minimum, most likely and maximum 1%, 1% and 2%/year [modelled as Pert distribution]	Source: expert panel [Supplementary Table 2],[5,15]; resulting in a total increase of minimum, most likely and maximum 5%, 5% and 10%, respectively, over the simulated period 20152019
Subtype of anti-TNF compounds in new anti-TNF users	Humira®: 20% Infliximab: 80% Remicade®: 20% biosimilars: 80%	Assumptions
Biosimilar price in relation to Remicade® price of the year 2014[a]	Pert[9] [30%. 40%, 60%], and modelled as a gradual exponential decrease in price	Source: Supplementary Table 2. The numbers are presented as the residual percentages of the original price. This price reduction was assumed to be quickly reached [modelled as an exponential function] after biosimilar introduction
Remicade® price in relation to Remicade® price of the year 2014[a]	Pert [40%, 50%, 70%], and modelled as a gradual linear decrease in price	Source: expert panel [Supplementary Table 1]. This price reduction was assumed to be reached linearly after biosimilar introduction
Humira® price in relation to Humira® price of the year 2014[a]	Pert [40%, 50%, 90%], and modelled as a gradual inverse exponential decrease in price	Source: expert panel [Supplementary Table 2] . This price reduction was assumed to be reached slowly [modelled as an inverse exponential function] after biosimilar introduction
Remicade® and Humira® users switching to biosimilars		Source: expert panel [Supplementary Table 2]
Applicable when biosimilars are less than % of the original price	Pert [30%, 50%, 80%]	
When this threshold price reduction is reached, …% of Remicade® and Humira® will switch to biosimilars	Uniform [80%, 85%], gradually reached	
Hospitalizations and other health care consumptions		
Development of hospitalization consumption 2015–2019	Uniform [0%, 10%]	Assuming no [0%] up to moderate decline of maximum 10% in 5 years' time[5]
Development of other health care costs 2015–2019	No further increase or decrease	Assuming other health care consumptions to remain stable over the next 5 years. Only price inflation correction was applied[5]

TNF, tumour necrosis factor.

[a]rices for biosimilars, Remicade® and Humira® were assumed to be highly correlated [r = 0.95].

4. The expert panel expected Remicade® and Humira® to remain more expensive than biosimilars over time. However, the manufacturers of these compounds were expected to respond to the market entry of biosimilars [price competition] by gradually reducing their prices towards 50% of the original price with a minimum of 40% and a maximum of 70% in Remicade® and a minimum of 40% and maximum of 90% in Humira® [Pert distribution] [concerning real purchasing prices]. Humira® prices were assumed to decrease more slowly, because no direct competitor of this compound is presently available on the market. The expected price development of biosimilars, Remicade® and Humira® are depicted in Figure 1. In order to account for the fact that prices of biosimilars, Remicade® and Humira® are interrelated, the simulated prices were modelled to be highly correlated [r = 0.95]. This means that when, for example in one of the iterations, the price for biosimilars is drawn out of the middle of the underlying distribution, then the other two prices will be drawn out of the middle, out of their underlying distributions as well.
5. Concerns regarding efficacy and safety of newly introduced biosimilars caused the expert panel to expect a relative high price reduction of 50% [minimum 30% and maximum 80%, Pert distribution] necessary to induce a switch to biosimilars in anti-TNF users. When this threshold price reduction would be reached, a minimum of 80% and maximum of 85% [uniformly distributed] of anti-TNF users would be expected to gradually switch towards biosimilar therapy. Furthermore, it was assumed that in many hospitals, switching anti-TNF users to biosimilar therapy would be an active process, forced by regulatory arrangements in the organization.
6. Hospitalization costs were assumed to decrease gradually over time with a minimum of 0 and a maximum of 10% reduction compared with the year 2014, modelled with uniform distribution.

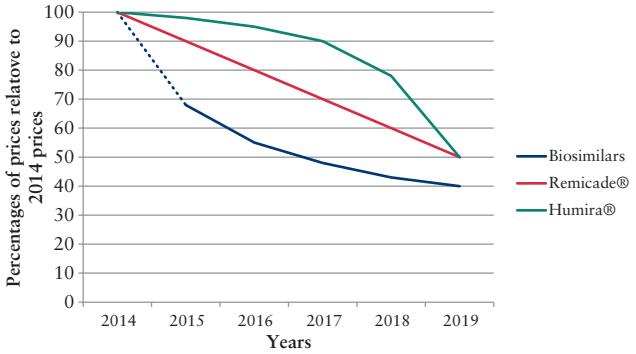

Figure 1. Expected development of anti-TNF compound prices in 2015-2019 relative to 2014 prices due to the introduction of biosimilars (base case scenario).

2.5. Sensitivity analyses

One-way sensitivity analyses were conducted to test the robustness of our model [see Table 3]. In each analysis, one of the components was adjusted relative to the base case scenario, and all other variables remained unchanged. Parameters that were varied in the sensitivity analyses included: a] a higher market uptake of anti-TNF

Table 3.

Sensitivity analysis, Nr	Assumption/point estimation/distribution	Explanation
1] Use of anti-TNF compounds 2015–2019	Most likely increase over 5 years of 10% [vs 5%]	Impact of high market uptake anti-TNF compounds due to decline in prices
2] Subtype of anti-TNF compounds in new anti-TNF users	Humira®: 20% Infliximab: 80% Remicade®: 0% [vs 20%] Biosimilars: 100% [vs 80%]	Impact of new infliximab users to all start with biosimilar therapy
3] Biosimilar price in relation to Remicade® price of the year 2014	Price difference immediately reached [vs gradually]	Impact of immediate maximum price reduction of biosimilars
4] Anti-TNF price in relation to Remicade® price of the year 2014	Modelled as a range of point estimators from 80% to 30% [vs Pert [30%. 40%, 60%] for biosimilars, Pert [40%, 50%, 70%] for Remicade® and Pert [40%, 50%, 90%] for Humira®]	Impact of a range in price reduction of anti-TNF therapy [including biosimilars, Remicade® and Humira®], starting with 20% reduction [80% remaining of price of originator in 2014] up to 70% reduction [30% remaining of price of originator in 2014]
5] Remicade® and Humira ® price in relation to 2014 prices	100% [vs Pert [40%, 50%, 70%] for Remicade® and Pert [40%, 50%, 90%] for Humira®]	Impact of no price reductions of Remicade® and Humira® after introduction of biosimilars
6] Remicade® and Humira® users switching to biosimilars		
6A] Applicable when biosimilars are less than …% of the original price	95% [vs Pert [30%, 50%, 80%]]	Impact of physicians switching to biosimilars on even a very small price reduction
6B] Applicable when biosimilars are less than …% of the original price	30% [vs Pert [30%, 50%, 80%]]	Impact of physicians only switching to biosimilars on a high price reduction
6C] When the threshold price reduction is reached, …% of Remicade® and Humira® will switch to biosimilars	Uniform [5%, 10%] [vs Uniform [80%, 85%]]	Impact of only a small proportion of patients switching to biosimilars when the threshold price reduction of reached
6D] When the threshold price reduction is reached, …% of Remicade® and Humira® will switch to biosimilars	Uniform [90%, 100%] [vs Uniform [80%, 85%]]	Impact of a large proportion of patients switching to biosimilars when the threshold price reduction is reached

TNF, tumour necrosis factor.

compounds [+10% in 5 years]; b] new infliximab users all starting on biosimilars [100%]; c] immediate maximum price reduction of biosimilars; d] a range of price reductions of anti-TNF therapy [between 20% and 70%]; e] physicians switching towards biosimilar therapy on high or low price reductions of biosimilars [705%]; f] only a small, or a large, proportion of patients switching towards biosimilar therapy once threshold prices are reached [5/10%90/100%]; and g] Remicade® and Humira® not reducing their prices after biosimilar market entry.

2.6. Outcomes

Health care costs for the reference case, the base case and the different sensitivity analyses were presented per CD or UC patient, for the total Dutch IBD population, per 100 000 inhabitants for the different years [2014–2019] and as sum over the total simulated period of 5 years. The differences in health care costs between scenarios and the reference case represented the economic impact of the introduction of biosimilars.

3. Results

3.1. Base case compared with reference

In the base case scenario, the introduction of biosimilars for anti-TNF resulted in gradual inclining cost savings towards a total of €9,850 per CD patient and €2,250 per UC patient over the simulated 5 years, equalling a 33% and 19% reduction in total costs per patient, respectively [Table 4]. In the base case, the introduction of biosimilars yielded total health care savings of €493 million over the total 5 simulated years after the introduction in The Netherlands, equalling a 28% reduction in total costs [Figure 2]. Cost savings reached €2.93 million per 100 000 inhabitants within the total 5 years. The percentage of the mean annual costs of anti-TNF compounds relative to the total health care costs declined from 62% to 18%. Detailed results of the base case scenario are presented in Supplementary Table 3, available as Supplementary data at *ECCO-JCC* online.

3.2. Sensitivity analyses

In Figure 3, a Tornado graph is depicted, including the components to which the economic impact of the introduction of biosimilars would be most sensitive. The economic impact was influenced mostly by price reductions of anti-TNF therapy, but was also subject to the prescription behaviour of the physician. If physicians would switch to biosimilars in case of only limited relative price reductions, an additional €121 million could be saved as compared with the base case scenario. Conversely, if switching to biosimilars only occurred after large price reductions, cost savings could be expected to be substantially lower. The amount of switching towards biosimilars, once the threshold price reduction was reached, would also influence the final economic impact but to a lesser extent. Even in the case that price reductions would cause a market uptake of biologics of 10% in 5 years instead of a steady market growth of 5%, total cost savings over 5 years would reach €472 million. Mean total cost savings per alternative scenario are presented in Supplementary Table 4, available as Supplementary data at *ECCO-JCC* online.

In Figure 4, a range in potential anti-TNF price reductions is depicted with corresponding total cost savings over 5 years for the Dutch IBD population. Larger price reductions were associated with higher corresponding cost savings.

Table 4. Mean results of the reference [no biosimilars] and base case scenario and simulated differences for the separate years and for the total simulated period.

	2014	2015	2016	2017	2018	2019	In 5 years [total]
IBD-specific health care costs per CD patient [mean, €]							
Reference	5,950	5,960	5,970	5,980	5,990	6,000	29,900
Base case	5,950	5,710	5,010	3,900	2,990	2,450	20,000
Difference	-	-250	-970	-2,080	-3,000	-3,550	-9,850
IBD-specific health care costs per UC patient [mean, €]							
Reference	2,330	2,330	2,340	2,350	2,380	2,360	11,800
Base case	2,330	2,250	2,100	1,870	1,690	1,590	9,500
Difference	-	-81	-240	-480	-670	-770	-2,250
IBD-specific health care costs per IBD patient [mean, €]							
Reference	3,960	3,970	3,970	3,980	3,990	4,000	19,900
Base case	3,960	3,810	3,410	2,780	2,280	1,980	14,200
Difference	-	-160	-570	-1,200	-1,720	-2,020	-5,700
Health care costs for the total Dutch IBD population [mean, € in millions]							
Reference	344	345	346	346	347	348	1,732
Base case	344	331	296	242	198	172	1,239
Difference	-	-14	-49	-105	-149	-176	-493
Cost difference per 100 000 population[33] [mean, € in millions][a]							
Difference	-	-0.08	-0.29	-0.62	-0.89	-1.05	-2.93
Percentage of costs of anti-TNF/total health care costs in IBD patients [mean, %]							
Reference	61	61	61	61	61	61	
Base case	61	60	55	44	29	18	

In The Netherlands, switching from originator to biosimilar is regulated at local level. The health budget is decided on in consultations between insurance companies and hospitals. Local choices regarding prices of biologic therapy are negotiated between hospitals and pharmaceutical companies.

A specification of medians and 90% confidence intervals of the base case scenario can be found in Supplementary Table 3. Reference represents no introduction of biosimilars for anti-TNF therapy.

TNF, tumour necrosis factor; IBD, nflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitits.

[a]Calculated for the Dutch population in 2014: 16 829 inhabitants. Costs were rounded to three digits. Of note, negative costs represent cost savings.

4. Discussion

This study showed that the introduction of biosimilars for infliximab results in substantial savings for IBD-specific health care costs within the first few years. For the Dutch IBD population, total cost savings may amount to €493 million within 5 years after the introduction of biosimilars [equalling a reduction in 28% of total health care costs and €2.93 million cost savings per 100 000 inhabitants]. The economic impact of biosimilars is most sensitive to the factual price reductions of anti-TNF therapy, but also depends highly on the threshold price reduction from which physicians switch patients towards biosimilars, and on the extent to which switching takes place once threshold prices are reached.

Over the past few years, multiple different biosimilars have been introduced, of which biosimilars for infliximab were the first to be approved in the field of gastroenterology.[9,16] Price reductions between 10% and 35% have previously been observed,[9] but actual implemented price reductions are uncertain, since data on prices only represent ceiling prices. Non-transparent pricing, due to contracting with hospitals, can lead to large price fluctuations which will not be publicly available.[15] Three budget impact studies have recently been performed: for biosimilars for infliximab; for the treatment of CD in eastern European countries[17]; for the treatment of autoimmune diseases in five European countries[18]; and for the treatment of rheumatoid arthritis in central and eastern European countries.[19] These studies all projected significant cost savings. Concerning eastern European countries, it is mentioned[17] that the introduction of biosimilars may offset the inequity in access to biologic therapy for CD between central and eastern European countries. Concerning the studies performed in central and Western Europe,[18,19] we made some methodological choices that are different compared with those of the previous models: 1] additional to drug-related costs, we added costs for hospitalizations, surgeries, diagnostics and outpatient clinic visits; 2] we projected a longer time horizon of 5 years instead of 1 and 3 years; 3] we added Humira® therapy as a significant market competitor; 4] we added price reductions of the originators as a response to the introduction of the new competitors; and 5] in contrast with previous studies, we did not presume a steady state of the potential market for biosimilars. With respect to the latter argument, the assumption that the introduction of biosimilars, accompanied by a reduction in prices, will only lead to a shift from the use of originators to biosimilars may not be realistic. We argue that the availability of lower-priced biosimilar versions of anti-TNF may lead to a reappraisal of current treatment algorithms, potentially resulting in an increase of top-down strategies in IBD patients.[20] Therefore, the number of users might increase beyond trend as prices fall.[21]

In the two previous budget impact studies on biosimilar-infliximab market entry,[18,19] modest price reductions of maximum 30% were modelled. Although we included a range of possible price reductions in the sensitivity analyses of our study, our base case scenario was based on increasing price reductions towards 60% for biosimilars and 50% for Remicade® and Humira®. However, it might take time to

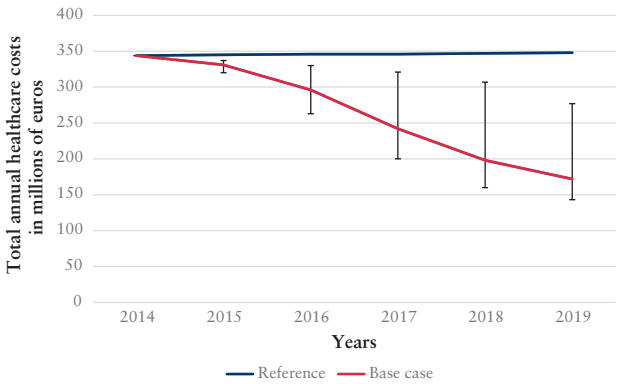

Figure 2. Development of total annual healthcare costs of Dutch IBD population according to the base case scenario over the years 2014-2019 (mean euros, presented in millions). Error bars represent 90% confidence intervals of the mean.

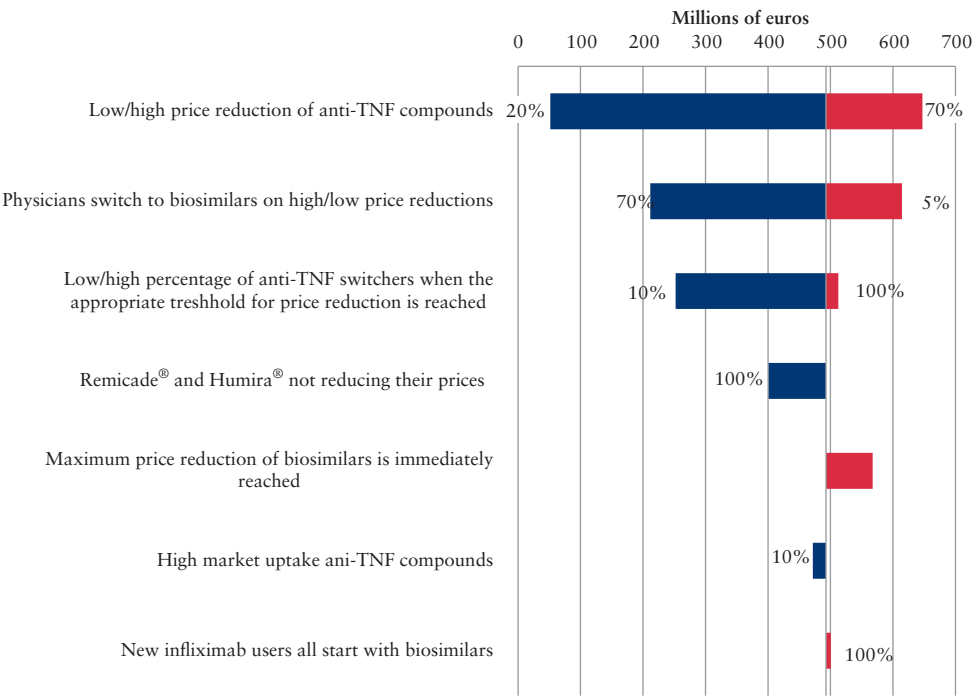

Figure 3. Sensitivity analyses in comparison to base case results. Alternative scenario-analyses depicted in a Tornado diagram. The x-axis shows the effect of changes in selected variables on the total cost savings relative to the Base case scenario. The y-axis shows the model parameter that was varied. The bars indicate the change in total cost savings caused by changes in the value of the indicated variable holding all other parameters similar.

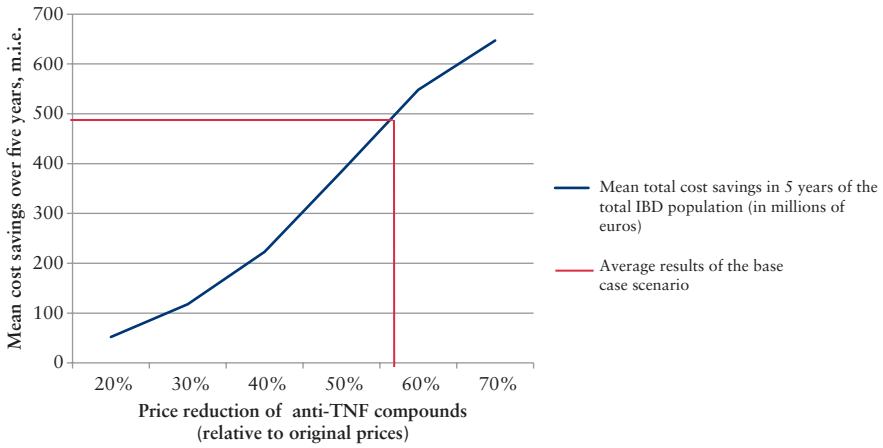

Figure 4. Mean cost savings over five years for different price reductions of all anti-TNF compounds. Including equal price reductions of biosimilars, Remicade® and Humira®, with the assumption of exponential price decline in biosimilars, a linear price decline in Remicade® and an inverse price decline of Humira®.

reach these price reductions, as assumed in our model, so that initial price reductions in the first years after the introduction of biosimilars are comparable to those of previous studies. Irrespective of considerable differences regarding the design of our study, the main findings are fairly similar: the entrance of biosimilars for infliximab is projected to cause substantial cost savings for the health care system.

Several assumptions were required in order to simulate our results. For example, we assumed the incidence rate of IBD to remain stable. Furthermore, population ageing was not taken into account. We do not expect population ageing to influence IBD-specific health care costs within the next 5 years, because the average costs incurred by elderly IBD patients are considerable lower than those incurred by younger patients.[12,22–24] As input in our model, we considered the health care costs as calculated in the COIN study representative for the domain of our study. Patients of the COIN study were derived from seven academic and seven general hospitals, and data were obtained during more than 2 years of follow-up. The validity of the self-report method used in this study was underscored by our recent study, in which we showed that calculated costs are highly concordant with data from the electronic patient record.[25] Moreover, we previously assessed the representativeness of the COIN study by performing a non-responder study and could not detect major differences in demographic or disease characteristics between responders and non-responders.[4] Therefore, we believe that these data are largely generalizable to the whole Dutch IBD population. Furthermore, we assumed a decrease in IBD-related hospitalizations over the next few years. This assumption is in line with observations from several studies, and has been ascribed to an increase in anti-TNF prescription rates.[5,7] The use of anti-TNF compounds was projected to increase with 5% over the next few years, extrapolated from an annual increase of 1% over 2 years of follow-up in the COIN study.[5] This increase may be attributed to the fact that a plateau of anti-TNF use has still not been reached in IBD.[15] We feel that a market uptake up to 13%, as calculated in previous studies,[18,19] might however be overestimated.

Second to the direct effect of price reductions of anti-TNF compounds, both the prescription behaviour and the procurement policies regarding switching of patients will substantially affect total health care costs. In the base case scenario, high price reductions were required for a physician to switch towards biosimilars. However, once concerns regarding interchangeability, safety and effectiveness of biosimilars are eliminated, barriers towards switching patients may diminish.[26,27] Substitution of originator for biosimilar is regulated at the country level[a] and, due to local budget, policies regarding substitution will differ as well.[28]

In the following years, many biosimilars are expected to enter the market.[29] Corresponding price reductions may force pharmaceutical companies to lower prices of originators and therapies which share the market. Substantial cost savings can therefore be anticipated and biologics may become available for a larger number of patients. In this era of rapidly changing treatment options, the findings of our study are highly relevant and may contribute to a better understanding of future developments. Since real purchasing prices of biologics and biosimilars are not publicly accessible, the components of our model and the corresponding outcomes provide clarity and transparency on this subject.

Other strengths of this study include the specification of the economic impact of the introduction of biosimilars for IBD-related health care, including not only costs directly related to the medication, but also IBD-specific hospitalizations, outpatient clinic visits and surgeries. Our model included various aspects of the market entry of a biosimilar, including price reductions, the potential market uptake, competition with adalimumab therapy, prescription behaviour and switching policies. Moreover, as cost savings are presented per 100 000 inhabitants, our results can be extrapolated to other countries. However, there are limitations to our analysis that warrant comment. Our model is founded on several assumptions [e.g. for price reductions], resulting in the introduction of uncertainty and translating into broad confidence intervals. Furthermore, we did not include more infliximab biosimilars that are yet to be introduced, the market uptake of novel biologics such as integrin antagonists[30] or the introduction of biosimilars for Humira®, of which the patent is due to expire within the next few years.[8] The emergence of these biosimilars can be expected to cause a similar shift in the cost profile in IBD, hence a further reduction of anti-TNF related costs.

In summary, IBD entails a high economic burden to society, which is predominantly determined by the use of biologics. The introduction of biosimilars for infliximab can be expected to result in substantial cost reductions for IBD-related health care. In turn, anti-TNF therapy may become available for a larger number of patients.

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Conflict of Interest

MS has no competing interests. BO has acted as a consultant for AbbVie, Takeda and MSD and received payment for lectures from Ferring, MSD and AbbVie. AAvB has acted as a consultant for AbbVie, Ferring, MSD-Merck and Tramedico, and received payments for lectures from AbbVie, Ferring, Pfizer and Takeda. PDS has no competing interests. MJJM has no competing interests.

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Author Contributions

Study concept and design: MS, MJJM, BO. Acquisition of data: MS, MJJM, BO. Model building: MS, MJJM. Interpretation of data: MS, MJJM, BO. Drafting of manuscript: MS. Critical revision of the manuscript: all authors. Final approval of the submitted manuscript: all authors.

Supplementary Data

Supplementary data are available at *ECCO-JCC* online.

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