Treatment patterns and costs of biologic therapy in inflammatory bowel disease: analysis of German pharmacy prescription data

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Background

- Crohn's disease (CD) and ulcerative colitis (UC) are the most prominent inflammatory bowel diseases (IBD) in Germany, with more than 300.000 affected persons.
- Current guidelines recommend therapy using pharmacological agents of increasing potency, with biologics at the end of the treatment algorithm. The TNFα-inhibitors Infliximab (IFX) and Adalimumab (ADA) and the anti-integrin antibody Vedolizumab (VDZ) are the most commonly used biologics. In case of non-response or failure, dose is escalated or therapy is switched between the biologic agents.
- Recent findings indicate that prescribed treatment depends on previous therapy, primarily prior exposition to biologic agents (bio-experienced vs. bio-naïve) (Ehehalt et al. 2017).
- IBD are a considerable burden on the German healthcare budget, mainly due to high costs of biologics (Prenzler et al. 2011).

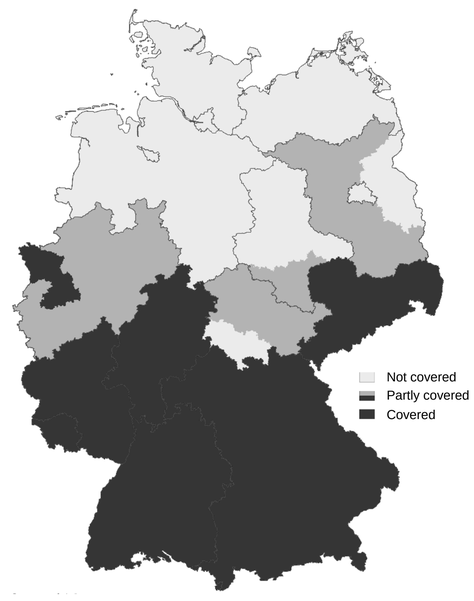
Objective

- To evaluate real-world treatment patterns and costs of bio-naïve and bio-experienced IBD patients treated with VDZ or TNFα-inhibitors.

Methods

- Anonymized German outpatient prescriptions which are collected at pharmacy data processing centers for the purpose of billing statutory health insurance funds were analyzed in this study. Regional coverage is shown in Figure 1.
- Cases with an initial prescription for VDZ or TNFα-inhibitors (ADA, IFX) between 01 July and 31 December 2015, and at least one prescription for VDZ, ADA, or IFX by a gastroenterologist during the entire study period were included.
- The follow-up period was 12 months from the initial prescription, with a 12 month pre-observation period to determine treatment history.
- Treatment duration was assessed on a monthly basis; dosing, co-medication and medication costs were evaluated on an annual basis.
- Discontinuation of therapy was defined as no further prescription within 12 months. Medication costs were based on the pharmacy retail price.
- For cases with 12 months of continuous initial (index) treatment, dosing, co-medication and costs were analyzed.
- Analyses were primarily descriptive; biologic dose is reported as mean annual mg and co-medication with azathioprine and methotrexate as percentage of patients; corticosteroids are reported as percentage and mean annual Daily Defined Dose (DDD). Treatment duration was evaluated using the Kaplan-Meier (KM) method.
- Analyses were stratified by previous biologic therapy in bio-naïve (no prescription 12 months prior baseline) and bio-experienced (at least one prescription 12 months prior baseline) cases.

Figure 1. Regions covered by the prescription database



Results

- 1.749 cases with an initial prescription of VDZ, ADA or IFX were included; 364 cases (21%) received VDZ, 705 (40%) ADA and 680 (39%) IFX. 34%, 86% and 80% of respective cases were bio-naïve.
- Overall, 963 cases (55%) stayed on index treatment for 12 months; 203 (56%) under VDZ, 382 (54%) and 378 (56%) under ADA and IFX, respectively. The distribution of bio-naïve cases in each treatment group is analogous to the total cohort. Slightly more bio-naïve cases stayed on therapy for 12 months than bio-experienced cases (VDZ: 59% vs. 52%, ADA: 53% vs. 47%, IFX: 55% vs. 48%).
- KM plots of the probability of continuing index treatment of VDZ, ADA or IFX in the first 12 months stratified by prior biologic treatment are shown in Figure 2.
- VDZ was prescribed at a mean annual dose of 2.535mg (median: 2.400mg, min.: 600mg, max.: 4.200mg). ADA and IFX were prescribed at mean doses of 1.194mg (med.: 1.200mg, min.: 80mg, max.: 3.360mg) and 3.121mg (med.: 3.000mg, min.: 300mg, max.: 9.800mg), respectively (Figure 3). Similarly, in the bio-naïve cohort the mean annual dose of VDZ was 2.522mg, ADA was 1.187mg and IFX was 3.082mg with comparable distribution parameters.
- Corticosteroid, azathioprine and/or methotrexate co-medication was prescribed in 53% (VDZ), 47% (ADA) and 60% (IFX) of all cases and 54%, 46% and 59% of cases in the bio-naïve cohort, respectively (Figure 4).
- Mean annual medication costs varied between €22.763 and €28.526. Mean costs of bio-naïve cases were marginally lower in all groups except for IFX Biosimilars; cost ranges overlap, however (Table 1 and Figure 5).

Table 1. Mean medication costs p.a. by biologic agent and subgroup

Biologic agent (N = all / naïve / exper.)	Mean medication costs p.a. (€) [range [a]]		
	All cases	Bio-naive cases	Bio-experienced cases
VDZ (N= 203 / 76 / 127)	25.243 [16.434 – 35.998]	25.123 [17.181 – 35.429]	25.315 [15.836 – 36.282]
ADA (N= 382 / 331 / 51)	26.332 [9.402 – 45.908]	26.153 [9.016 – 46.188]	27.490 [14.970 – 41.565]
IFX (N= 378 / 306 / 72)	25.879 [11.305 – 43.459]	25.637 [11.333 – 42.765]	26.907 [13.613 – 45.808]
Original (N= 174 / 145 / 29)	28.526 [13.521 – 49.893]	27.838 [12.800 – 48.944]	31.965 [21.248 – 49.957]
Biosimilars (N= 212 / 141 / 71)	22.763 [8.812 – 39.389]	23.116 [9.625 – 39.297]	22.063 [9.043 – 39.573]

[a] range is defined as the mean costs of cases with the lowest dosing and the highest dosing
[b] case numbers on IFX Original and IFX Biosimilars are not additive due to switching, with no continuous therapy on original or biosimilar, but continuous therapy on either of both agents
exper. = experienced

Figure 2. Time on index treatment compared by biologic agent for all cases and stratified by previous biologic treatment

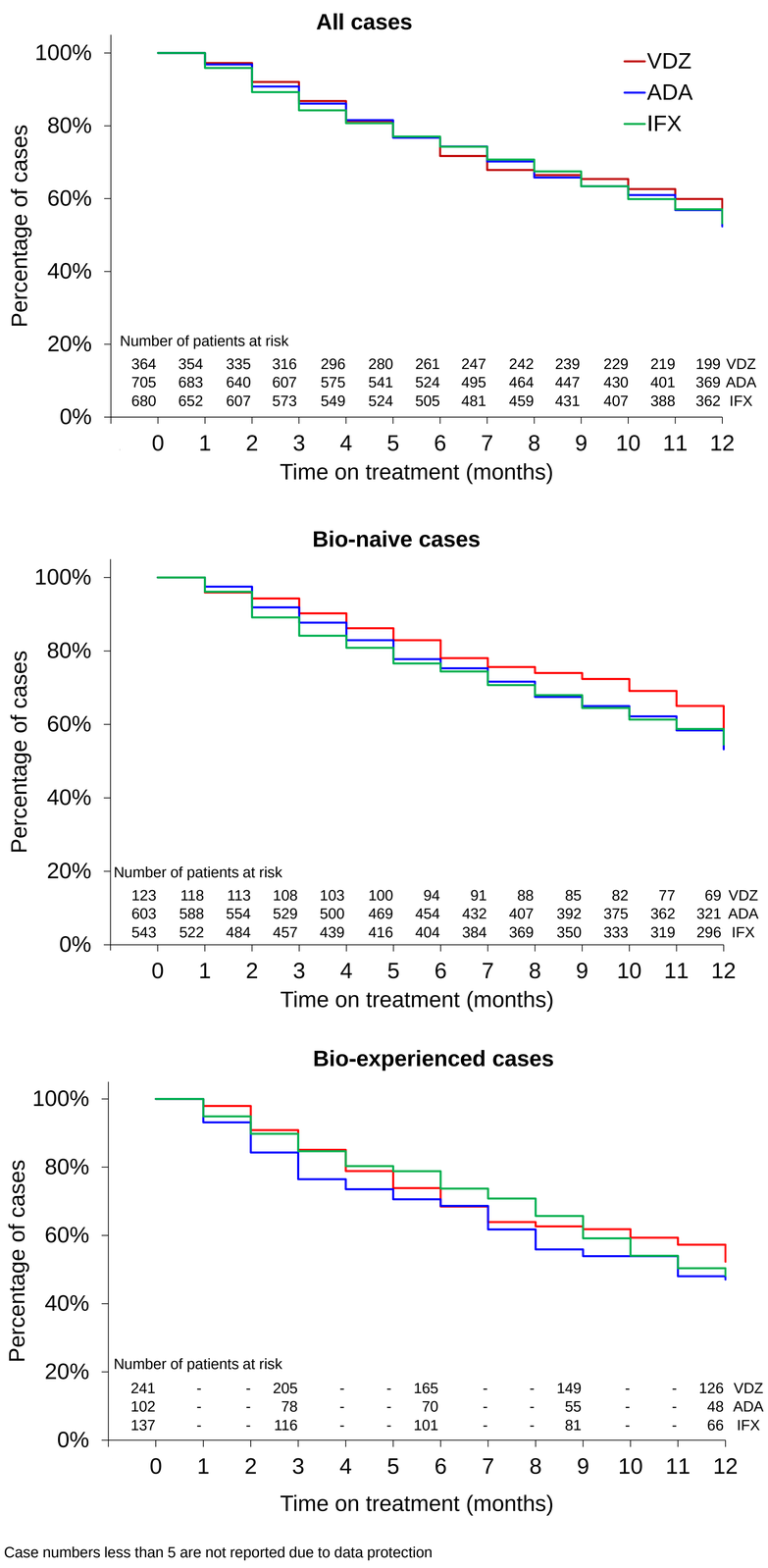


Figure 3. Distribution of mean annual dose by biologic agent

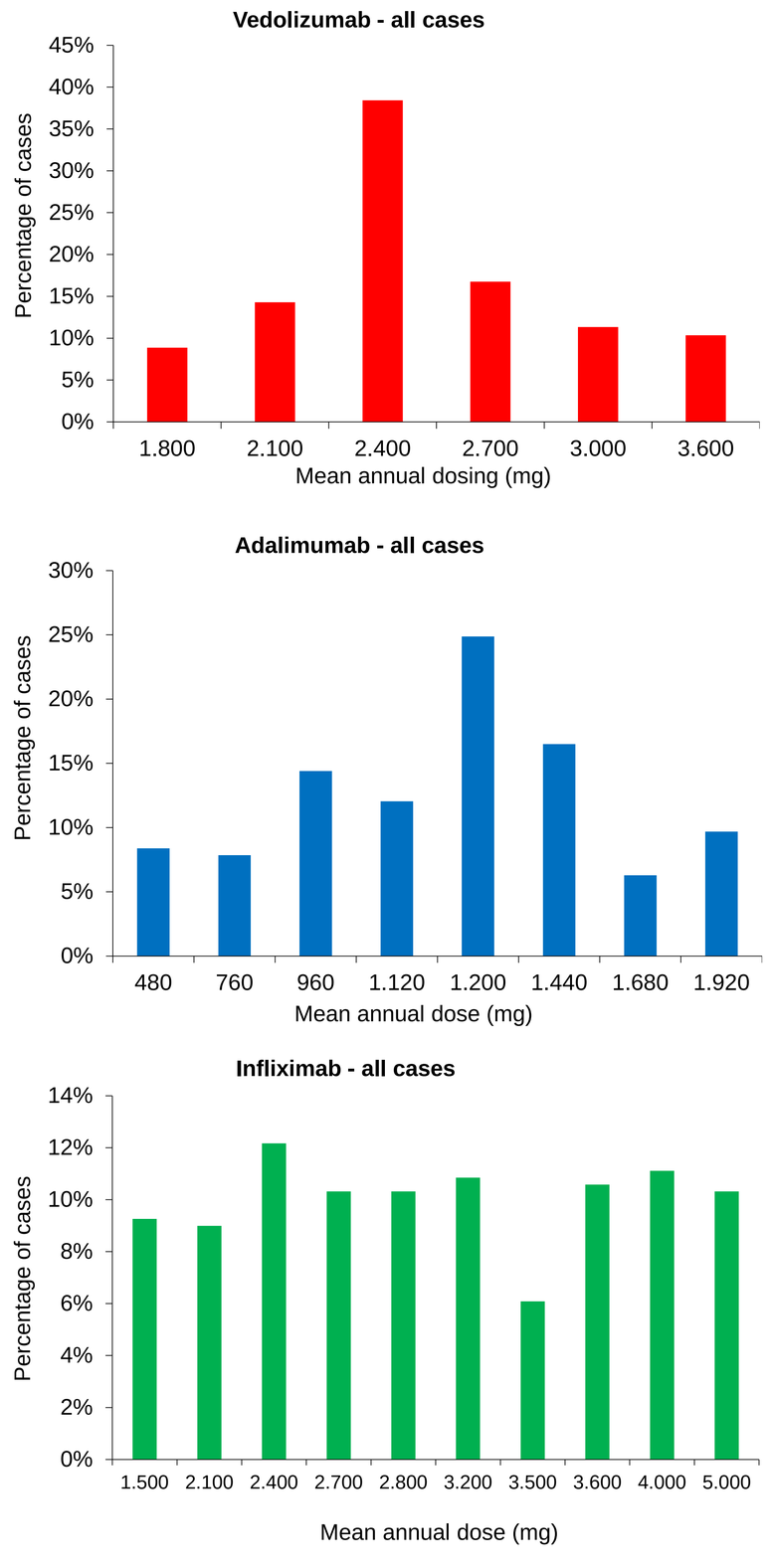


Figure 4. Percentage of cases with at least one prescription of a concomitant medication

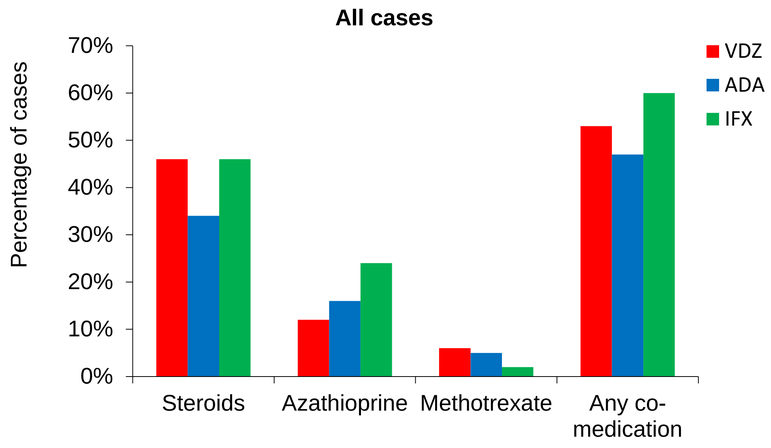
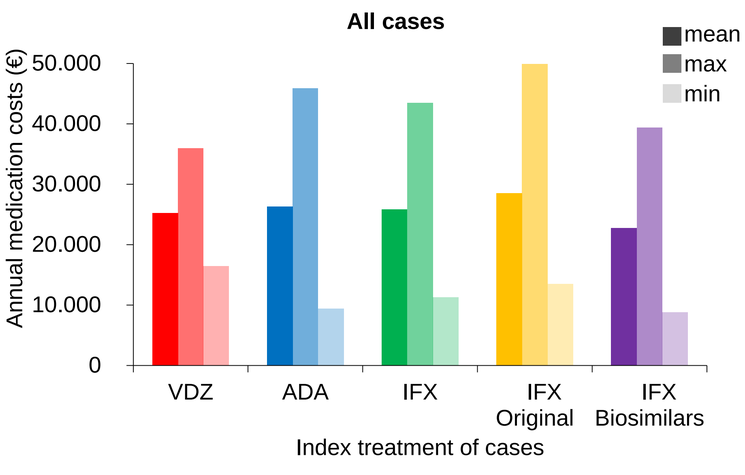


Figure 5. Total medication costs p.a. (€)



(-) Case numbers less than 5 are not reported due to data protection

Strengths and Limitations

- To the best of our knowledge this is the first observational study in Germany to describe real-world treatment patterns and costs of IBD treatment in a large, representative cohort based on prescription data.
- The lack of diagnostic data was met by including only cases with at least one prescription issued by a gastroenterologist. Stratification by CD and UC diagnosis was not possible due to lack of diagnostic information on prescriptions.
- There were no data on therapy-relevant patient characteristics, such as age, gender, weight or disease severity, included in the data set. Disease duration and the number of prior TNFα-inhibitors could not be established.
- Comparability of groups was accomplished by analyzing cases with an initial prescription in the same period and with the same follow-up duration.

Conclusions

- The study cohort included a high proportion of bio-naive cases (73%), with a noticeable difference between VDZ (34%) and ADA (86%) / IFX (80%).
- The KM plots show that, overall, the probability of continuing treatment was comparable between VDZ and TNFα-inhibitor cases, despite the comparatively lower rate of VDZ-treated bio-naïve patients. In the bio-naïve cohort comparably more cases stayed on VDZ treatment in the first 12 months (59% vs. 53% / 55%).
- Based on the summary of product characteristics the recommended annual biologic dose can be deduced. The recommended annual dose is 2.325mg for VDZ, 1.140mg for ADA and 3.100mg for IFX (assuming a dose of 400mg per interval). Based on that, the percentage of cases with a higher annual dose compared to the recommendation can be estimated in this study. Estimates were similar between groups (33% VDZ, 38% ADA and IFX).
- Overall, an increased biologics dose was accompanied by an increase in co-medication with corticosteroids, azathioprine and / or methotrexate, regarding the proportion of cases as well as the dosage (data not shown).
- In all groups a higher annual biologics dose was associated with higher annual medication costs, as overall medication costs were mainly determined by the costs of the biologic therapy.
- Cases under IFX Biosimilars and VDZ had the lowest medication costs, while cases under IFX Original had the highest.
- Against the background of the ongoing price discussion regarding biologic therapy, it's worth mentioning that the costs of cases under IFX were not lower than that of the other biologic agents, despite an IFX Biosimilar rate of 56%.

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References

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