Prevalence and Incidence Estimations in German AMNOG Applications: The Role of Real-world Evidence (RWE)

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BACKGROUND

- 90% of the German population is insured in the Statutory Health Insurance (SHI), which covers nearly all healthcare services with only little co-payments for patients.
- German health insurance claims data therefore constitute an important basis for RWE on morbidity and healthcare costs.
- In 2011, the Act on the Reform of the Market for Medicinal Products (AMNOG) was enacted in Germany to counter rising healthcare costs.
- The AMNOG obliges pharmaceutical companies to submit a benefit dossier to the Federal Joint Committee (FJC) at market launch, estimating prevalence, incidence, and annual therapy costs and providing granular data on medical benefits in terms of mortality, morbidity, and health-related quality of life. All information must be underpinned with current, high-quality evidence.
- Pharmaceutical companies are entitled to negotiate a national reimbursement price only if the FJC declares an additional benefit over the selected comparator therapy.
- Until now, the role of RWE in German AMNOG applications in terms of utilization, quality, and impact on benefit ratings and price discounts is unclear.

OBJECTIVE

- The aim of this study was to investigate the extent to which RWE was used for estimation of prevalence and incidence in German AMNOG assessments and also its impact on benefit ratings and price discounts.

METHODS

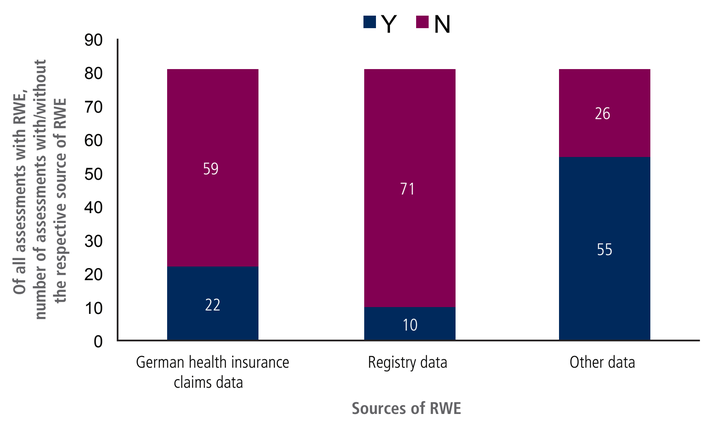
- All German AMNOG applications with published benefit ratings until the end of August 2015 were included.
- They were screened for use of RWE in assessing the prevalence/incidence and structure/size of target populations.
- After description and discussion of methods and data sources used, statistics were applied to explore the potential influence of use of RWE data on benefit ratings and level of price discounts.
- Price discounts were calculated using the official tariff list (Lauertaxe) by computing the change of ex-factory price before and after price negotiations.

RESULTS

Types of RWE data

- In total, 167 AMNOG assessments were included in the analyses.
- RWE was incorporated in 49% (n=81) of these dossiers to assess prevalence and incidence, and the size of target populations. German health insurance claims data were employed in 22 dossiers (27%); registry data in 10 dossiers (12%); and other data sources like IMS, Delphi panels, Kantar Health data, INSIGHT Health data, and Megapharm data in 55 dossiers (68%). IMS data were included in 44 of these assessments. Multiple data sources were used in 6 dossiers.

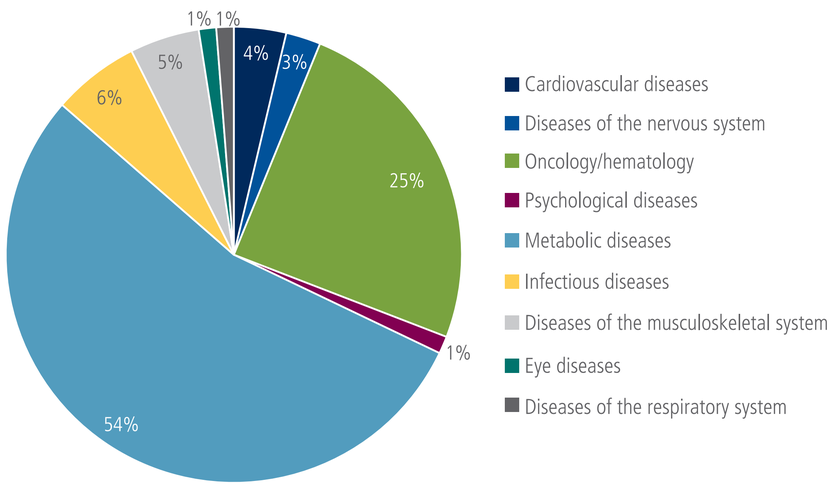
Figure 1. Data Sources of RWE in AMNOG Assessments



Key: AMNOG – Act on the Reform of the Market for Medicinal Products; RWE – real-world evidence.

- RWE was mostly considered in 2 disease areas: metabolic diseases (44 dossiers) and oncology/hematology (20 dossiers).
- German claims data and other data sources also were mainly used for metabolic diseases (9 dossiers and 35 dossiers, respectively) and in oncology/hematology (7 dossiers and 9 dossiers, respectively).
- All but 2 registry data analyses were performed in the field of oncology/hematology.

Figure 2. Disease Areas for RWE in AMNOG Assessments



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- The majority of RWE analyses assessed the prevalence of the underlying disease and size of the target population; only a few tried to analyze the incidence.
- Prevalence was estimated in 21 of 22 dossiers specifically using German health insurance claims data and in 53 of 55 dossiers using other data sources, whereas incidence was estimated in 5 and 4 dossiers, respectively.
- Registry data, however, were used both to assess prevalence (7 of 10) and incidence (6 of 10).

Assessment of populations

- The regulator will evaluate the RWE data in a dossier and discuss the findings, finally setting epidemiological numbers together with the ruling on clinical efficacy. As potential price negotiations will also factor in the potential budget impact, it is important not to inflate potential patient numbers. Hence, a sound, realistic, and robust estimate is of paramount importance from the perspective of the pharmaceutical company.
- Having said that, the SHI target population was accepted as correct in 44% of the AMNOG assessments using RWE, while it was considered to underrate in 31% and overrate in 25%.
- Of all dossiers that included claims data, the target population was accepted in 64% and underrated in 36%.
- None of the German claims data analyses overrated the SHI target population, whereas overestimations were observed in 21% of dossiers not using German claims data.
- The target population was considered by regulators to be overrated in 35% of the assessments that employed other data sources, mostly IMS data (80%).
- Particularly with regard to the subsequent price negotiations, smaller target populations might be an advantage.

Table 1. SHI Target Population: Estimates Stated in the Dossiers Compared to Estimates Stated by the FJC

N=167		Underrated		Accepted as given*		Overrated		Total
		n	%	n	%	n	%	
RWE	Y	25	31%	36	44%	20	25%	81
	N	23	27%	53	62%	10	12%	86
German health insurance claims data	Y	8	36%	14	64%	0	0%	22
	N	40	28%	75	52%	30	21%	145
Registry data	Y	4	40%	5	50%	1	10%	10
	N	44	28%	84	54%	29	18%	157
Other data	Y	17	31%	19	35%	19	35%	55
	N	31	28%	70	63%	11	10%	112

*A margin of +10% was assumed.

Key: FJC – Federal Joint Committee; RWE – real-world evidence; SHI – Statutory Health Insurance.

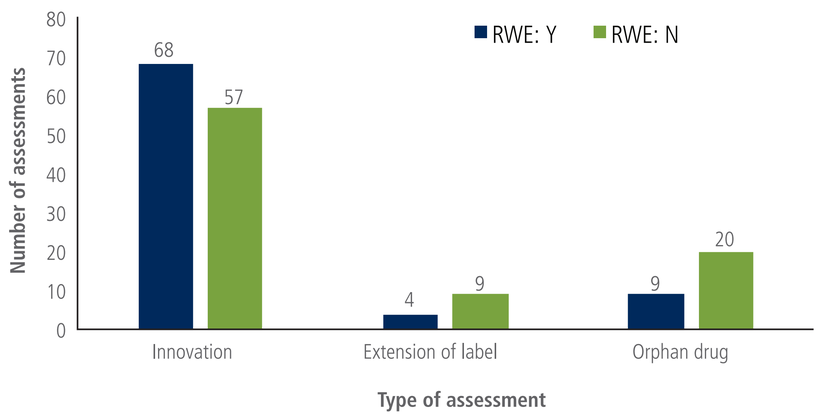
Benefit rating and price discount

- Of all AMNOG assessments using RWE, 40% were declared to prove an additional benefit of the new pharmaceutical over the selected comparator.
- However, a causal relationship between the use and quality of RWE and the benefit rating is equivocal, as the benefit rating mostly depends on clinical evidence. Rather, RWE on incidence and prevalence, as well as size of target populations, is more important for the subsequent price negotiations, as it has influence on the budget impact.
- Price negotiations were completed for 99 AMNOG assessments.
- A *t*-test evaluating the association between the use of RWE and negotiated price discounts revealed no statistically significant difference between assessments that did incorporate RWE data and assessments that did not (P=0.18).
- The *t*-tests remained inconclusive after stratification by data source (claims data, registry data, and other data).

Orphan drugs

- Innovation was the most common objective for submitting a dossier (125 dossiers), while only 13 dossiers aimed at an extension of the label.
- An orphan drug status was given in 29/167 dossiers, of which 9 used RWE for assessing target populations and 20 did not.
- In these orphan drug dossiers, RWE in terms of claims data was included in 67% (6 of 9), registry data in 44% (4 of 9), and other data in 11% (1 of 9) of cases.
- In 97% (28 of 29) of the orphan drug dossiers, the target population was considered as being underrated or accepted as reported by the company. Inclusion of RWE resulted in only 2 cases of underestimating and 7 correct estimates.
- Disease areas for orphan drug dossiers using RWE comprised oncology/hematology (7 of 9), psychological diseases (1 of 9), and cardiovascular diseases (1 of 9).

Figure 3. Use of RWE Stratified by Type of Assessment



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CONCLUSIONS

- German health insurance claims data comprise comprehensive information such as demographics, outpatient and inpatient care, prescriptions, devices and aids, incapacity to work, and sick leave payments.
- German claims data are particularly useful for prevalence and incidence analyses, since diagnoses, procedures, and prescriptions are documented routinely and patient histories can be evaluated over longer time periods. This is of special value regarding the target population and cost estimations, which are of paramount importance in price negotiations following the AMNOG assessment.
- German claims data constitute a reliable and valid data source for assessing epidemiologic evidence in German AMNOG assessments. Indication-specific claims data analyses are a meaningful complement to literature research.
- Additional benefit ratings are most likely driven by clinical evidence, whereas price negotiations depend heavily on estimations of target populations, which should be backed up by robust real-world evidence.

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