

The burden of adverse drug reactions reported in the Dutch ADR Monitor

J.M. Quik¹, H.R. Gosselt¹, J.A. van Lint¹, L.J. Kosse¹, P.M. ten Klooster², H.E. Vonkeman^{2,3}, B.J.F. van den Bemt^{4,5}, N.T. Jessurun¹

Introduction

Adverse drug reactions (ADRs) can negatively impact patients' lives in different manners:

- Decrease Quality of Life
- Lead to non-compliance
- Prolong length of hospital stay
- Economic impact

Information on the burden patients experience from ADRs is scarce. Insight in the burden of ADRs can help optimize treatment options and can aid in improving health related quality of life and compliance.

Since November 2022, the Netherlands Pharmacovigilance Centre Lareb has been systematically collecting patient reported ADRs through the **Dutch ADR Monitor** (Bijwerkingmonitor) system. This is a web-based cohort event monitoring system developed to gain insight into ADRs from the patients' perspective.

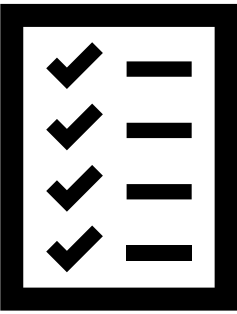
The aim of this research is to investigate the burden of ADRs on 7 different domains in patients using various drugs for different chronic conditions.

Methods

The Dutch ADR Monitor is an observational, prospective cohort event monitoring system. Participants received web-based questionnaires every 2 months during 1 year. The questionnaires included questions on chronic disease and disease activity, therapies, comorbidities, demographic information, overall health and questions about ADRs experienced in the last 2 months.

Lareb developed a multifactorial burden measurement instrument for the Dutch ADR Monitor to score the burden of ADRs on 7 domains:

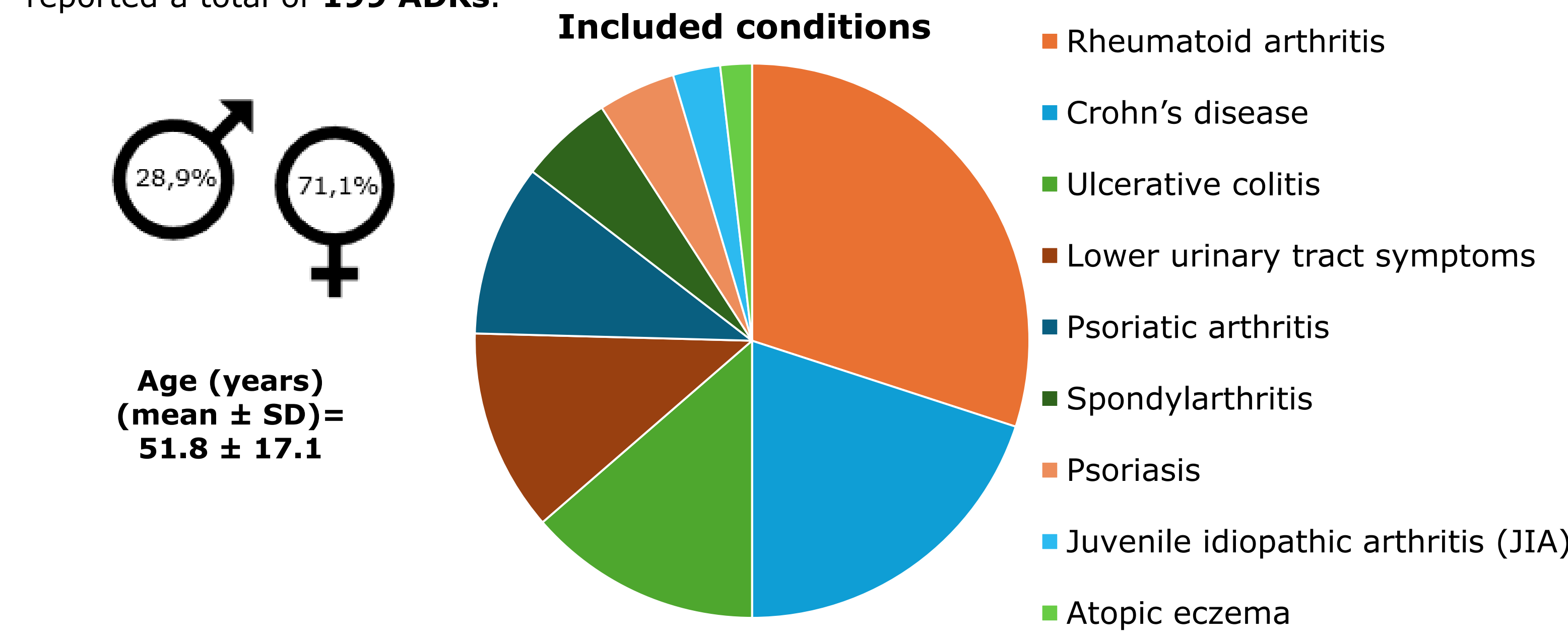
- **Appearance**
- **Medical treatment**
- **Daily life**
- **Fatigue**
- **Mental consequences**
- **Physical consequences**
- **Course of the ADR**



For all domains, except for the course of the ADR, patients were first asked to report whether the ADR affected the specific domain or not, using a dichotomous yes/no question. If patients answered 'yes' to the question if the domain was affected by the ADR, they were asked to assign a score from 0 ('No burden at all') to 10 ('Highest possible burden') to the burden they experienced on this domain. The distributions of these burden scores was demonstrated in Likert plots. The burden between persistent and recurrent ADRs was compared using the Cochran-Armitage test for trend. Patients could further explain on burden in an open text field.

Participants

A total of 149 patients participated in the Dutch ADR Monitor between November 2022 and May 2023. **92 patients** reported one or more 1 ADRs and were included. These patients reported a total of **199 ADRs**.



Methotrexate 28 (30,4%)	Adalimumab 22 (23,9%)	Hydroxychloroquine 9 (9,8%)	Other 47 (51,1%)
-----------------------------------	---------------------------------	---------------------------------------	----------------------------

Results

Impact on daily life (70%) and fatigue (66%) were experienced most frequently by the participating patients over **all reported ADRs (figure 1)**. The highest median burden score was reported on the domain fatigue (median=8, IQR=2).

For **most reported types of ADRs**, patients reported they experienced an impact on the domains fatigue and daily life most frequently (**figure 2**). For skin and subcutaneous disorders impact on appearance and mental consequences were experienced most frequently (respectively 74% and 70%). For most types of ADRs, patients experienced the highest burden on the domains daily life and fatigue.

No statistically significant difference in burden scores between persistent and recurrent ADRs was found (p=0.59) (**figure 3**).

Quotes from the open tekst field

- 'Little energy, so my social life next to work is minimal'** (female, 61 yrs., burden score 9 on fatigue).
- 'The eczema is visible and also gives a reduction in self-confidence. (...)'** (male, 38 yrs., burden score 8 on appearance and burden score 7 on mental consequences)
- 'From all complaints, seeing your hair reduce is psychologically a thing. (...)** (female, 57 yrs., burden score 8 on appearance and burden score 6 on mental consequences).
- 'Nausea is unpredictable. (...) I fear that I will be overtaken by it again when I am not at home'** (female, 29 yrs., burden score 10 on course)

Results

General burden of reported ADRs

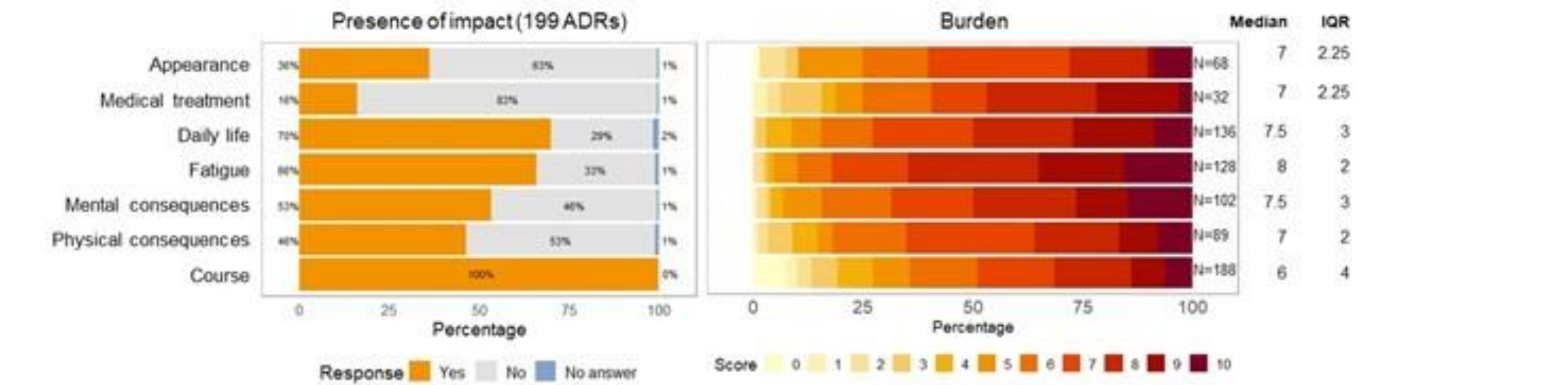


Figure 1. Distribution of the percentage of patients that experienced an impact on the domains (left) and the Likert plot of the distribution of the burden scores for all reported ADRs together on 7 domains (right).

Burden of the most reported types of ADRs

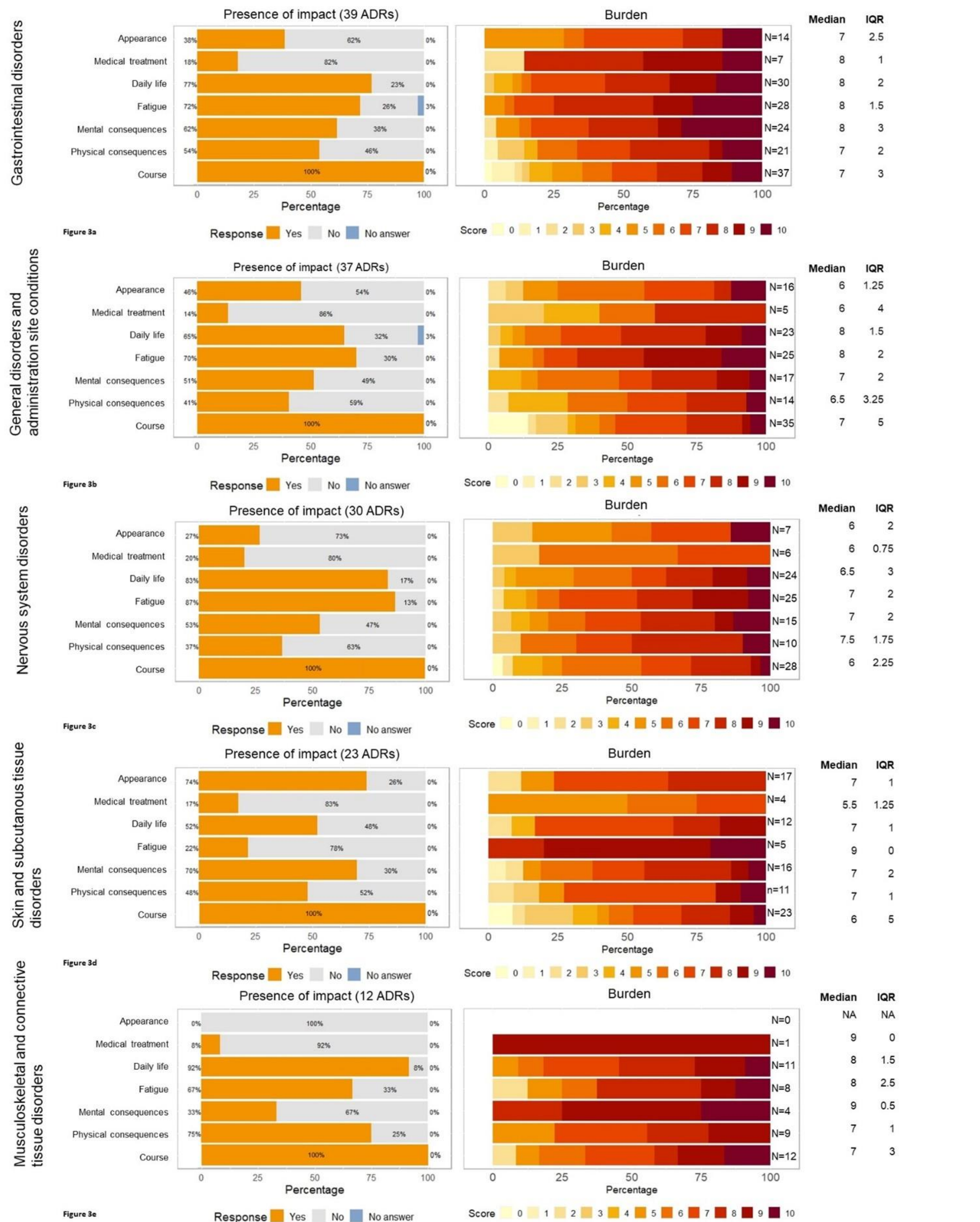


Figure 2. Distribution of the percentage of patients that experienced an impact on the domains and the Likert plots of the distribution of the burden scores for (a) gastrointestinal disorders, (b) general disorders and administration site conditions, (c) nervous system disorders, (d) skin and subcutaneous disorders and (e) musculoskeletal and connective tissue disorders.

Burden of the course of reported ADRs

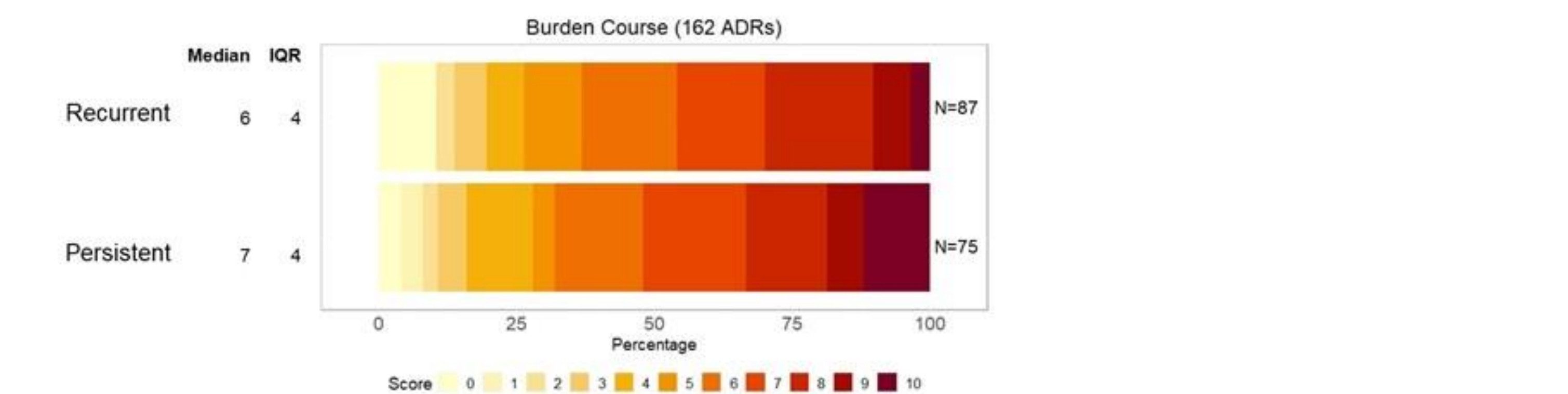


Figure 3. Likert plot of the distribution of the burden scores for the ADRs with a persistent and recurrent course.

Conclusions

These results give insight into the burden patients experience from different kinds of ADRs and can help health care professionals to better understand the factors contributing to the burden of ADRs.

- **Impact on the domains fatigue and daily life were experienced most frequently**, except for skin and subcutaneous tissue ADRs, where impact on appearance and mental consequences were experienced most frequently
- **Fatigue was considered the most burdensome domain.**
- No difference in burden was found between persistent (median=7, IQR=4) and recurrent ADRs (median=6, IQR=4, p=0.59).

Further analysis of the explanations in the open text field is recommended. These explanations give more detailed information about how patients experience the burden of ADRs and the burden of the course.