Development and validation of the General Attitude towards Medication Questionnaire (GAMQ)

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Abstract (MAXIMUM 250 words, now 250 words)

Background: Attitudes towards medication can affect treatment outcomes and adherence through mechanisms such as placebo and nocebo effects. Although both negative and positive attitudes towards medication are of importance, previous research mainly investigated the impact of negative attitudes towards medication. This focus is also reflected in existing self-report scales, most of which measure negative beliefs about medication in general and/or focus on specific medication. To assess both negative and positive attitudes towards medication in general, the General Attitude towards Medication Questionnaire (GAMQ) was developed.

Method: For the GAMQ, 12 items largely based on existing questionnaires were selected. It was validated in 4 Dutch samples: 2 samples of 508 and 279 respondents of the general population, and 2 samples of 121 patients with rheumatoid arthritis and 70 patients with atopic dermatitis.

Results: Factor analyses indicated three subscales representing “Trust in medication”, “Concerns about medication”, and “Reluctance to use medication”, which were structurally stable across the samples. The total scale showed good internal consistency. Medium to strong correlations with other measures of general medication attitude (e.g. BMQ-G), indicated good convergent validity. Furthermore, exploring its predictive validity indicated that the GAMQ correlated with expected medication outcomes.

Conclusion: Results suggest that the GAMQ is suitable for assessing general medication attitudes, both negative and positive, in a wide variety of research settings and in various patient populations. Due to its balanced nature, the GAMQ may be especially informative when investigating predictors of treatment outcomes and adherence, as well as determinants of placebo and nocebo effects.

Keywords: Medication, Attitude, Questionnaire development, Expectancies, Placebo effects, Nocebo effects

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Introduction

Attitudes towards medication have been identified as important predictors of treatment outcomes (1-3) and adherence to prescribed medication regimens (4, 5). Limited beneficial treatment outcomes, harmful side effects, and non-adherence are major problems in healthcare worldwide, linked with poor health outcomes and increasing healthcare costs (1, 6, 7). Negative attitudes towards medication have been associated with the occurrence of negative medication (side) effects (1, 2) and, partially resulting from that, non-adherence (8). This association between negative attitudes toward medication and medication side effects may be explained by nocebo effects, as it also occurs in response to inert treatments (7). In addition to the lack of negative attitudes, positive attitudes towards medication may increase medication effectiveness (3, 7, 9), akin to how positive outcome expectancies of a specific treatment can contribute to placebo effects (8, 10, 11). Having a positive attitude towards medication in general, trusting the effectiveness of the medication, and being convinced that the treatment is needed, has also been associated with increased adherence (4, 5). Ultimately, fostering positive attitudes towards medications could help in optimizing the effects of pharmacotherapy and preventing nocebo-induced side effects and non-adherence (7, 12).

Despite these indications that both negative and positive attitudes towards medication are of importance, current research mainly focuses on the impact of negative attitudes towards and beliefs about medication (1, 2, 7). This focus on negative attitudes is also reflected in the instruments currently available to assess attitudes towards medication (e.g. Beliefs about Medicines Questionnaire-General (13)). Other questionnaires, assessing positive as well as negative attitudes, are concerned with attitudes towards specific medication such as pain or anti-psychotic medication (Beliefs about Medicines Questionnaire-Specific; 13, Pain Medication Attitude Questionnaire; 14, 15; Drug Attitude Inventory-10; 16, 17) and are as such highly valuable in specific contexts but do not allow comparisons across diverse settings and samples.

To enable research into negative and positive attitudes of medication in a variety of settings and samples, a questionnaire that assesses negative as well as positive attitudes towards medication in general is needed. The current paper describes the development of such a questionnaire, the General Attitude towards Medication Questionnaire (GAMQ) and the evaluation of its psychometric properties in both healthy and patient samples (rheumatoid arthritis, RA, and atopic dermatitis, AD). Patients with RA and AD often experience chronic pain or itch for which many use medication for an extended period of time. Both pain and itch are known for their responsiveness to placebo and nocebo effects (10, 18, 19), and thus might be specifically sensitive to beliefs and attitudes about medication. To evaluate the psychometric properties of the GAMQ, the stability of the factor structure across samples was tested (20) in two general and two patient samples. Furthermore, the internal consistency

of the questionnaire, convergent validity (association with existing medication attitude questionnaire), predictive validity (association with expected effectiveness and side effects of medication), and associations with demographic and health-related characteristics were analyzed in each of the four samples.

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Method

Respondents

To ensure the availability of representative general samples and samples of patients with RA and AD, the GAMQ was administered as part of different questionnaire studies. For the validation of the GAMQ, data from these studies were combined. The specific methods used to recruit participants and collect data varied between studies. Also, the studies differed with regard to additional questionnaires that were assessed. See Table A.1. in the Supplemental Digital Content for an overview of the relevant questionnaires per sample. Data from a general sample (Gs1) (21) and samples of patients with Rheumatoid Arthritis (RAs) and Atopic Dermatitis (ADs) were obtained in a study investigating expectations about negative and positive effects of different routes of medication administration (in the RA patients sleep quality and the circadian rhythm were investigated as well). A second general sample (Gs2) was obtained from an online experimental and questionnaire study on imagery and the induction of pain medication outcome expectations by verbal suggestion. Both studies were approved by the relevant local ethics committee.

General sample 1 (Gs1)

A general sample that was representative of the adult Dutch population in terms of gender, age, and province of residence was recruited via an online service (Qualtrics, Provo, UT, USA) in September 2015. All respondents were asked to fill in a battery of online questionnaires, including the GAMQ, taking approximately 20 minutes.

General sample 2 (Gs2)

A second general sample that was representative of the Dutch population in terms of gender and age was recruited via posters and flyers at various public locations (e.g., library, gym, pharmacy), social media, participant recruitment websites, and personal networks in the Netherlands. Data collection took place from March to June 2016. Respondents filled in a battery of online questionnaires, including the GAMQ, taking approximately 35 minutes via Qualtrics.

Rheumatoid arthritis sample (RAs)

Patients with RA fulfilling the 1987 ACR criteria were recruited from the Leiden Early Arthritis Clinic (EAC) cohort (22), a population-based prospective cohort. Patients were approached via email and could choose whether they wanted to fill out the battery of questionnaires via Qualtrics or using paper and pencil. Data collection took place in October 2015. Filling out the questionnaires took approximately 45 minutes.

Atopic Dermatitis sample (ADs)

Patients with AD who visited the Department of Dermatology of the Leiden University Medical Center in the preceding year were approached via regular post from January to March 2016. They could choose whether they wanted to fill out the battery of questionnaires via Qualtrics or using paper and pencil. Completing the questionnaires took participants around 30 minutes.

General Attitude towards Medication Questionnaire (GAMQ)

Respondents of all samples completed the General Attitudes towards Medication Questionnaire (GAMQ). To reflect both negative and positive attitudes towards medication, 6 positively and 6 negatively worded items were created. Items for the GAMQ were adapted from other questionnaires measuring attitudes towards and beliefs about medication or were newly developed. Questionnaires that provided inspiration for items were: the general and specific scales of the Beliefs about Medicines Questionnaire (BMQ, 13), the Pain Medication Attitude Questionnaire (PMAQ; 14), the Drug Attitude Inventory (DAI, 16, 17), and a study-specific attitude towards pain medication scale (15). Selection and adaptation of existing items and development of new items was done by authors KP and JT with assistance of AE, AvL, and MP. The goal was to select and create around 10 items that are easy to understand and clearly reflect a personal view ("I think..."). To create a balanced scale assessing negative as well as positive attitudes, an equal number of positive and negative items was included in the questionnaire. The introduction with instructions on how to fill in the GAMQ as well as the answering options were adapted from the BMQ-G (13). Participants are requested to rate each item on a 5-point Likert scale, ranging from 1 ("strongly disagree") to 5 ("strongly agree").

The GAMQ was formulated and tested in Dutch. The English version was obtained by forward-backward translation. The initial forward translation from Dutch to English was done by a native speaker and certified translator in collaboration with the authors JT and KP. After consensus was achieved about the first English version, native Dutch author HvM, who was blinded for the original Dutch version, translated the first English version back to Dutch. Comparison of this backward translation to the original Dutch questionnaire and the first English translation by the translator and authors JT and KP led to minor adjustments in the final English translation provided in Table 1. For the Dutch version, please see Supplemental Digital Content Table A.2.

Table 1. The English translation of the General Attitude towards Medication Questionnaire (GAMQ) including instruction and response options.

We want to ask you some questions about what you think about medication in general. We are interested in your views about medication that has been prescribed for you by your doctor. Please indicate to what extent you agree or disagree with the following statements. There are no right or wrong answers. We are interested in your views.

	Strongly disagree	Disagree	Uncertain	Agree	Strongly agree
1) I am concerned about the side effects of medication.	☐	☐	☐	☐	☐
2) I think that medication can help with my symptoms.	☐	☐	☐	☐	☐
3) I am afraid that medication has a harmful effect on my body.	☐	☐	☐	☐	☐
4) If I have symptoms, I readily take medication for them.	☐	☐	☐	☐	☐
5) I find it unnatural to take medication.	☐	☐	☐	☐	☐
6) I trust that it is safe to take medication.	☐	☐	☐	☐	☐
7) I only take medication if there is absolutely no other option.	☐	☐	☐	☐	☐
8) I have no problem with taking medication if I have symptoms.	☐	☐	☐	☐	☐
9) I would rather endure my symptoms than take medication.	☐	☐	☐	☐	☐
10) I trust in the effectiveness of medication.	☐	☐	☐	☐	☐
11) I am afraid of becoming addicted if I take medication for an extended period.	☐	☐	☐	☐	☐
12) For me the advantages of medication outweigh the disadvantages.	☐	☐	☐	☐	☐

Materials and measures

General beliefs about medication

Beliefs about medication in general were measured using the Beliefs about Medicines Questionnaire – General (BMQ-G, 13) in all of the investigated samples. The BMQ-G consists of two subscales, the General-Harm and the General-Overuse scales, measuring general beliefs about the harmfulness of medication (e.g., “All medicines are poisons”) and doctor’s over-prescription of medication (e.g., “Doctors use too many medicines”), respectively. Each of the scales consists of 4 items that are rated on a 5-point Likert scale, ranging from 1 (“strongly disagree”) to 5 (“strongly agree”). Summing these items per scale results in scores ranging from 4 to 20, with higher scores

reflecting more negative beliefs. Internal consistency as indicated by Cronbach's alpha for the General-Harm subscale ranged from $\alpha=.65$ (questionable) in RAs to $\alpha=.73$ (acceptable) in Gs1. For the General-Overuse subscale, Cronbach's alpha was acceptable in all samples, ranging from $\alpha=.71$ in ADs to $\alpha=.78$ in Gs1 and Gs2.

Medication attitude visual analogue scale (VAS)

Respondents of all samples were also asked to rate their general attitude towards medication ("How do you think about medication in general?") on a visual analogue scale (VAS) ranging from 0 ("very negatively") to 100 ("very positively").

Expectations regarding medication

Participants of the Gs1, RAs, and ADs rated their expectations about the effectiveness for pain and itch relief as well as about side effects of different routes of medication administration (oral, injection, and topical routes) on visual analogue scales ranging from 0 ("not at all") to 100 ("very much") (21). For the current study, VAS scores of the different routes of medication administration were averaged, resulting in three scores reflecting 1) the expected effectiveness of medication for pain relief, 2) the expected effectiveness of medication for itch relief, and 3) the expected side effects of medication.

Demographic and health-related characteristics

All respondents were asked to provide information about their age, gender, marital status, education level, religious affiliation, nationality, and fluency in Dutch language. Regarding health-related characteristics, respondents were asked whether they were currently undergoing treatment for any illness(es). Additionally, they were asked to rate the intensity of currently experienced pain or itch on a VAS ranging from 0 ("none at all") to 100 ("very much"). In the GS2, respondents only rated current pain intensity, on an 11-point numerical rating scale with identical anchors as the VAS.

Health-related quality of life was measured using the Short Form-12 (SF-12, 23) in the Gs1 and the Short Form-36 (SF-36) in the RAs and ADs. As the SF-36 contains all items included in the SF-12, responses on the SF-36 were used to compute the SF-12 scores. The SF-12 results in two scores, namely the physical health composite score (PCS), and the mental health composite score (MCS). The PCS consists of physical functioning, role limitations due to physical problems, bodily pain, and general health, and comprises items like "During the past 4 weeks, how much did pain interfere with your normal work (including work outside the home and housework)?". The MCS consists of mental health, role limitations due to emotional problems, social functioning, and vitality, and comprises items like "How much of the time during the past 4 weeks have you felt calm and peaceful?". Scores are

calculated based on item response theory, with regression weights standardized for the Dutch population (23).

To assess disease activity and impact in the patient samples, the Disease Activity Score 44 (DAS44, 24) was used in the RAs, while the respondents in the ADs completed the Patient Oriented Eczema Measure (POEM, 25). The DAS-44 is a measure of disease activity in rheumatoid arthritis combining symptoms of tenderness and swelling in 44 joints with the Erythrocyte Sedimentation Rate in mm/hour and a general health assessment expressed on a visual analogue scale ranging from 0 to 100. The DAS-44 scores of respondents in the RAs were determined during their last visit at the LUMC (approximately 24 weeks prior to filling in the questionnaire) which were made available for use in this study from the Leiden EAC Cohort (22). High scores on the DAS-44 reflect more disease activity, with scores below 1.6 indicating clinical remission. Cut off points for disease activity are low (≤ 2.4), moderate (> 2.4 to 3.7), and high (> 3.7) (26). The POEM was used to measure eczema severity in the ADs. It comprises seven items assessing on how many days of the past week the patient experienced 7 different symptoms of eczema. Each item is rated from 0 ("no days") to 4 ("every day"), resulting in a minimum score of 0 and a maximum score of 28, with higher scores indicating more severe eczema. Additionally, scores are banded into categories as follows: 0 to 2 clear or almost clear from eczema, 3 to 7 mild eczema, 8 to 16 moderate eczema, 17 to 24 severe eczema, and 25 to 28 very severe eczema. Internal consistency of the POEM in the current study was good ($\alpha=.89$).

Quality of the responses

The questionnaire sets for each sample contained items included to ensure the quality of the responses. For all samples, the questionnaire sets concluded with two items inquiring whether respondents were able to understand the questions asked in the questionnaire and whether respondents had read all questions well before answering. The questionnaire sets for both general samples included two additional control questions on which respondents were requested to give a pre-defined answer, to check whether they read the questions well.

Statistical analyses

Descriptive statistics, univariate analyses of variance (ANOVAs), chi-square tests, and Pearson correlations were calculated using SPSS version 25 (IBM Corporation, Armonk, NY, USA). Factor analyses were run using the Latent Variable Analysis software package (lavaan 0.6-3) in R (version 3.4.3). The significance level for all tests was set at $\alpha=.05$ (two-tailed). For correlations, cut-off values of $r=.10$, $.30$, and $.50$ were used to indicate small, medium, and large correlations, respectively (27). For ANOVAs, partial eta squared (η_p^2) was calculated as an indicator of the effect size. Cut off values of $\eta_p^2=.01$, $.06$, and $.14$ were used to indicate small, medium, and large effects, respectively (27). All

correlations and ANOVAs, including post-hoc tests, were tested for significance using simple bootstrap with 1000 samples and the bias corrected accelerator.

Between-sample differences in medication attitude scores, as well as demographic and health-related characteristics were analyzed using univariate ANOVAs for continuous variables and chi-square tests for categorical variables.

The factor structure of the newly developed GAMQ was investigated in all samples using the following procedure (20, 28, 29): First, an exploratory principal component analysis (PCA) using varimax rotation was run in a random subsample consisting of 60% of Gs1 (training sample, $n = 305$) to inform on the general component structure of the GAMQ. Next, the resulting structure was tested by a confirmatory factor analysis (CFA) in the same training sample with bootstrap (1000 draws), to obtain robust standard error estimates. This was repeated in the remaining 40% of Gs1 ($n = 203$). The generalizability of this factor structure was investigated by CFA, using 1000 bootstrap draws, in Gs2, and the RAs and ADs. As measures of fit, the Comparative Fit Index (CFI) (30, 31) for which $\geq .90$ indicates adequate fit and $\geq .95$ indicates excellent fit, as well as the Root Mean Square Error of Approximation (RMSEA; 32) and the Standardized Root Means Square Residual (SRMSR; 33) for both of which $\leq .08$ indicates adequate fit and $\leq .05$ indicates excellent fit (34), were calculated in each sample. Finally, the stability of the factor structure (measurement invariance) across the samples was tested using 5 different, progressively restrictive, models: 1) factor configuration, 2) factor loadings, 3) intercepts, 4) residuals, and 5) means (20).

As an indicator for internal consistency of the GAMQ, Cronbach's α was computed for the questionnaire as a whole and for all subscales identified by the factor analysis. Cut-off values for Cronbach's α were $\leq .50$: unacceptable, $.50-.60$: poor, $.60-.70$: questionable, $.70-.80$: acceptable, $.80-.90$: good, and $\alpha \geq .90$: excellent (35). Also, Cronbach's α if each individual item is omitted was reported for the GAMQ total and subscale scores. Furthermore, the distribution of scores and use of each item of the GAMQ was described. As indicators of convergent validity, correlations of the GAMQ total and subscale scores with the BMQ-G General-Harm and General-Overuse subscales and with respondent's medication attitude VAS score were calculated. To explore possible predictive validity of the GAMQ, associations with expected medication effects were analyzed. Finally, correlations of the GAMQ total and subscales with demographic and health variables were calculated.

Results

Sample characteristics

General sample 1 (Gs1)

Nine hundred four respondents reacted to the invitation for study participation. Of these, 112 (12%) never started filling out the questionnaires, 234 (26%) stopped filling out the questionnaires prematurely or were automatically excluded for failing to give the requested answer to one of the control questions. The remaining 558 (62%) filled out the questionnaires completely. Of these, two (<1%) indicated that they were not able to speak Dutch fluently and 40 (7%) respondents were over quota regarding gender, age, or province of residence. Five (1%) respondents completed the questionnaires in less than 1/3 of the median time (i.e. in under 6.4 min) and another three (<1%) indicated not having read or understood the questions well. These respondents were excluded, resulting in 508 (56% of the initial 904) respondents included in this study.

General sample 2 (Gs2)

In total, 690 respondents initiated participation in the study. Of these, nine (1%) respondents explicitly refused informed consent and 296 (43%) completed the questionnaires. Of those who completed the questionnaires, nine (3%) answered one or both of the control questions incorrectly and one (<1%) respondent did not speak Dutch fluently. Five (2%) respondents completed the questionnaires in less than 1/3 of the median time (<11 min). One (<1%) respondent indicated not having understood the questions well and one (<1%) did not give up his or her age, making it impossible to determine if the respondent was at least 18 years old (inclusion criterion). All these respondents were excluded, resulting in a total of 279 (40% of the initial 690) respondents.

Rheumatoid arthritis sample (RAs)

Of the 305 invited patients, 145 (48%) responded by filling out the questionnaires at least partially. Ninety-five (66%) of these respondents opted to fill out the questionnaires via an online service, while 50 (34%) filled out a paper and pencil version of the questionnaires and returned it via postal service. Of these 145 respondents, seven (5%) respondents explicitly refused to consent and ended participation. Eight (6%) respondents did not fill out the informed consent form, but since they filled out the questionnaires and took the effort to return them via postal service, consent was inferred. Of the remaining respondents, 126 (91%) filled out the GAMQ completely, making the response useful for this study. Of these, one (<1%) respondent indicated not being able to speak Dutch fluently and four (3%) did not indicate having understood or read the questions well. The remaining 121 (40% of the invited 305) respondents were included in this study.

Atopic Dermatitis sample (ADs)

Of the 300 invited respondents 79 (26%) filled out the questionnaires at least partially. Of these, 35 (44%) respondents opted to fill out the questionnaires via an online service, while 44 (56%) filled out and returned a paper and pencil version of the questionnaires. Five respondents (6%) explicitly refused informed consent. Two (3%) respondents did not fill out the informed consent form but completed and returned the questionnaires. Again, this was interpreted as informed consent to participate in the study. Of the remaining respondents, 71 (96%) filled out the GAMQ completely. All of these respondents indicated to be fluent Dutch speakers. One respondent (1%) who failed to indicate whether he or she had understood and read the questions well was excluded. The remaining 70 (23% of the invited 300) respondents were included in this study.

Sample comparisons demographic and health-related characteristics

See Table A.3 in the Supplemental Digital Content for an overview of the demographic and health-related characteristics per sample, including comparisons between the samples. Notable differences in demographic characteristics were: 1) the relatively older age of respondents in the RAs; 2) the larger proportion of women in the RAs; 3) the relatively high education level in especially the Gs2, but also the ADs; 4) the relatively high number of respondents who had no religious or ideological affiliation in the Gs2, particularly in comparison to the patient samples; and 5) the somewhat higher proportion of respondents in a relationship in the RAs.

Concerning health-related characteristics, notable differences were: 1) a relatively small proportion of the respondents in Gs2 was in treatment for long-lasting physical or mental complaints; 2) physical health-related quality of life was somewhat lower in the RAs than in the ADs and Gs1; while mental health-related quality of life did not significantly differ between the samples ; 3) as can be expected, current pain was higher in the RAs than all other samples; 4) likewise, current itch was notably higher in the ADs than in the Gs1 and the RAs. Furthermore, mean disease activity (DAS-44) in the RAs was close to clinical remission. In the ADs, POEM scores indicated the mean eczema severity to be moderate. Last, there were no substantial differences between expected effectiveness and expected side effects of medication between the samples.

GAMQ Factor structure and measurement invariance

An exploratory principal component analysis on 60% of the Gs1 suggested that the GAMQ consists of 3 underlying components; one component comprises items 2, 6, 8, 10, and 12 which represent Trust in medication (i.e., Trust; Eigenvalue = 3.06), the second consists of items 1, 3, and 11 which represent Concerns about medication (i.e., Concerns; Eigenvalue = 2.12), and the third contains items 5, 7, and 9 which represent Reluctance to use medication (i.e., Reluctance; Eigenvalue = 2.10).

Taken together, these three components explained 61% of the variance. The loadings of item 4 stayed below the threshold of 0.35 for all of the three components and was left out of the subsequent factor analyses, but kept in the total scale. Stricter evaluation using confirmatory factor analysis (CFA) confirmed the suggested 3-component structure in the 60% training sample as well as in the 40% validation set. The estimated standardized factor loadings obtained by CFA with bootstrap in the same 60% of Gs1, the remaining 40% of Gs1, Gs1 as a whole, Gs2, RAs, and ADs are presented in Table 2.

The CFI suggests an adequate fit of the factor structure for the ADs and Gs1 and a close to adequate fit in the other samples. The RMSEA, where smaller values indicate a better fit, was close to .08 in all samples, indicating a close to adequate fit. The SRMSR, which has the same cut-off values as the RMSEA, indicated an adequate fit (Table 2). Taken together, and considering the highly differential nature of the samples, the fit of the factor structure was deemed adequate for all samples.

Table 2. Items of the GAMQ with factor loadings derived from confirmatory factor analyses and estimates of fit for the factor model per sample.

Items	Factor loading					
	Gs1	Gs1 60% ¹	Gs1 40% ²	Gs2	RAs	ADs
Subscale 1 – Trust in medication						
8) I have no problem with taking medication if I have symptoms.	1.24	1.20	1.31	1.71	1.50	1.40
2) I think that medication can help with my symptoms.	1.10	1.05	1.18	0.92	0.86	0.57
6) I trust that it is safe to take medication.	1.09	1.05	1.17	1.32	1.06	1.38
12) For me the advantages of medication outweigh the disadvantages.	1.01	0.86	1.23	1.15	1.17	0.62
10) I trust in the effectiveness of medication.						
Subscale 2 – Concerns about medication						
3) I am afraid that medication has a harmful effect on my body.	1.13	1.21	1.05	0.98	0.87	0.94
11) I am afraid of becoming addicted if I take medication for an extended period.	0.71	0.86	0.53	0.50	0.39	0.41
1) I am concerned about the side effects of medication.						
Subscale 3 – Reluctance to use medication						
5) I find it unnatural to take medication.	2.50	2.59	2.43	1.27	3.22	2.66
9) I would rather endure my symptoms than take medication.	2.12	2.27	1.96	1.15	2.29	1.80
7) I only take medication if there is absolutely no other option.						
Indicators of model fit						

CFI	.91	-	.87	.89	.84	.90
RMSEA	.09	-	.12	.09	.10	.09
SRMSR	.06	-	.07	.05	.07	.08

Note. ¹ CFA in training sample. ² CFA in remaining 40% of Gs1. Gs1: General sample 1, Gs2: General sample 2, RAs: Rheumatoid Arthritis sample, ADs: Atopic dermatitis sample CFI: Comparative Fit Index, RMSEA: Root Mean Square Error of Approximation, SRMSR: Standardized Root Means Square Residual.

The measurement invariance tests across the samples for the proposed factor structure of the GAMQ (Table 3) indicated that the overall fit of the proposed factor structure (Model 1) is adequate (CFI = .90) or close to adequate (RMSEA = .09) and thus stable across samples. Adding more constraints to this model such as the loadings, intercept and residuals significantly decreased the fit indicated by the CFI (Models 2 to 5), indicating that these parameters differ across samples.

Table 3. Fit statistics testing the measurement invariance of the proposed factor structure across all samples.

Model	χ^2	Df	CFI	RMSEA	$\Delta\chi^2$ *	Δdf
1) Factor configuration invariant	495.60	164	.90	.09		
2) as above & loadings invariant	552.49	188	.89	.09	56.89	24
3) all of the above & intercept invariant	646.13	212	.87	.09	93.64	24
4) all of the above & residuals invariant	730.67	245	.85	.09	84.54	33
5) all of the above & means invariant	762.92	254	.85	.09	32.25	9

Note. * All $\Delta\chi^2$ significant at $p < .001$. χ^2 : Satorra-Bentler scaled statistic, CFI: Comparative Fit Index, RMSEA: Root Mean Square Error of Approximation.

Scoring of the GAMQ, frequency distribution of scores, and use of each item

To obtain the total score for the GAMQ, scores on the negatively worded items (items 1, 3, 5, 7, 9, 11) were reversed and the sum-score of all items was calculated. This resulted in scores with a theoretical minimum of 12 and maximum of 60. As the individual subscales determined during factor analysis (see below) contain either only positively or only negatively worded items, sum-scores were calculated and items were not reversed. Visual inspection of histograms indicated that the distribution of scores for the GAMQ total, and subscales was close to normal in all samples. Generally, the distribution of the total and subscale scores covered the full or almost full theoretical range. Frequency distribution of scores for each item indicated that for most items all answering categories were used in all samples. In case a response option was not used, this favored a more positive attitude towards medication.

Internal consistency GAMQ

Internal consistency of the GAMQ total scale, as indicated by Cronbach's alpha is displayed in Table 4. Cronbach's alpha was generally good for the total scale, but lower for the subscales, particularly Concerns and Reluctance, which included a smaller number of items. Cronbach's alpha if each separate item is omitted is reported in Supplemental Digital Content Table A.4 to A.7. For the total scale and subscales Trust and Reluctance no item stood out as significantly affecting the internal

consistency. For the subscale Concerns, omitting item 11 (“I am afraid of becoming addicted if I take medication for an extended period”) would increase Cronbach’s alpha. However, considering its content and fit in the total scale, item 11 was kept in the questionnaire.

Table 4. Cronbach’s alpha as indicator of internal consistency for the GAMQ total and subscale scores for each sample

Scale	Cronbach’s alpha			
	Gs1	Gs2	RAs	ADs
GAMQ Total	.84	.83	.78	.81
GAMQ Trust	.81	.78	.73	.74
GAMQ Concerns	.69	.59	.67	.71
GAMQ Reluctance	.67	.67	.56	.66

Note. Gs1: General sample 1, Gs2: General sample 2, RAs: Rheumatoid Arthritis sample, ADs: Atopic dermatitis sample.

Sample comparisons on medication attitude

See Table 5 for an overview of the medication attitude scores per sample. Comparisons of the samples on the GAMQ total and subscale scores, the BMQ subscale scores for Harm and Overuse and medication attitude VAS scores showed only minimal differences between the samples. On the GAMQ total score and subscale Trust, the Gs2 scored slightly lower than the other samples (total $p < .05$, Trust $p < .01$), which did not differ from each other. On the BMQ-G subscale Harm, the ADs scored slightly lower than all other samples ($p < .05$), while the Gs2 scored slightly lower than Gs1 ($p = .001$). On the General-Overuse subscale, Gs1 scored significantly higher than the Gs2 ($p < .05$), RAs, and ADs ($p < .01$); RAs and ADs scored significantly lower than Gs2 but did not significantly differ from each other. On medication attitude VAS scores Gs2 scored slightly lower than Gs1 ($p < .01$).

Table 5. Medication attitude for each sample – mean (SD)

	Gs1 (<i>n</i> = 508)	Gs2 (<i>n</i> = 279)	RAs (<i>n</i> = 121)	ADs (<i>n</i> = 70)	Sample comparisons
GAMQ Total	39.83 (7.01)	38.10 (7.23)	39.86 (6.23)	40.37 (6.73)	$F(3,974)=4.53$, $p=.004$, $\eta_p^2=.01$
GAMQ Trust	18.74 (3.15)	17.90 (3.29)	19.16 (2.85)	19.09 (3.01)	$F(3,974)=6.75$, $p<.001$, $\eta_p^2=.02$
GAMQ Concerns	8.76 (2.52)	9.08 (2.42)	9.11 (2.48)	8.74 (2.59)	$F(3,974)=1.38$, $p=.246$, $\eta_p^2=.00$
GAMQ Reluctance	8.85 (2.32)	9.23 (2.44)	8.83 (2.23)	8.71 (2.38)	$F(3,974)=1.94$, $p=.121$, $\eta_p^2=.01$
BMQ-G General-Harm	10.60 (2.74)	9.90 (2.62)	10.21 (2.45)	9.01 (2.66)	$F(3,968)=9.33$, $p<.001$, $\eta_p^2=.03$
BMQ-G General-Overuse	12.51 (3.00)	12.03 (3.13)	11.39 (2.68)	11.21 (3.01)	$F(3,970)=7.28$, $p<.001$, $\eta_p^2=.02$
Medication attitude VAS	63.55 (23.62)	58.58 (22.72)	63.76 (23.38)	63.34 (19.59)	$F(3,949)=3.07$, $p=.027$, $\eta_p^2=.01$

Note: Gs1: General sample 1, Gs2: General sample 2, RAs: Rheumatoid Arthritis sample, ADs: Atopic dermatitis sample. BMQ-G: general scale of the Beliefs about Medicines Questionnaire, VAS: visual analogue scale, GAMQ: General Attitude towards Medication Questionnaire.

Convergent validity: Associations of the GAMQ with measures of medication attitude

Convergent validity of the GAMQ was tested by investigating the associations of the GAMQ total and subscale scores with the BMQ-G General-Harm and General-Overuse scores and the medication attitude VAS. As visible in Table 6, a more positive general medication attitude according to the GAMQ Total consistently showed strong negative correlations with the BMQ-G subscales and correlated positively and strongly with a more positive medication attitude VAS score across samples. The positive GAMQ subscale Trust consistently correlated negatively with the BMQ-G subscale scores and positively with the medication attitude VAS score. The negative GAMQ subscales Concerns and Reluctance were positively correlated with both BMQ-G subscale scores and negatively correlated with the medication attitude VAS score in all samples. Most of these correlations were moderate to strong in all samples.

The GAMQ total correlated strongly with all of its subscales. As can be expected, correlations with Trust were positive, while correlations with Concerns and Reluctance were negative. The subscale Trust showed negative correlations with Concerns. This association was moderate in the general samples and weak in the patient samples. Trust also correlated strongly and negatively with Reluctance, except in the RAs where this association was moderate. Subscales Concerns and Reluctance correlated moderately and positively with each other in all samples.

General Attitude towards Medication Questionnaire

Table 6. Associations of the GAMQ with other indicators of beliefs about or attitudes towards medication and its own subscales.

	Gs1 (n = 508)				Gs2 (n = 279)				RAs (n = 121)				ADs (n = 70)			
	Total	Trust	Concerns	Reluctance	Total	Trust	Concerns	Reluctance	Total	Trust	Concerns	Reluctance	Total	Trust	Concerns	Reluctance
Medication attitude																
BMQ-G General-Harm, r	-.58*	-.46*	.46*	.51*	-.54*	-.44*	.44*	.47*	-.51*	-.31*	.47*	.49*	-.59*	-.44*	.39**	.56*
BMQ-G General-Overuse, r	-.58*	-.46*	.46*	.49*	-.57*	-.51*	.37*	.48*	-.50*	-.34*	.43*	.35*	-.53*	-.46*	.27*	.47*
GAMQ Total, r		.84*	-.70*	-.83*		.86*	-.67*	-.82*		.77*	-.68*	-.77*		.80*	-.61*	-.84*
GAMQ Trust, r			-.37*	-.57*			-.36*	-.57*			-.22	-.40*			-.17	-.59*
GAMQ Concerns, r				.43*				.39*				.40*				.31*
GAMQ Reluctance, r																
Medication attitude (VAS), r	.67*	.62*	-.46*	-.52*	.69*	.62*	-.40*	-.59*	.64*	.48*	-.45*	-.47*	.65*	.68*	-.28	-.47*

Note: Gs1: General sample 1, Gs2: General sample 2, RAs: Rheumatoid Arthritis sample, ADs: Atopic dermatitis sample. n.a. = data not available; * bootstrapped confidence intervals did not include 0. ¹ In treatment for long-lasting medical or psychological complaints or diseases other than Ra for RAs and AD for ADs. SF12 PCS: Short Form 12 Physical Component Score, SF-12 MCS: Short Form 12 Mental Component Score, DAS44: Disease Activity Score, POEM: Patient Oriented Eczema Measure, BMQ-G: general scale of the Beliefs about Medicines Questionnaire, VAS: visual analogue scale, GAMQ: General Attitude towards Medication Questionnaire. Medium and large effect sizes are printed in bold.

Predictive validity: Associations of the GAMQ with expected medication effects

All associations of the GAMQ total and subscale scores with expected medication effects can be found in the Supplemental Digital Content (Table A.8.) and only statistically significant, moderate associations are reported here. Expected effectiveness of medication for pain was positively associated with the GAMQ Total in the RAs and with the subscale Trust in the Gs1. Expected effectiveness of medication for itch was positively associated with the GAMQ Total and the subscale Trust in the ADs. Expected side effects were negatively correlated with the GAMQ Total and the subscale Trust, and positively associated with the subscale Reluctance in the ADs.

Associations between the GAMQ and demographic and health variables

All associations of the GAMQ total and subscale scores with demographic and health variables can be found in the Supplemental Digital Content (Table A.8.). Only statistically significant, moderate associations are reported here. Religious or ideological affiliation was moderately associated with the GAMQ Total in the RAs. Respondents who were not affiliated with any religion or who identified as Christian had a more positive attitude towards medication than respondents affiliated with other religions. Religious or ideological affiliation was also moderately associated with the GAMQ subscale Trust in the RAs, however post-hoc pairwise comparisons between the different affiliations were statistically non-significant. Concerning health, in the ADs, respondents who had comorbidities scored moderately higher on the subscale Trust.

Discussion

Attitudes towards medication are important predictors of treatment outcome and adherence (1-5). Current research and measures mainly focus on negative attitudes towards medication which may be involved in nocebo effects and affect treatment outcomes and adherence negatively (1, 2, 7, 8, 13). Positive attitudes toward medication, however, may increase medication effectiveness (3, 7, 9) and adherence (4, 5) partially through mechanisms that are also involved in placebo and nocebo effects. To facilitate research into the effects of both positive and negative attitudes towards medication in general, the General Attitude towards Medication Questionnaire (GAMQ) was developed and its psychometric properties were investigated in two general and two patient samples (rheumatoid arthritis, RAs, and atopic dermatitis, ADs).

The results of our study show that the GAMQ has satisfactory psychometric properties in terms of stability across the investigated samples, internal consistency, and convergent as well as predictive validity. Therefore, it is suggested to be suitable for assessing general medication attitudes, both negative and positive, in a wide variety of research settings and in various patient populations. The balanced nature of the GAMQ, and brevity render it a promising tool for investigating predictors of medication outcomes and adherence, as well as placebo and nocebo effects.

Exploratory and subsequent confirmatory factor analyses indicated that the GAMQ comprises three subscales that were named Trust in medication (i.e., Trust), Concerns about negative effects of medication (i.e., Concerns), and Reluctance to use medication (i.e., Reluctance). One item (item 4) could not be included in any of the subscales but was left in the total scale considering its content and its contribution to the internal consistency. Another item (item 11) affected the internal consistency of the subscale Concerns but was left in the scale as it addresses the topic of addiction to medication, which is deemed highly relevant for this questionnaire. The adequate, or close to adequate, fit of the factor structure in all four samples and the measurement invariance tests indicate that the GAMQ measures the same underlying construct in both general and patient populations (20). This consistency of the GAMQ factor structure across samples is not due to a lack of diversity of the investigated samples, as they differed with regard to important demographic factors (e.g., age, gender, and education) as well as health variables (chronic medical complaints, physical health-related quality of life, current pain and itch) and medication attitude (BMQ-G and GAMQ), although the latter differences were small. The internal consistency of the GAMQ total scale was generally good, and that of the Trust subscale was generally acceptable. The subscales Concerns and Reluctance, however showed relatively low internal consistency, which is probably due to the limited number of items contained in these subscales. However, taking into account the stability of the GAMQ's factor structure including these

subscales, the subscale scores convey important information about specific aspects of general medication attitudes in addition to the total score.

Convergent validity of the GAMQ total scale and subscales was good, as indicated by the strength and direction of associations with the BMQ-G and a single item measure of medication attitude in all samples. This demonstrates the suitability of the GAMQ to measure general positive attitudes towards medication in addition to negative ones. Predictive validity of the GAMQ was investigated by examining its association with expectations about effectiveness of medication for pain and itch relief and expected side effects of medication. Overall, a positive attitude toward medication, seemed to be stronger and more consistently associated with expected effectiveness and side effects of medication than a negative attitude toward medication. This provides indications for the additional value of measuring general positive attitudes to medication. It may also hint towards a possible link between positive attitudes toward medication and expectancy induced placebo and nocebo effects. Notably, associations of the GAMQ total and subscale scores with expected effectiveness of medication for pain were mostly stronger than for itch in the RA sample including many respondents who were experienced with taking pain medication, while the opposite was true for the AD sample including many respondents who were experienced with taking medication against itch. These findings suggest that the GAMQ total score might also be informative in predicting people's medication-specific expectations, although further research is required to confirm this. Furthermore, GAMQ was not consistently or strongly associated with demographic or health related characteristics, but correlations that were found (i.e., associations with religious or ideological affiliation, with the presence of a (co-morbid) illness, and quality of life in some samples) were largely consistent with research on other measures of general medication attitudes such as the BMQ-G (36-40).

The GAMQ was developed and validated in Dutch, and an English version of the questionnaire, obtained by forward-backward translation with the help of a certified translator and native speaker, is provided in this article. As other questionnaires assessing general medication attitudes are valid across different languages and cultural backgrounds (e.g. 41, 42-45), the same could be expected for the GAMQ. However, further research is needed to confirm this. The sample sizes of the patient samples were small for validation purposes. However, including the patient samples allowed for the GAMQ to be investigated in four distinct populations which differed from each other in important demographic and health characteristics and thus yielded valuable information about the usability of the GAMQ across diverse samples and generalizability of the results. Furthermore, the brevity of the GAMQ (12 items) enables its use in patient populations in which more lengthy questionnaires would be too tiring. Moreover, the balance between positive and negative items and their wording, clearly reflecting a personal view rather than a general truth, make it suitable for use in cross-sectional as well as experimental research and possibly clinical practice. Especially when it is important not to bias the

responses of the participants by overly extreme and one-sided items and when general positive attitudes toward medication are equally as important as negative ones, as is the case in placebo and nocebo research, the GAMQ can be considered a suitable instrument. To conclude, the newly developed GAMQ is a sufficiently reliable and valid measure of positive and negative attitudes towards medication in general, and suitable for use in general and clinical populations.

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Supplemental Digital Content

Table A.1. Overview of questionnaires per sample.

	Gs1	Gs2	RAs	ADs
Attitude towards medication				
GAMQ	x	x	x	x
BMQ-G	x	x	x	x
Medication attitude VAS	x	x	x	x
Health-related characteristics				
SF-12 PCS	x		x	x
SF-12 MCS	x		x	x
POEM				x
DAS-44			x	
Current pain intensity	x	x	x	x
Current itch intensity	x		x	x
In treatment for long- lasting medical or psychological complaints or diseases (other than RA for RAs and AD for ADs)	x	x	x	x
Expectancies regarding medication	x		x	x

Note. Gs1: General sample 1, Gs2: General sample 2, RAs: Rheumatoid Arthritis sample, ADs: Atopic dermatitis sample, GAMQ: General Attitude towards Medication Questionnaire, BMQ-G: General scale of the Beliefs about Medicines Questionnaire, VAS: Visual Analogue Scale, SF-12: Short Form 12, PCS: Physical health Composite, MCS: Mental health Composite, POEM: Patient Oriented Eczema Measure, DAS44: Disease Activity Score-44.

Table A.2. Dutch version of the General Attitude toward Medication Questionnaire (Attitude ten opzichte van Medicijnen Vragenlijst)

Wij willen u nu een aantal vragen stellen over hoe u denkt over medicijnen in het algemeen.

Wij zijn geïnteresseerd in uw mening over medicijnen die u op doktersvoorschrift gebruikt.

Wilt u aangeven in hoeverre u het eens of oneens bent met onderstaande uitspraken?

Er zijn geen goede of foute antwoorden. Wij zijn benieuwd naar uw mening.

	helemaal mee oneens	mee oneens	geen duidelijke mening	mee eens	helemaal mee eens
1. Ik ben bezorgd over de bijwerkingen van medicijnen	☐	☐	☐	☐	☐
2. Ik denk dat medicijnen mij goed kunnen helpen tegen klachten	☐	☐	☐	☐	☐
3. Ik ben bang dat medicijnen schadelijk zijn voor mijn lichaam	☐	☐	☐	☐	☐
4. Als ik klachten heb, neem ik daar gemakkelijk medicijnen voor	☐	☐	☐	☐	☐
5. Ik vind het onnatuurlijk om medicijnen te gebruiken	☐	☐	☐	☐	☐
6. Ik vertrouw er op dat het veilig is om medicijnen te gebruiken	☐	☐	☐	☐	☐
7. Ik gebruik medicijnen alleen als er echt geen andere mogelijkheid is	☐	☐	☐	☐	☐
8. Ik heb er geen moeite mee om medicijnen te gebruiken als ik klachten heb	☐	☐	☐	☐	☐
9. Ik onderga mijn klachten liever dan dat ik medicijnen gebruik	☐	☐	☐	☐	☐
10. Ik vertrouw op de werkzaamheid van medicijnen	☐	☐	☐	☐	☐
11. Ik ben bang verslaafd te raken als ik medicijnen langdurig gebruik	☐	☐	☐	☐	☐
12. Voor mij wegen de voordelen van medicijnen op tegen de nadelen	☐	☐	☐	☐	☐

Table A.3. Demographic and health-related characteristics for each sample.

	Gs1 (n = 508)	Gs2 (n = 279)	RAs (n = 121)	ADs (n = 70)	Sample comparison *
Demographic characteristics					
Age (years) mean (SD), range	47.00 (16.06) 18-75	41.12 (14.18) 18-65	58.63 (13.15) 22-85	47.49 (20.45) 19-82	F(3, 971)=35.10, p<.001, $\eta_p^2=.10$
Gender, n (%) of men	247 (48.6%)	130 (46.6%)	31 (25.6%)	31 (44.3%)	$\chi^2(3)=21.36$, p<.001
Educational level, n (%)					$\chi^2(3)=64.28$; p<.001
Secondary	310 (61.0%)	95 (34.1%)	81 (66.9%)	32 (45.7%)	
Tertiary	198 (39.0%)	184 (65.9%)	40 (33.1%)	38 (54.3%)	
Nationality, n (%)					$\chi^2(6)=7.46$; p=.281
Dutch	497 (97.8%)	263 (94.3%)	116 (96.7%)	67 (95.7%)	
Other	6 (1.2%)	10 (3.6%)	3 (2.5%)	2 (2.9%)	
Multiple	5 (1.0%)	6 (2.2%)	1 (0.8%)	1 (1.4%)	
Religious or ideological affiliation, n (%)					$\chi^2(6)=39.99$; p<.001
None	300 (59.1%)	204 (73.1%)	59 (49.2%)	29 (42.0%)	
Christian	178 (35.0%)	65 (23.3%)	57 (47.5%)	37 (53.6%)	
Other	30 (5.9%)	10 (3.6%)	4 (3.3%)	3 (4.3%)	
Marital status, n (%)					$\chi^2(3)=11.40$; p=.010
Single	175 (34.4%)	89 (31.9%)	22 (18.6%)	20 (28.6%)	
In relationship	333 (65.6%)	190 (68.1%)	96 (81.4%)	50 (71.4%)	
Health-related characteristics					
In treatment for long-lasting medical or psychological complaints or diseases (other than RA for RAs and AD for ADs), n (%)	218 (42.9%)	88 (31.5%)	54 (45.5%)	31 (44.3%)	$\chi^2(3)=12.08$; p=.007
SF-12 PCS, mean (SD)	47.94 (11.46)	n.a.	42.91 (10.41)	48.82(9.05)	F(2,696)=10.99, p<.001, $\eta_p^2=.03$
SF-12 MCS, mean (SD)	46.34 (12.11)	n.a.	44.88(11.84)	47.01(9.48)	F(2,696)=0.95, p=.386, $\eta_p^2<.01$
DAS-44, mean (SD)	n.a.	n.a.	1.67 (0.82)	n.a.	n.a.
POEM, mean (SD)	n.a.	n.a.	n.a.	13.21 (8.28)	n.a.
Current pain intensity, mean (SD)	25.93 (30.40)	18.92 (25.07)	34.85 (30.28)	19.58 (23.77)	F(3,973)=9.97, p<.001, $\eta_p^2=.03$
Current itch intensity, mean (SD)	12.01 (21.66)	n.a.	9.72 (19.28)	52.92 (29.47)	F(2,691)=105.95, p<.001, $\eta_p^2=.24$

Expectancies regarding medication					
Expected effectiveness of medication for pain relief, mean (SD)	67.85 (13.42)	<i>n.a.</i>	62.81 (12.02)	62.50 (14.86)	$F(2,671)=9.35, p<.001, \eta_p^2=.03$
Expected effectiveness of medication for itch relief, mean (SD)	63.04 (15.37)	<i>n.a.</i>	60.66 (14.81)	57.21 (17.93)	$(F(2, 669)= 4.21, p=.014, \eta_p^2=.01$
Expected side effects of medication, mean (SD)	48.20 (12.62)	<i>n.a.</i>	51.93 (12.36)	48.03 (11.49)	$F(2, 665)=2.97, p=.052, \eta_p^2=.01$

Note: Gs1: General sample 1, Gs2: General sample 2, RAs: Rheumatoid Arthritis sample, ADs: Atopic dermatitis sample. Available data are reported, missing values were disregarded from analyses. SF-12 PCS: short form 12 physical component score, SF-12 MCS: short form 12 mental component score, DAS-44: disease activity score, POEM: patient oriented eczema measure, *n.a.*: not assessed, SD: standard deviation.

Table A.4. Cronbach's alpha of the GAMQ total scale if item omitted.

Item	Gs1	Gs2	RAs	ADs
1) I am concerned about the side effects of medication. <i>(rev)</i>	.84	.82	.76	.80
2) I think that medication can help with my symptoms.	.83	.82	.77	.81
3) I am afraid that medication has a harmful effect on my body. <i>(rev)</i>	.83	.82	.76	.80
4) If I have symptoms, I readily take medication for them.	.83	.82	.76	.79
5) I find it unnatural to take medication. <i>(rev)</i>	.82	.82	.74	.77
6) I trust that it is safe to take medication.	.83	.82	.76	.78
7) I only take medication if there is absolutely no other option. <i>(rev)</i>	.84	.82	.79	.80
8) I have no problem with taking medication if I have symptoms.	.82	.81	.75	.78
9) I would rather endure my symptoms than take medication. <i>(rev)</i>	.82	.81	.75	.78
10) I trust in the effectiveness of medication.	.83	.82	.77	.79
11) I am afraid of becoming addicted if I take medication for an extended period. <i>(rev)</i>	.85	.85	.78	.82
12) For me the advantages of medication outweigh the disadvantages.	.83	.82	.76	.81
Total scale	.84	.83	.78	.81

Note: Gs1: General sample 1, Gs2: General sample 2, RAs: Rheumatoid Arthritis sample, ADs: Atopic dermatitis sample. *(rev)* indicates items for which scores were reversed.

Table A.5. Cronbach's alpha of the GAMQ subscale Trust if item omitted.

Item	Gs1	Gs2	RAs	ADs
2) I think that medication can help with my symptoms.	.77	.76	.71	.72
6) I trust that it is safe to take medication.	.78	.74	.69	.66
8) I have no problem with taking medication if I have symptoms.	.80	.74	.70	.67
10) I trust in the effectiveness of medication.	.76	.74	.67	.66
12) For me the advantages of medication outweigh the disadvantages.	.78	.74	.67	.75
Total scale	.81	.78	.73	.74

Note: Gs1: General sample 1, Gs2: General sample 2, RAs: Rheumatoid Arthritis sample, ADs: Atopic dermatitis sample.

Table A.6. Cronbach's alpha of the GAMQ subscale Concerns if item omitted.

Item	Gs1	Gs2	RA	AD
1) I am concerned about the side effects of medication.	.55	.37	.35	.45
3) I am afraid that medication has a harmful effect on my body.	.48	.41	.50	.48
11) I am afraid of becoming addicted if I take medication for an extended period.	.74	.68	.80	.85
Total scale	.69	.59	.67	.71

Note: Gs1: General sample 1, Gs2: General sample 2, RA: Rheumatoid Arthritis sample, AD: Atopic dermatitis sample.

Table A.7. Cronbach's alpha of the GAMQ subscale Reluctance if item omitted.

Item	Gs1	Gs2	RA	AD
5) I find it unnatural to take medication.	.49	.56	.35	.51
7) I only take medication if there is absolutely no other option.	.71	.60	.60	.65
9) I would rather endure my symptoms than take medication.	.46	.56	.38	.51
Total scale	.67	.67	.56	.66

Note: Gs1: General sample 1, Gs2: General sample 2, RA: Rheumatoid Arthritis sample, AD: Atopic dermatitis sample.

General Attitude towards Medication Questionnaire

Table A.8. Associations of the GAMQ with expected medication effects, demographic and health variables.

	Gs1 (n = 508)				Gs2 (n = 279)				RAs (n = 121)				ADs (n = 70)			
	Total	Trust	Concerns	Reluctance	Total	Trust	Concerns	Reluctance	Total	Trust	Concerns	Reluctance	Total	Trust	Concerns	Reluctance
Demographic characteristics																
Age (years), r	.04	.12*	<.01	-.01	.02	.02	-.01	-.03	.02	-.02	<.01	-.05	-.03	.01	.06	.06
Gender, η_p^2	.02**	.01**	.03***	.01*	.01	.01	.01	.00	.03	.03*	.00	.03	.00	.00	.04	.00
Men, mean (SD)	40.94 (6.47)	19.14 (3.09)	8.28 (2.36)	8.60 (2.21)	38.78 (7.55)	18.19 (3.50)	8.85 (2.51)	9.11 (2.45)	41.52 (6.53)	20.03 (3.04)	9.00 (2.53)	8.23 (2.32)	39.97 (7.64)	19.26 (3.36)	9.35 (2.78)	8.77 (2.68)
Women, mean (SD)	38.79 (7.34)	18.37 (3.17)	9.21 (2.59)	9.10 (2.39)	37.50 (6.92)	17.65 (3.08)	9.28 (2.32)	9.34 (2.44)	39.29 (6.05)	18.87 (2.74)	9.14 (2.48)	9.03 (2.17)	40.69 (6.00)	18.95 (2.73)	8.26 (2.36)	8.67 (2.14)
Educational level, η_p^2	.01	.01	.00	.00	.00	.00	.00	.00	.01	.02	.00	.01	.02	.01	.04	.00
Secondary, mean (SD)	40.23 (6.96)	18.93 (3.12)	8.68 (2.48)	8.80 (2.26)	37.46 (7.20)	17.61 (3.47)	9.24 (2.55)	9.39 (2.48)	40.33 (6.05)	19.43(2.71)	9.14(2.60)	8.69(2.26)	39.38 (7.42)	18.78 (3.25)	9.28 (2.99)	8.88 (2.12)
Tertiary, mean (SD)	39.22 (7.05)	18.44 (3.19)	8.88 (2.59)	8.94 (2.41)	38.35 (7.19)	18.05(3.19)	8.99 (2.35)	9.15(2.43)	38.90 (6.54)	18.62 (3.08)	9.05 (2.26)	9.10 (2.17)	41.21 (6.06)	19.34 (2.80)	8.29 (2.14)	8.58 (2.60)
Nationality, η_p^2	.01	.01	.01	.01	.00	.01	.01	.01	.02	.02	.02	.03	.03	.04	.03	.03
Dutch, mean (SD)	39.86 (6.97)	18.76 (3.14)	8.75 (2.50)	8.86 (2.32)	38.14 (7.24)	17.98 (3.30)	9.12 (2.41)	9.23 (2.43)	39.96 (6.21)	19.22 (2.87)	9.12 (2.50)	8.79 (2.20)	40.52 (6.73)	19.15 (3.01)	8.66 (2.56)	8.69 (2.39)
Other, mean (SD)	35.17 (9.83)	16.67 (4.76)	10.17 (3.66)	9.50 (2.35)	36.30 (6.78)	16.70 (2.67)	8.80 (2.53)	9.80 (2.70)	35.67 (4.93)	16.67 (1.53)	8.00 (1.73)	10.33 (2.31)	40.50 (4.95)	19.50 (0.71)	11.00 (4.24)	8.00 (0.00)
Multiple, mean (SD)	42.80 (5.40)	19.20 (2.05)	7.60 (2.79)	7.20 (1.64)	39.33 (8.21)	16.67 (3.67)	7.83 (2.56)	8.33 (2.94)	33.00 (n=1)	19.00 (n=1)	12.00 (n=1)	12.00 (n=1)	30.00 (n=1)	14.00 (n=1)	10.00 (n=1)	12.00 (n=1)
Religious or ideological affiliation, η_p^2	.01	.00	.01	.01	.00	.00	.00	.00	.07*	.07*	.02	.04	.06	.02	.07	.04
None, mean (SD)	40.19 (6.79)	18.74 (3.05)	8.67 (2.43)	8.66 (2.28)	38.11 (7.42)	17.95 (3.41)	9.03 (2.52)	9.31 (2.49)	39.69 (5.46)	19.20 (2.62)	9.34 (2.25)	8.93 (2.09)	41.21(6.49)	19.45 (2.80)	8.31 (2.51)	8.69 (2.47)
Christian, mean (SD)	39.61 (7.18)	18.87 (3.10)	8.78 (2.55)	9.15 (2.37)	38.08 (6.05)	17.83 (2.83)	9.26 (1.86)	9.00 (2.22)	40.49 (6.57)	19.37 (2.77)	8.79 (2.74)	8.63 (2.30)	40.51 (6.83)	19.05 (3.16)	8.84 (2.62)	8.54 (2.38)
Other, mean (SD)	37.63 (7.84)	18.00 (4.30)	9.53 (3.10)	9.00 (2.24)	38.00 (10.69)	17.40 (3.75)	8.90 (3.48)	9.10 (3.03)	31.25 (6.18)	15.25 (5.12)	10.50 (1.73)	11.00 (1.83)	33.00 (4.00)	17.67 (2.08)	11.67 (2.08)	11.00 (0.00)
Marital status, η_p^2	.00	.00	.00	.00	.00	.01	.00	.00	.00	.00	.01	.00	.04	.02	.03	.03
Single, mean (SD)	39.55 (6.61)	18.61 (3.03)	8.88 (2.62)	8.85 (2.22)	37.51 (7.89)	17.52 (3.56)	9.01 (2.64)	9.44 (2.59)	40.23 (6.71)	19.27 (2.49)	8.55 (3.05)	8.95 (1.91)	42.45 (5.96)	19.80 (2.59)	8.05 (2.39)	8.05 (2.65)
In relationship, mean (SD)	39.98 (7.21)	18.81 (3.21)	8.70 (2.47)	8.86 (2.37)	38.38 (6.91)	18.08 (3.15)	9.11 (2.31)	9.13 (2.37)	39.50 (5.85)	19.05 (2.91)	9.30 (2.28)	8.90 (2.23)	39.54 (6.90)	18.80 (3.14)	9.02 (2.64)	8.98 (2.24)

General Attitude towards Medication Questionnaire

Health variables																
long-lasting medical or psychological complaints ¹ , η_p^2	.02**	.04***	.01	.02**	.00	.01	.01	.00	.00	.00	.00	.00	.05	.09*	.00	.03
No, mean (SD)	39.10 (7.06)	18.21 (3.28)	8.60 (2.40)	9.13 (2.33)	37.88 (7.68)	17.69 (3.45)	8.92 (2.47)	9.33 (2.58)	39.72(6.52)	19.15 (3.09)	9.15 (2.44)	8.86 (2.24)	39.08 (7.27)	18.31 (3.10)	8.82 (2.49)	9.05 (2.62)
Yes, mean (SD)	40.81 (6.83)	19.45 (2.82)	8.97 (2.67)	8.48 (2.25)	38.58 (6.15)	18.36 (2.87)	9.42 (2.28)	9.01 (2.11)	40.31 (6.00)	19.20 (2.59)	9.02(2.58)	8.79 (2.24)	42.00 (5.69)	20.06 (2.61)	8.65 (2.75)	8.29 (2.00)
SF-12 PCS, r	.00	-.08*	-.18*	.04	n.a.	n.a.	n.a.	n.a.	.20*	.14	-.17	-.20*	-.15	-.12	-.03	.21
SF-12 MCS, r	.06	.04	-.23*	.07	n.a.	n.a.	n.a.	n.a.	.14	-.01	-.29*	-.15	-.06	-.04	-.10	.19
DAS44, r	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	-.24*	-.21	.16	.23*	n.a.	n.a.	n.a.	n.a.
POEM, r	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	.01	.08	.10	-.03
Current pain intensity, r	-.02	.03	.14*	-.01	.00	.02	.09	-.00	-.07	-.05	.08	.07	.08	.13	.20*	-.24
Current itch intensity, r	.02	.00	.04	-.05	n.a.	n.a.	n.a.	n.a.	-.09	-.04	.17*	.08	-.08	.05	.20	.08
Expectancies regarding medication																
Expected effectiveness of medication [in general] for pain relief, r	.26*	.30*	-.14*	-.16*	n.a.	n.a.	n.a.	n.a.	.30*	.18	-.23*	-.21*	.07	.21	.10	-.05
Expected effectiveness of medication [in general] for itch relief, r	.24*	.27*	-.15*	-.13*	n.a.	n.a.	n.a.	n.a.	.08	-.03	-.07	-.12	.35*	.48*	-.03	-.26*
Expected side effects of medication [in general], r	-.23*	-.20*	.22*	.14*	n.a.	n.a.	n.a.	n.a.	-.24*	-.16	.27*	.14	-.42*	-.36*	.24	.36*

Note: Gs1: General sample 1, Gs2: General sample 2, RAs: Rheumatoid Arthritis sample, ADs: Atopic dermatitis sample. GAMQ theoretical range of scores: Total 12 - 60 (12 items) Trust 5 - 25 (5 items), Concerns 3 - 15 (3 items), Reluctance 3 - 15 (3 items). n.a. = data not available; For ANOVAs: *p<.05, **p<.01, ***p<.001; For correlations: * bootstrapped confidence interval did not include 0. ¹ In treatment for long-lasting medical or psychological complaints or diseases other than Ra for RAs and AD for ADs. SF12 PCS: short form 12 physical component score, SF-12 MCS: short form 12 mental component score, DAS44: disease activity score, POEM: patient oriented eczema measure. Medium and large effect sizes are printed in bold.