Development of a novel instrument for assessing intentional non-adherence to official medical recommendations (iNAR-12): a sequential mixed-methods study in Serbia

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ABSTRACT

Objectives We aimed to (1) develop a novel instrument, suitable for the general population, capturing intentional non-adherence (iNAR), consisting of non-adherence to prescribed therapy, self-medication and avoidance of seeking medical treatment; (2) differentiate it from other forms of non-adherence, for example, smoking; and (3) relate iNAR to patient-related factors, such as sociodemographics, health status and endorsement of irrational beliefs (conspiratorial thinking and superstitions) and to healthcare-related beliefs and experiences (including trust and negative experiences with the healthcare system, normalisation of patient passivity).

Design To generate iNAR items, we employed a focus group with medical doctors, supplemented it with a literature search and invited a public health expert to refine it further. We examined the internal structure and predictors of iNAR in an observational study.

Setting Data were collected online using snowball sampling and social networks.

Participants After excluding those who failed one or more out of three attention checks, the final sample size was n=583 adult Serbian citizens, 74.4% female, mean age 39.01 years (SD=12.10).

Primary and secondary outcome measures The primary, planned outcome is the iNAR Questionnaire, while smoking was used for comparison purposes.

Results Factor analysis yielded a one-factor solution, and the final 12-item iNAR Questionnaire had satisfactory internal reliability (alpha=0.72). Health condition and healthcare-related variables accounted for 14% of the variance of iNAR behaviours, whereas sociodemographics and irrational beliefs did not additionally contribute.

Conclusions We constructed a brief yet comprehensive measure of iNAR behaviours and related them to health and sociodemographic variables and irrational beliefs. The findings suggest that public health interventions should attempt to improve patients’ experiences with the system and build trust with their healthcare practitioners rather than aim at specific demographic groups or at correcting patients’ unfounded beliefs.

INTRODUCTION

From a pile of medicines they [patients] should take, they decide which they should give priority to and to which they should not ... More often than not, supplements and probiotics are prioritized at the expense of medicines which could really solve their health issues.

Public health expert, when asked about intentional non-adherence in a focus group

According to the WHO, adherence is defined as “the extent to which a person’s behaviour ... corresponds with agreed recommendations from a healthcare provider”; with non-adherence being its opposite pole. It encompasses a range of health behaviours from non-adherence to treatment recommendations and avoidance to seek medical treatment to self-medication and disregarding public health recommendations. The consequences of non-adherence can be dire: antibiotic overuse and vaccine hesitancy are listed as the top 0 global health
threats. Thus, there is a growing need for a better understanding and management of non-adherence to medical recommendations.3

The majority of non-adherence research focuses on only one aspect of non-adherence such as taking medication4–6 and often targets people with specific health conditions. However, non-adherence might constitute a broader construct of non-adhering to medical recommendations in general, also including behaviours such as avoiding and delaying treatment, self-medication and non-adherence to public health recommendations. Regarding all these types of recommendations, non-adherence can be intentional and unintentional. While unintentional non-adherence is a consequence of various barriers7–9 (eg, socioeconomic, healthcare system-related, cognitive), we consider intentional non-adherence (iNAR) to be a result of a decision-making process and therefore more psychologically rooted. Understanding whether different iNAR behaviours form a unitary construct, as well as what are significant predictors of this behavioural tendency, could prove to be useful for designing future health interventions aimed at the general population.

According to the WHO report,1 non-adherence to treatment recommendations is a global problem only expected to increase with the rising burden of chronic diseases. A failure to adhere to treatment threatens its effectiveness and can lead to poorer health outcomes and decreased quality of life. It is a risk factor for premature mortality,7 the spread of infectious diseases8 and a higher burden on healthcare systems.9 Achieving treatment adherence is a consequence of various barriers9–11 (eg, socioeconomic, healthcare system-related, cognitive), we consider intentional non-adherence (iNAR) to be a result of a decision-making process and therefore more psychologically rooted. Understanding whether different iNAR behaviours form a unitary construct, as well as what are significant predictors of this behavioural tendency, could prove to be useful for designing future health interventions aimed at the general population.

Avoidance or delay in seeking medical treatment leads to late detection of disease, which worsens prognosis and treatment options.10

Self-medication is another widespread issue.11–14 Excessive use of antimicrobials has led to microbial resistance to infections such as pneumonia, tuberculosis, gonorrhoea and salmonellosis.15 The use of psychotropic medicines also presents a significant public health problem14–15 and has increased in the past decade.16 These trends are tracked worldwide, with Serbia being at the top of the list of European countries.17–18 Serbian citizens also reported the highest consumption of benzodiazepines in Europe.16–18 While self-medication practices do differ by country, they nevertheless represent a global issue (eg, Limaye and Novak et al20 for a review).

Non-adherence to public health recommendations, such as regularly applying sunscreen, which protects from UV radiation as a known carcinogen22–23 or using fluoride-based dental products which protects from caries24 has been extensively studied. Vaccine hesitancy leads to dire public health consequences: outbreaks of infectious diseases such as measles and pertussis25 and, recently, the spread of COVID-19.26 Moreover, recent studies regarding non-adherence to COVID-19 preventive guidelines (eg, face-mask wearing and social distancing) indicated that non-adherence behaviours are mutually related, that is, that individuals who chose not to adhere to the preventive recommendation disregarded all of them rather than adhering to some and not to others.27–28

Reasons for non-adherence to medical recommendations

Factors leading to non-adherence can be divided into several broad categories. WHO suggests five: patient-related, social/economic, condition-related, therapy-related and health-system related.1 Given that our study focuses on the general population and on non-disease-specific behaviour, we investigate patient-related, social/economic and health-system-related factors as potential predictors. Empirical research suggests that healthcare system factors shown to be related to adherence include appointment efficacy, treatment duration and its costs.1 Those are likely to improve patients’ experiences with the healthcare system. On the other hand, avoidance/delay in seeking treatment has been related to dislike or distrust in practitioners and general dislike of medical treatment,25 while greater adherence to treatment is related to clinicians who provide clear information, emotional support and empathy, and treat patients as partners in the process.30–31 Despite the benefits of such a model of physician–patient partnership, within some contexts (especially non-Western Educated Industrialised Rich and Democratic, that is, non-WERID), adherence is positively related to obedience and treatment satisfaction.32–33 This suggests that, in certain contexts, patients’ passivity is normalised or even expected, thus making the relation with adherence less clear. Furthermore, adherence is consistently related to patients’ trust in the healthcare system and healthcare providers: trusting patients are more likely to adhere to treatment and follow public health recommendations (see Chandra et al34 for a review).

Patient-related factors can comprise a wide range of constructs, including psychological ones. Some studies looking at disease-specific adherence have suggested the role of personality traits and mental health (eg,35–37). The focus has also been on illness and medication-related beliefs.38 However, even though psychological factors are sometimes taken into account (see systematic reviews45, their scope is limited and does not consider the accumulating evidence that different types of irrational beliefs predict specific health behaviours. There is evidence that believers in ‘Big Pharma’ or ‘population control’ conspiracy theories go to fewer health and dental check-ups and are reluctant to use sunscreen.39 During the COVID-19 pandemic, adherence to public health recommendations and, especially, vaccine hesitancy have been repeatedly tied to conspiratorial thinking (see van Mulukom et al40 for a review). Superstition was also shown to be positively related to the use of complementary medicines,41–42 but its relationship with non-adherence has not yet been investigated. Such an ‘irrational mindset’—a set of epistemologically unfounded beliefs, can lead patients...
to deviate from scientifically based practices and thus be predictive of non-adherence to medical and public health guidelines in the general population.43-45

**Study objectives**

The first goal of the current study was to develop a novel instrument measuring iNAR behaviour to medical recommendations and explore its factorial structure and reliability. This instrument encompassed a broader range of non-adherence behaviours than the existing adherence scales typically address, such as: (1) not adhering to treatment directly recommended by a healthcare provider, such as terminating therapy early or changing the dosage of a prescribed therapy; (2) self-medication; (3) avoiding to seek medical help and (4) not adhering to public health advice, such as refusing child vaccination or not following preventive public health guidelines, in a general population. Our goal was to investigate whether these different types of non-adherence form a homogeneous category of behaviours. The behaviours were selected to reflect iNAR, but excluded non-adherence encompassing lifestyle-related habit-like behaviours that are also a result of psychological factors (eg, personality traits such as conscientiousness) but are not necessarily intentional, such as smoking, sedentary lifestyle and unhealthy diet.38 47 48 To confirm the latter distinction, we examined whether iNAR captured by the instrument is different when compared with a representative of such behaviour—smoking, that is, whether these two types of behaviours have different precursors.

The second goal of the current study was to relate iNAR to irrational beliefs such as conspiracy theories and superstition as patient-related factors, as well as to healthcare system and provider-related factors. Drawing from previous research, we preregistered the following hypotheses: people who are more prone to conspiracy theorising (H1),39 44 49 with less trust in the healthcare system (H2a) and less trust in healthcare professionals, that is, interpersonal trust (H2b) and less prone to normalise patient passivity (H3) will more frequently engage in non-adherence behaviours—this part of the analysis was exploratory.

**METHODS**

The design and confirmatory analyses plan were preregistered and uploaded on OSF: https://osf.io/pnugm. We deviated from the preregistration on only two minor points that are outlined in a separate document https://osf.io/bfmqn).

**Development of the INAR Questionnaire**

To compile a comprehensive initial pool of non-adherence behaviours, we obtained input from medical experts and searched the relevant literature.

**Input from medical experts**

In April 2022, we conducted a focus group with seven medical doctors with expertise in psychiatry, neurology, pulmonology, public health, gynaecology, epidemiology and forensics. We aimed to represent various specialties, in particular clinicians (ie, doctors who communicate directly with patients in their practice). The focus group was conducted by two members of the research team, the moderator being a trained clinician. A semistructured interview guide that defined general themes and prompt questions, but also allowed for a spontaneous flow of the conversation was used. The group was convened online (due to the restrictions imposed by the pandemic) and the conversation lasted for approximately 3 hours. The contents of the conversation were then transcribed (by three team members) and analysed by systematising the answers to the interview guide questions. Most importantly for the present study, we focused on when and why patients fail to adhere to the prescribed treatment. Specifically, participants described instances in which their patients either failed to follow or directly violated their recommendations. For instance, they mentioned non-adherence to the prescribed medications, taking self-prescribed medications or self-initiated modification of the prescribed treatment (eg, stopping the use of medication when a patient starts feeling better, modifying the dosage or deciding which medicine one needs), as well as some public health recommendations such as refusing mandatory vaccination for children. These behaviours constituted the basis for our instrument. A detailed report on focus group results is available in Serbian at https://osf.io/8hf5y/.

**Literature search**

We conducted a literature search using the following keywords: health behaviors, questionable health behaviors, unhealthy behaviors, medical adherence, medical compliance, non-adherence, non-compliance, instrument, assessment, measurement, to inform inclusion of any additional behaviors that were not mentioned by the experts. We observed that previous studies either focused on single behaviours or, less often, attempted to encompass a wide range of very different behaviours that might, in our opinion, be rooted in different factors/reasons.32-34 That is why, among these, we sought to capture only behaviours where patients intentionally decided not to follow a recommendation or to avoid/delay seeking treatment, rather than due to unintentional reasons such as demographics, forgetfulness, complexity of regimens or patient–provider relationships.49 Following this logic, we did not include unhealthy behaviours such as not eating recommended servings of fruits and vegetables or not getting enough exercise or
sleep (eg, Breslow and Enstrom and von Bothmer and Fridlund[35,56]).

Revision of the initial list of items
Eight members of the research team rated an initial list of 73 items extracted from previous studies or suggested by the medical doctors in the focus group, according to whether they reflected iNAR, as we previously defined it. The items that were rated favourably by at least five raters were added to the preliminary expert list. Any inconsistencies in ratings were discussed with the whole team until consensus was reached for the final list.

Face and content validity assessment
The final version of the non-adherence behaviours list was sent to a public health expert (a lecturer of university-level public health courses at the Faculty of Medicine with a PhD in public health) for comments and suggestions. The expert judged the item content as adequate and suggested slight changes in wording. The final list had 22 items, with the following response options: It has never happened to me, It has happened to me more than a year ago/ in the past year/the past 2 weeks (see https://osf.io/yzr8j).

Participants and procedures
We calculated that a sample size of 300 respondents enables performing factor analyses on the data, according to the rule of thumb of 3–20:1 participant-to-variable ratio. In addition, it enabled us to detect at least one incidence of rare events with 1% frequency, with a power of 95% and alpha=0.05. A sample size of n=475, however, enables the detection of at least two incidences of events with 1% frequency with a power of 95% and alpha=0.05.

Data were collected online, from July to August 2022, using the snowball method and social networks. To increase the representativeness of the sample, we targeted different population categories as seeds (participants of different gender, age and education). The recruited participants were asked to disseminate the call for the study to their friends and professional contacts. Respondents were not compensated for their participation. To be included in the sample, participants had to be over 18 years of age and have residence in Serbia.

As per preregistration, data collection was terminated when we reached both mandatory conditions: (1) the sample size was at least 475, and (2) there were no new entries in the database for five consecutive days. This left us with the initial sample of n=646. We included three attention checks to screen out inattentive respondents (eg, ‘To show you are paying attention, select the response it has happened to me in the past year’). After we excluded participants who failed one or more out of three attention checks, 583 participants remained. There were no other exclusions. The mean age of the final sample was 39.01 years (SD=12.10; age range: 18–79), 74.4% female. Average education duration was 17.11 years (SD=2.66). The socioeconomic status (SES) of the participants ranged from 1 (we struggle to cover basic food expenses on a monthly basis) to 6 (money is never an issue in our household); the mean was 4.06 (SD=0.86). About one-third (29%) of the respondents reported having one chronic medical condition, 9.8% reported two, and 3.3% three and more, with an average of 0.61 chronic conditions per respondent.

Patient and public involvement
The patients were not involved in the design of the study. However, we reached out to the two largest patient associations in Serbia at the very beginning, and their representatives attended the stakeholder meetings at later stages. The report from the focus groups was distributed to their participants, and their feedback was solicited. The manuscript based on the main study was publicly posted. Lay summaries from both focus groups and the main study were disseminated via media and social networks.

Instruments/variables
All instruments are available at https://osf.io/w4s8w/. Internal consistencies of all multi-item instruments are provided in the Results section.

iNAR Questionnaire comprised 22 behaviours (eg, did not take prescribed therapy, avoided going to a medical check-up, self-medicated with antibiotics, etc). For each behaviour, participants reported whether it has happened to them and when. Four items included a conditional logic: only women were asked about attending gynaecological check-ups, participants who indicated having children were asked two items regarding child vaccination and participants with chronic health conditions were asked about non-adhering to their therapy. The total score is calculated by averaging all items.

COVID-19-specific behaviours were assessed with two items14, (1) the number of doses of any vaccine against COVID-19 (none to four) and (2) adhering to COVID-19 guidelines (eg, keeping a physical distance, wearing masks, maintaining hand hygiene) (1 Not at all to 5 Completely).

Health status was assessed via a self-reported evaluation of health on a five-point Likert scale (1 Very poor to 5 Very good) and presence of any chronic disease/condition using a checklist (eg, cardiovascular, neurological, gastrointestinal).

Body mass index (BMI) was calculated using participants’ self-reported height (in cm) and weight (in kg).

Smoking was measured as the number of cigarettes smoked per day.

Trust in the healthcare system and healthcare professionals was assessed with a total of four items with the highest loadings on the Generalised (mis)trust in the healthcare system, and Particularised (interpersonal) trust in healthcare professionals factors from the Women’s trust and confidence in Healthcare System — WITCH scale, two items from each subscale (1 Completely disagree to 5 - Completely agree).

Normalisation of patient passivity contains two items with high loadings, appropriate for the general
population, adapted from the Passivity Normalisation During Childbirth scale.\textsuperscript{51} The items are rated on a five-point scale (1 \textit{Completely disagree} to 5 - \textit{Completely agree}).

Experiences with the official healthcare system were assessed using a nine-item measure assessing the frequency of positive (four items) and negative experiences (five items) with the healthcare system (1 \textit{Never} to 5 - \textit{Every time}).\textsuperscript{51}

Belief in generic conspiracy theories was assessed using the Conspiracy Mentality Questionnaire (CMQ\textsuperscript{58}, Serbian version by Lukić \textit{et al.}\textsuperscript{60}) consisting of five items (eg, \textit{Many important things happen in the world, which the public is never informed about}) rated on a five-point scale (1 \textit{Completely disagree} to 5 - \textit{Completely agree}).

Superstition was assessed via five items of the Superstition scale (eg, \textit{I would never show on my own body where someone else got injured}) with the highest loadings on the general factor as reported in the original paper.\textsuperscript{60} The items are rated on a five-point scale (1 \textit{Completely disagree} to 5 - \textit{Completely agree}).

Sociodemographic variables included gender, age, number of years of education and SES.

Data transformations
Prior to analysing the data, we binarised all iNAR items to obtain information on whether or not participants have ever exhibited the behaviour. These binarised items were subsequently used in the factor analysis as well as for calculating the overall iNAR score. The number of COVID-19 vaccine doses was also binarised into ‘vaccinated’ and ‘not vaccinated’, as was the ‘presence/absence of chronic disease/condition’ based on participants’ responses on the corresponding checklist item. The number of smoked cigarettes was winsorised so that values higher than 20 were replaced with 20 smoked cigarettes a day. All transformations and analyses were performed using R statistical software (R-V.4.2.0\textsuperscript{63}).

RESULTS

Missing data
There were no missing data for the iNAR items while some participants did not finish the questionnaire, dropping out at different stages. The minimal number of participants for either of the variables was n=524. Correlations between variables were calculated using the maximum available information for each correlation that is, pairwise deletion. All regression analyses models were tested on a subsample with no missing data on either of the variables, that is, listwise deletion, resulting in n=524.

Factorial validity and reliability assessment of iNAR
The most prevalent iNAR behaviours in our sample were not applying sunscreen when exposed to sun/UV rays, reluctance to visit a healthcare professional despite the presence of symptoms and skipping regular medical check-ups (table 1). In contrast, the least prevalent iNAR behaviours were refusing child vaccination and taking high blood pressure medication without a prescription, both observed in less than 5\% of participants. Postponing child vaccination and avoiding dental filling were among the least prevalent iNAR behaviours as well.

Factorial structure
To explore the factorial structure of iNAR, we first performed an initial single-factor exploratory factor analysis on the tetrachoric correlation matrix for the full set of 22 behaviours (table 1). We excluded items referring to child vaccination (Items 4 and 5), due to their poor factor loadings, low correlations with all other items and low frequency. The Scree plot for the remaining 20 items suggested either a one-factor or a three-factor solution with an approximately equal number of items per factor (table 1). In either of these solutions, items regarding use of sunscreen and avoiding fluoride toothpaste (Items 6 and 7) had poor loadings showing that they are poor indicators of both general, as well as any specific manifestation of iNAR, so we excluded them as well. The three-factor solution, however, led to overall poorer factor reliability (Gronbach’s alpha from 0.45 to 0.62 for the best 3–4 items per factor and .62 for the total score). Additionally, items with the highest loadings on the respective factors had significant content overlap that could artificially inflate their correlations, so we opted for a single-factor solution.

Further shortening of the scale
For the final version of the instrument, we decided to exclude or merge some of the items based on either their prevalence, factor loadings or their conceptual and/or empirical (indicated by intercorrelations) overlap. We merged items referring to skipping regular check-ups by different specialists (Items 1 and 3); not taking prescribed therapy for chronic or acute conditions (Items 15 and 16), and taking high blood pressure or other medication without prescription (Items 11 and 13). We also excluded Item 22 (avoiding dental filling) which had low frequency as well as a low loading on the main factor. The lowest loading items of the remaining 14 behaviours were two items regarding self-medication (antibiotics and anxiotytics) as well as two items regarding check-ups (Items 2 and merged Items 1 and 3). We kept self-medication items due to their practical importance but excluded check-up attendance items. Factor loadings for the final 12-item version of the iNAR Questionnaire (see https://osf.io/6rjtj9) were all higher than 0.35 (see table 1).

Reliability assessment
This final set of 12 behaviours showed good internal consistency as indicated by both alpha (\(\alpha=0.72\)) as well as the omega coefficient (\(\omega=0.73\)). It was also highly correlated with the initial item set (\(r=0.92\)), showing that the reduction in the number of iNAR behaviours was warranted.
Descriptive statistics and intercorrelations for all variables

As Table 2 shows, almost all scales showed good reliability. Since all distributions significantly deviated from the normal distribution, we opted for Spearman correlations, as per preregistration.
iNAR behaviours were most strongly related to negative experiences with the healthcare system and to self-reported health status. In line with our hypothesis (H2), iNAR was also significantly related to trust in the healthcare system—positively to mistrust to the system as a whole (H2a), and negatively to trust in healthcare professionals (H2b), as well as to the normalisation of patient passivity (H3). We also observed a significant correlation between iNAR and the presence of chronic disease and smoking, as well as lower adherence to COVID-19 guidelines. Finally, iNAR showed weak, but significant correlations with conspiracy mentality, in line with our prediction (H1), as well as with superstition.

Contrasting predictors of iNAR and smoking behaviour

To test whether iNAR behaviours have different predictors compared with other psychologically determined non-adherence behaviours, we ran two hierarchical regressions with iNAR and smoking as outcomes. In the first step, we included sociodemographics (gender, age, education and SES) as predictors, followed by health condition variables (self-reported health status, BMI and presence of chronic disease) in the second step. Next, we included variables concerning healthcare-related beliefs and experience, such as general and interpersonal (mis)trust in the healthcare system, normalisation of patient passivity and negative experiences with the medical system. Finally, we added variables assessing an irrational mindset (conspiracy mentality and superstition).

With iNAR as the outcome variable, sociodemographics did not contribute to the prediction, but the model was significant in the second step, accounting for 8% of the variance (table 3). In the third step, healthcare-related beliefs and experiences contributed significantly over and above the other predictors, accounting for an additional 6% of the variance. Finally, the irrational mindset did not add to the prediction when controlling for the other predictors in the fourth step. The model, in total, explained 14% of the variance of smoking, with only education contributing significantly to prediction. Additionally, superstition marginally contributed in the expected direction.

DISCUSSION

In the present study, we developed a novel measure of iNAR to medical recommendations, thus accomplishing our first goal. The final version of the instrument consisting of 12 behaviours, demonstrated good factorial validity and reliability and correlated strongly with the
## Table 3  Hierarchical regressions with iNAR-12 and smoking as outcomes

<table>
<thead>
<tr>
<th>Block 1</th>
<th>iNAR-12</th>
<th>Smoking</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$b$ (95% LLCI, ULCI)</td>
<td>$\beta$ (95% LLCI, ULCI)</td>
</tr>
<tr>
<td>Intercept</td>
<td>0.50 (0.20, 0.81)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender</td>
<td>0.00 (0.00, 0.00)</td>
<td>0.00 (0.09, 0.09)</td>
</tr>
<tr>
<td>Age</td>
<td>0.00 (0.00, 0.00)</td>
<td>-0.03 (0.12, 0.06)</td>
</tr>
<tr>
<td>Education</td>
<td>0.00 (0.00, 0.00)</td>
<td>-0.05 (0.14, 0.03)</td>
</tr>
<tr>
<td>SES</td>
<td>0.01 (0.02, 0.03)</td>
<td>0.02 (0.06, 0.11)</td>
</tr>
<tr>
<td>$F$ (df)</td>
<td>0.781 (4, 519)</td>
<td></td>
</tr>
<tr>
<td>$\Delta R^2_{adj}$</td>
<td>-0.002</td>
<td>0.018</td>
</tr>
</tbody>
</table>

| Block 2 | | |
|---------|---------|---------|---------|
| Health self-evaluation | -0.05 (0.08, 0.03) | -0.17 (0.26, 0.09) | <0.001 | -0.66 (1.45, 0.13) | -0.08 (0.17, 0.01) | 0.195 |
| Chronic disease | 0.05 (0.01, 0.09) | 0.11 (0.02, 0.19) | 0.020 | -0.08 (1.30, 1.14) | -0.01 (0.10, 0.09) | 0.802 |
| BMI | 0.00 (0.00, 0.01) | 0.03 (0.06, 0.12) | 0.497 | -0.08 (0.22, 0.07) | -0.05 (0.14, 0.05) | 0.395 |
| $F$ (df) | 16.018 (3, 516)** | 1.166 (3, 516) | | |
| $\Delta R^2_{adj}$ | 0.080 | 0.001 |

| Block 3 | | |
|---------|---------|---------|---------|
| General mistrust | 0.00 (0.03, 0.02) | -0.01 (0.11, 0.09) | 0.849 | 0.54 (0.19, 1.28) | 0.08 (0.03, 0.18) | 0.241 |
| Interpersonal trust | 0.00 (0.03, 0.03) | 0.00 (0.10, 0.11) | 0.983 | -0.14 (0.93, 0.64) | -0.02 (0.13, 0.09) | 0.846 |
| Normalisation of patient passivity | -0.03 (0.05, 0.00) | -0.10 (0.19, 0.01) | 0.034 | -0.5 (1.22, 0.21) | -0.07 (0.16, 0.03) | 0.181 |
| Negative experiences | 0.08 (0.05, 0.11) | 0.25 (0.15, 0.35) | <0.001 | 0.23 (0.70, 1.17) | 0.03 (0.08, 0.13) | 0.601 |
| $F$ (df) | 9.692 (4, 512)** | 2.187 (4, 512) | | |
| $\Delta R^2_{adj}$ | 0.058 | 0.009 |

| Block 4 | | |
|---------|---------|---------|---------|
| Conspiracy mentality | 0.00 (0.02, 0.03) | 0.01 (0.08, 0.10) | 0.866 | 0.44 (0.33, 1.21) | 0.06 (0.04, 0.15) | 0.266 |
| Superstition | 0.02 (0.00, 0.05) | 0.08 (0.00, 0.17) | 0.056 | -0.37 (1.08, 0.35) | -0.05 (0.14, 0.04) | 0.313 |
| $F$ (df) | 1.985 (2, 510) | 0.945 (2, 510) | | |
| $\Delta R^2_{adj}$ | 0.003 | -0.001 |
| $R^2_{adj}$ | 0.140 | 0.028 |

The reported $F$ statistics are from the ANOVAs comparing the two steps. For all steps of the hierarchical regression models, see online supplemental table 2.

*p<0.05, **p<0.01, ***p<0.001.

BMI, body mass index; iNAR, intentional non-adherence; SES, socioeconomic status.
total score from the initial item pool, indicating practically no loss of information after the abridgement.

Importantly, a single common latent dimension was found to underlie a diverse set of non-adhering behaviours, suggesting that adherence is a unitary construct, broader than medication-taking behaviour. Namely, self-medication, changing or adapting the prescribed therapy without or contrary to medical advice, ignoring symptoms and postponing seeking treatment proved to form a relatively homogeneous category of behaviours reflecting the same general tendency to disregard official medical recommendations.

Non-adherence to public health and other health recommendations, such as avoiding using sunscreen or toothpaste with fluoride, rejecting tooth filling, refusing or postponing a child’s vaccination proved not to be a part of the same construct as the rest of the iNAR behaviours. There was also virtually no correlation between iNAR and vaccination against COVID-19 and only a weak negative correlation with following guidelines to protect against COVID-19. Taken together, our results suggest that these types of non-adherence behaviours have somewhat different precursors.

iNAR behaviours were more strongly negatively related to both self-reported health status and the presence of chronic diseases. It is possible that participants with more health issues have had more opportunities to disregard health recommendations than people who are generally healthy. Likewise, it may be that iNAR behaviours contributed to negative health outcomes.

**Relationship between iNAR, irrational beliefs and experiences with the healthcare system**

As for our second goal, iNAR correlated only modestly with conspiracy mentality and superstition, while there was no relationship between iNAR and COVID-19 vaccination, which has previously been strongly related to a conspiratorial worldview. This suggests that the reasons for iNAR to medical recommendations do not primarily stem from core irrational beliefs, but from other individual or contextual factors.

In our study, the irrational mindset did not significantly improve the prediction of non-adherence when other predictors were accounted for. This might be because, in our study we have used general conspiracy beliefs rather than medical conspiracy beliefs which have previously been found to be related to some health behaviours. Perhaps more specific medical conspiracy beliefs would have had stronger relations with non-adherence behaviours. It is important to note that, while our findings clearly suggest that other factors such as experiences with the healthcare system are of critical importance for non-adherence, we did observe zero-order correlations between iNAR and both conspiracy mentality and superstition. Superstition remained a marginally significant predictor when other predictors were controlled for, indicating a role, although small, of an irrational mindset in iNAR. Another reason why we did not observe a more substantial role of irrational mindset, might be that iNAR could be rational under certain circumstances, such as stopping use after experiencing side-effects or due to inability to cover treatment expenses.

iNAR behaviours were consistently rooted in negative healthcare-related beliefs and experiences. Negative correlations of iNAR behaviours with trust in the healthcare system and trust in healthcare practitioners are in line with previous findings that individuals with higher trust are more prone to follow medical recommendations (see Birkhäuser et al. for a review). Further, a negative correlation between the normalisation of patients’ passivity and iNAR indicates that the individuals who are more likely to hand over decision-making to their physicians are less prone to iNAR behaviours. When it comes to the predictive power of this set of beliefs and experiences, only negative experiences and, to a lesser extent, normalisation of patients’ passivity contributed to the explanation of iNAR behaviours. This supports previous findings that patients who experienced poor communication with their physicians are less likely to adhere to therapy. It also suggests that giving up personal control over the treatment contributes to higher adherence to the therapy, which was found to be the case in healthcare systems in developing countries. It is possible that an unequal relationship between the patient and the medical professional benefits patients who are more submissive in a relation to their physicians, but repels patients who value autonomy and agency, who may thus refuse the medical recommendation they are given. Striving for shared decision-making about the treatment would likely benefit both types of patients in improving their health outcomes.

The lack of additional predictive power of trust in the healthcare system and professionals might have occurred due to their relatively high correlations with experiences with the healthcare system. Although the literature proposes that trust is one of the key determinants of (non)adherence to the prescribed treatment, it also documents a relatively high overlap between trust and previous experiences (eg, Keating et al.), similarly to the pattern we observed.

Importantly, iNAR behaviours were shown to be distinct from an unhealthy habit-like non-adhering behaviour, that is, smoking, as demonstrated by a weak relationship between the two. In addition, our novel iNAR measure and smoking were predicted by entirely different sets of variables. For instance, while educational level correlated negatively with smoking, consistently with previous internationally and locally relevant findings, we did not observe any sociodemographic differences in iNAR. It seems that system-related, rather than patient-related predictors are important for this type of behaviour: non-adherence is mainly rooted in negative experiences and distrust of the medical system.
Limitations and future research
While we found meaningful relations between iNAR on one side, and health status, healthcare-related beliefs and experiences, and irrational beliefs on the other, the correlations were only weak to moderate. One reason might be that in order to obtain the clinically most relevant measure, we focused on behaviours instead of, for example, attitudes or intentions. The variability of behaviours is, on the other hand, dependent on a myriad of internal and external factors such as opportunity and available resources. To confirm the validity of the iNAR instrument, future studies should examine its relationship with other adherence scales.

Despite their brevity, almost all of our measures showed adequate reliability, except for the Normalisation of Patient Passivity scale. Since this scale was adapted from the longer Passivity Normalisation During Childbirth scale, this might have affected its reliability. Future studies should thus aim to replicate the finding on its relation with iNAR using scales that are longer and developed to measure generalised normalisation of patient passivity.

As for the scale format, we opted to exclude the ‘non-applicable’ option in our iNAR scale, which could have led to us capturing ‘accidental’ adherence—participants who had no opportunity to adhere were clumped together with those who always adhered to recommendations. We excluded this option since we assumed that most people were at some point in their life in a situation where adherence was required and that those who had no opportunity to adhere (eg, take medication or visit a dentist) were very rare.

Since we used only smoking as a representative of other psychologically determined non-adherence behaviours, future studies could include a more comprehensive set (eg, sedentary behaviour, unhealthy diet) to better disentangle the differences between these two types of non-adherence. In addition, although patient-related factors examined here did not prove central for predicting iNAR, these behaviours might be rooted more deeply; personality traits, such as conscientiousness and agreeableness, could also be tested as predictors. Future research could also test the predictive power of medical or digital literacy.

Even though the snowball sampling procedure led to decreased representativeness and sampling bias, we still had a large and relatively diverse sample. As we aimed to develop a novel measure of iNAR (ie, we primarily focused on psychometric properties and its relationships with the irrational mindset and experiences with the healthcare system), and not to explore the prevalence of these behaviours in the population, a convenience sample was optimal for this stage of research. Moreover, while some studies did find gender and age group differences in medical non-adherence (eg, Mahmoudi et al and Thunander Sundbom and Bingeford), our data show no correlation between iNAR and either of the sociodemographic variables. Based on this, we should expect to replicate the structure and predictors of iNAR on a sample representative of Serbia. Nevertheless, to gain further insights into the prevalence of iNAR, future studies should use probability samples and test the effects cross-culturally.

Implications
The results of the current study suggest that interventions need to focus on establishing trust in the healthcare system, the medical profession and prescribed therapies. Implementing systemic changes in healthcare to support patients and build trust is a long-term process; broken trust is difficult to repair. Although our results indicated that passive patients are less likely to engage in iNAR, we would not suggest fostering further passivisation. Instead, we would focus on improving patients’ experiences with the system and their healthcare providers: non-adhering patients reported mistrust in the healthcare system and repeated negative experiences, which proved to be more important than positive ones. This may seem self-evident, but our study demonstrated that such negative experiences are by far the strongest predictor of iNAR, outperforming those proven relevant to other types of questionable health behaviours: for example, sociodemographic for smoking, or irrational beliefs for the use of traditional, complementary medicine.

CONCLUSIONS
The novel inventory measuring iNAR to official medical recommendations—iNAR-12—demonstrated good internal consistency, a clear factorial structure and meaningful correlations with relevant constructs. We show that various behaviours, including non-adherence to treatment, self-medication and avoiding seeking medical advice from a homogenous construct, while non-adherence to public health recommendations did not constitute its part. Importantly, iNAR proved to be clearly differentiated from smoking. As a brief assessment tool, iNAR-12 can be particularly useful in large, for example, epidemiological studies. It can also be informative when proposing interventions aimed to improve adherence, given that our results strongly suggest that iNAR to recommendations is primarily related to malleable factors in patients’ interactions with the healthcare system.

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11
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