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Patient use, understanding, and behaviour toward patient information leaflets for medicines: a cross-sectional study of adults in Italy

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Abstract

Background Patient information leaflets (PILs) for medicines are legally required across the European Union to support safe medicine use, informed decision-making, and treatment adherence. However, they are often criticised for complexity, poor readability, and anxiety-inducing descriptions of side effects. Health literacy (HL), the ability to access, understand, appraise, and apply health information, may affect how patients engage with PILs. Italy has a high prevalence of limited HL, yet population-based evidence on its influence remains scarce. This study examined patterns of PIL use, comprehension, and related behaviours in the Italian adult population, accounting for HL differences.

Methods A cross-sectional survey was conducted between October 2024 and April 2025 among 1,977 adults (mean age 46.5 years; 63% women). Recruitment combined social media dissemination with general practitioner collaboration to reach older and less digitally active individuals. The questionnaire collected sociodemographic data, HL (using the six-item HLS-EU-Q6 and a single-item functional HL screener), and indicators of PIL engagement, including reading frequency, reasons for non-consultation, comprehension of extracts, anxiety, therapy discontinuation, risk interpretation, and perceptions of commercial influence. Data were analysed using descriptive and inferential statistics.

Results 66% of respondents reported always reading PILs for prescription medicines, and 71% did so for over-the-counter products. Overall, 17.2% had inadequate HL, 52.4% problematic, and 30.4% sufficient. Among sociodemographic variables, only education differed by HL level (2.09 vs. 2.02; $p = 0.04$). Higher HL was associated with more frequent PIL reading, greater confidence in medicine use (mean 2.22 vs. 1.94; $p < 0.001$), and lower anxiety (2.21 vs. 1.97; $p < 0.001$). In contrast, respondents with lower HL more often discontinued therapies after reading PILs (37% vs. 28%; $p = 0.02$) and overestimated vaccine risks compared with analgesics (25% vs. 9%). Perceiving PILs as commercially influenced was also more common among those with limited HL ($p < 0.001$).

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Conclusions HL significantly shapes how Italian adults use and interpret PILs, influencing engagement, confidence, anxiety, and therapy behaviours. Current formats may inadvertently widen inequalities by overburdening readers with limited HL. Public health efforts should prioritise simplification, plain language, balanced risk communication, and perceptions of neutrality to promote equitable and safe medicine use.

Keywords Patient information leaflets, Package leaflets, Drug inserts, Health literacy, Risk communication, Public health

Text box 1. Contribution to the literature

- This study provides the first national evidence on how Italian adults read, understand, and react to patient information leaflets (PILs) for medicines.
- It suggests that people with lower health literacy feel more anxious, trust PILs less, and are more likely to stop treatment after reading them.
- The findings reveal that current PIL formats may unintentionally worsen health inequalities by being too complex.
- The study highlights the need for clearer, simpler, and more trustworthy PILs to support safe and confident medicine use.
- It offers practical insights for public health communication and medicine regulation in Europe.

Background

Patient information leaflets (PILs) for medicines constitute a legally required component of all medicines authorised for marketing in the European Union. They are intended to provide patients with accurate, accessible, and non-promotional information on the safe and effective use of medications [1], including the drug's intended use, instructions for administration, contraindications, and potential adverse effects [2]. Within this regulatory framework, PILs are expected to support more autonomous and safer medicine-taking by helping patients understand how to use a prescribed drug correctly and recognise potential risks. However, they do not, in their current design, provide the balanced, comparative information on benefits and harms across all available options that would be required for fully informed treatment decisions, and the way adverse reactions are presented may even foster overestimation of risk [3].

Over the last two decades, various studies have demonstrated that PILs can improve short-term patient recall and satisfaction, particularly when used as a supplement to professional counselling [4, 5]. However, the mere presence of a PIL does not guarantee its effective use, and significant proportions of patients either avoid reading the PIL or report difficulties in understanding its content [5]. A growing body of international research indicates that many PILs can be linguistically inaccessible to patients, particularly those with lower education or limited health literacy [5–8]. Numerous studies have found that the readability of PILs remains well above recommended levels [2]. The European Commission's guidelines advise that PILs should be comprehensible to the general public [1] and undergo user testing [9, 10], but independent evaluations consistently report that most PILs exceed the acceptable threshold of readability (typically aligned with the 6th to 8th grade reading level) [9, 10, 11–13]. Likewise, evaluations of PILs for chronic conditions, such as hypertension or diabetes, revealed that the vast majority scored poorly on user-focused design metrics and required advanced reading skills [12].

In addition to structural and linguistic complexity, other known barriers to effective PIL use include small font size, information overload, rigid formatting, lack of plain language, and failure to differentiate between critical and ancillary information, all of which reduce patient engagement and contribute to misinterpretation of vital instructions [13, 14]. More recently, attention has shifted towards the emotional and psychological effects of PIL content, particularly regarding the communication of risks. Research suggests that how side effects are described in PILs, whether qualitatively or quantitatively, can significantly affect a patient's perception of danger, trust in the medication, and willingness to adhere to treatment [15]. In many cases, lengthy and detailed descriptions of rare but severe side effects lead to confusion or alarm, triggering disproportionate levels of anxiety [16]. This phenomenon has been linked to the so-called nocebo effect, in which patients experience adverse symptoms or discontinue treatment due to negative expectations generated by reading risk-related information, potentially leading to therapy interruption [17, 18].

The regulatory use of verbal probability descriptors (e.g. "common", "rare", "very rare") has also been shown to increase risk perception, particularly in patients with low numeracy or health literacy [19, 20]. In the UK, a study by Webster et al. found that patients greatly overestimated the likelihood of side effects based on these labels, especially for symptoms described as "common" [21]. The misinterpretation of such language not only distorts patients' understanding of drug safety but may also reduce adherence and fuel unnecessary consultations with healthcare providers.

These challenges are particularly relevant in populations with limited health literacy. Defined as the ability to access, understand, appraise, and apply health information, health literacy (HL) is increasingly recognised as a social determinant of health and a critical predictor of health outcomes [22]. The European Health Literacy

Survey (HLS-EU) revealed that almost 47% of the population across eight EU countries had either inadequate or problematic HL, with significant disparities by age, education, and socioeconomic status [23]. Italy, in particular, has been identified as having a high prevalence of low HL: in a multicentre study involving over 8,000 participants, Palumbo et al. found that only 28% of Italians exhibited sufficient HL, with older adults and individuals with lower education being most at risk [24]. This has important implications for medicine use, as patients with low HL may be less likely to engage with written drug information, more prone to misunderstand instructions, and more likely to experience medication errors [25].

Despite growing international interest in this topic, Italy has lacked large-scale, empirical research on how patients engage with PILs and how this engagement is influenced by HL or sociodemographic characteristics. Existing Italian studies have primarily focused on qualitative or quantitative linguistic aspects of PILs [26–29], while behavioral and emotional outcomes related to their use remain largely unexplored. No population-based study has yet investigated how HL, operationalised via a validated instrument such as the HLS-EU-Q6, relates to patients' reading habits, comprehension of PILs, emotional responses to risk information, or treatment behaviours such as medication avoidance. This represents a significant research gap with both clinical and public health implications, particularly in a country with a large elderly population, regional disparities in healthcare access, and well-documented challenges in health communication [30].

To address this gap, we conducted a national cross-sectional survey of Italian adults to examine how they use, understand, and perceive PILs, and to characterise the distribution of HL and its relationship with these outcomes. Specifically, the analysis considered PIL reading habits, reasons for non-consultation, perceived comprehension, emotional reactions (such as anxiety), and behavioural outcomes (including therapy discontinuation) across HL levels and key sociodemographic subgroups. It also explored how HL shapes the interpretation of risk information and trust in the neutrality of PIL content. By addressing these dimensions, the study provides the first national-level evidence on how Italians interact with PILs and offers actionable insights for tailoring public health communication to improve comprehension of written medicine information and support safe medication use across diverse patient populations.

Methods

This cross-sectional study was conducted among adults in Italy between October 26, 2024, and April 30, 2025, using the LimeSurvey platform [31] for anonymous data collection. The study is reported in accordance with the checklist for reporting results of internet e-surveys (CHERRIES) [32], and the completed checklist is provided in the supplementary materials (SM1). Because the survey was voluntary and distributed online, it was not possible to precisely define the target population or calculate a formal response rate. Nevertheless, the study design followed standard recommendations for surveys estimating proportions. A large sample size was intentionally targeted in order to improve the precision and stability of the estimates. Specifically, a predefined goal of at least 1,000 completed questionnaires was established prior to data collection, in order to ensure sufficient precision of the estimates [33]. Eligibility was restricted to participants aged 18 years or older who fully completed the questionnaire. Participants had the option to withdraw consent at any time prior to submitting responses. The study adhered fully to national and European data protection regulations (D.Lgs 101/2018; EU Regulation 679/2016). Recruitment was based on a snowball sampling approach: the survey was disseminated through social media, personal and professional networks, and with the collaboration of local general practitioners. The involvement of general practitioners was particularly valuable for ensuring also the inclusion of older adults and individuals less accustomed to online platforms, thereby broadening reach to less digitally active adults.

The survey, was designed to capture key demographic and behavioral variables relevant to PILs and HL. It comprised three principal sections:

1) Sociodemographic characteristics:

This section comprised questions on age, gender, region of residence, educational level, occupational status (distinguishing healthcare from non-healthcare professions), self-reported proficiency in the Italian language, and the frequency of medication use.

2) HL assessment:

General HL was assessed using the six-item European Health Literacy Survey Questionnaire (HLS-EU-Q6) [34], which evaluates individuals' perceived ability to access, understand, appraise, and apply health information across multiple domains, and has been validated for use in Italian [35]. The six items respectively ask how easy it is (1) to find information on treatments of illnesses that concern you, (2) to understand what your doctor says, (3) to judge which everyday behaviours are related to your health, (4) to judge when you may need a second opinion from another doctor, (5) to use information from your doctor to make decisions about your illness, and (6) to follow instructions from your doctor or pharmacist. Items 1–2 reflect the health promotion

domain, items 3–4 the disease prevention domain, and items 5–6 the healthcare domain. Each item is scored on a four-point Likert scale (1 = 'very difficult' to 4 = 'very easy'), with higher values indicating greater HL. According to validated thresholds, scores were classified as 'inadequate' (<1.5), 'problematic' (1.5–2.49), or 'sufficient' (≥2.5). Functional health literacy (FHL) in the written domain was assessed with a single item by asking participants how difficult it was to read health information leaflets or brochures. Responses were recorded on a five-point Likert scale (1 = 'very difficult' to 5 = 'very easy'). We considered limited HL a score ≤ 3. For formal statistical evaluation, the HLS-EU-Q6 was employed as the primary continuous measure of HL to leverage its multidimensional properties and validated cut-offs. Spearman correlation analysis between the FHL single item and the overall HLS-EU-Q6 score was performed.

3) Use and perception of PILs:

This section comprised questions addressing: (a) how often participants read the PIL the first time they use a medicine, separately for prescription and over-the-counter medicines, and ranked reasons for non-reading; (b) which standard PIL sections are read most frequently and which are perceived as most difficult; (c) emotional and behavioural responses, including confidence in medicine use after reading the PIL and anxiety elicited by the PIL (both on five-point scales), whether respondents had ever stopped or not started a medicine after reading the PIL, and, where applicable, ranked reasons for discontinuation; (d) a blinded risk-appraisal task based on two authentic, anonymised adverse-reaction excerpts labelled 'Medicine A' and 'Medicine B', taken respectively from the ibuprofen and Comirnaty COVID-19 vaccine PILs, in which participants indicated which medicine they perceived as more risky or selected 'I don't know', with responses coded into three categories for analysis; (e) behavioural intentions in response to a drowsiness warning and an antibiotic safety warning, elicited through choice and ranking questions; and (f) perceptions of medicine risk and commercial influence, including ranking vaccines, painkillers/anti-inflammatory medicines, antibiotics, blood-pressure medicines, and anxiolytics according to perceived seriousness of side effects, and agreement on a five-point scale that information in PILs is influenced by commercial interests.

The full questionnaire, in the original Italian version and the English translation, is provided in supplementary material (SM2). Development of the survey was informed by an extensive review of existing research in HL and health communication. The instrument was piloted with a preliminary group of 10 individuals to evaluate its comprehensibility and suitability, and no major revisions were deemed necessary as a result of this process.

Participation was entirely voluntary and anonymous, and no personally identifiable data were collected. Electronic informed consent was obtained from all respondents prior to survey access. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. In line with the General Authorisation to Process Personal Data for Scientific Research Purposes issued by the Italian Data Protection Authority [36] and the internal regulations of the Ethics Committee for Research involving Humans at the University of Brescia (DR. 863/2025 prot. n. 307740/2025) [37], formal ethics committee approval was not required because the study consisted of anonymous, non-interventional survey research on adult participants and did not collect sensitive personal health information.

Descriptive statistics (means, standard deviations, frequency distributions) were calculated for all variables. The HLS-EU-Q6 score was treated as a continuous variable and further examined within sociodemographic and behavioral subgroups. Between-group comparisons were conducted using independent samples t-tests for continuous variables and chi-square tests for categorical variables, with statistical significance set at $p < 0.05$. After checking for normal distribution using Shapiro-Wilk test, ANOVA analysis test was applied for the comparison of three or more independent mean values. Analyses included stratification by region, gender, education, healthcare background, PIL reading habits, anxiety response, perceived confidence in medicine use, therapy discontinuation, and risk perception. A binary logistic regression model was conducted to predict the likelihood of selecting the correct response "Ibuproben" to the question related to perception of medication risk. The outcome variable was coded as 1 for selection of response "Ibuproben" and 0 for selection of response "Vaccine" or "Don't know". All predictors statistically significant in univariate analysis were entered simultaneously into the model.

The covariates to be included into the final model were selected using a backword selection process, with a univariate $p < 0.05$ as the main criterion. To check for collinearity among variables, the Spearman correlation test was used. The results of logistic regression have been reported with adjusted odds ratios and 95% confidence intervals. A p-value less than 0.05 was considered as statistically significant for all analyses. Considering that internal consistency could be sample-specific, HLS-EU-Q6 was tested for reliability using the Cronbach's alpha with a range between 0.70 and 0.95 considered acceptable [38]. Statistical analyses were performed using Stata [39].

Table 1 Sociodemographic characteristics of adults participating in a national survey on patient information leaflets for medicines in Italy, October 2024–April 2025

Study sample, *n* = 1977 **Mean age: 46.5 ± 14.5; range: 18–98 years.**			
Variable	**Category**	***N***	**(%)**
Gender	Male	730	36.9
	Female	1,237	62.6
	Not specified	10	0.5
Region of residence	Northern Italy	1,219	61.7
	Central Italy	394	19.9
	Southern Italy and Islands	364	18.4
Educational attainment	Secondary education or less	525	26.6
	University degree or higher	1,452	73.4
Healthcare education or employment	No	1,583	80.1
	Yes	394	19.9
Self-reported Italian language proficiency	Low	114	5.8
	Advanced	693	35.1
	Excellent	1,170	59.2

Results

Sample characteristics

A total of 1,977 adults completed the survey (mean age 46.5 years, SD 14.5, range 18–98) and 23 did not give consent to participate. 580 questionnaires were excluded because incomplete. Women represented nearly two-thirds of the sample (62.6%); most respondents resided in Northern Italy (61.7%). The majority (73.4%) reported having a university degree and 19.9% indicated current or past study or employment in the healthcare sector. Self-reported Italian proficiency was predominantly advanced/excellent. Detailed sample characteristics are presented in Table 1.

Medicine use and PIL engagement

As shown in Table 2, overall, with respect to medicine use, about 40% reported taking medicines once per day or more (38.7%). A clear pattern emerged in the reasons for not reading PILs: respondents most often preferred to rely on doctors or pharmacists, whereas lower-ranked positions more frequently reflected structural and trust-related barriers, such as perceived language complexity and lack of trust in PILs. Regarding which sections of the PIL are read, "What the medicine is and what it is used for" most commonly occupied the top rank, while "Contents of the package and other information" was typically ranked last; these same sections also anchored perceived difficulty, with the former more often judged difficult and the latter easiest to understand.

Table 2 Frequency of medicine use and rank-order responses related to engagement with patient information leaflets for medicines among adults in Italy, October 2024–April 2025

Variable	**Category**	***N***	**(%)**
Frequency of medicine use	Less than once per month	664	33.6
	At least once per month	415	21.0
	At least once per week	134	6.8
	At least once per day	494	25.0
	More than once per day	270	13.7
Reason why PIL is not read*			
First	I prefer to ask to the doctor or pharmacist	336	41.8
Second	That's too long	273	34.0
Third	The characters are too small	169	21.0
Fourth	The language is too complex	342	42.5
Fifth	They are not trustworthy	489	60.8
Frequency with which the various sections of the PIL are read*			
First	What the medicine is and what it is used for	1122	56.8
Second	The drug's dosage and method of administration	647	32.7
Third	What I need to know before taking the drug	588	29.7
Fourth	Possible side effects	597	30.2
Fifth	Storage and composition	875	44.3
Sixth	Contents of the package and other information	1137	57.5
Understanding the sections of the PIL: from the most difficult to the least difficult*			
First	What the medicine is and what it is used for	554	28.0
Second	What I need to know before taking the drug	478	24.2
Third	Possible side effects	410	20.7
Fourth	The drug's dosage and method of administration	431	21.8
Fifth	Storage and composition	541	27.4
Sixth	Contents of the package and other information	851	43.1

* For rank-order items, values refer to the option most frequently chosen for each position. Percentages indicate the share of respondents assigning that option to that rank; they are position-specific and not additive

HL scores and distribution

HL, assessed with the HLS-EU-Q6, indicated overall moderate difficulty (mean 2.07, SD 0.72). Item means ranged from lower scores on judgment-oriented tasks (e.g. deciding when a second opinion is needed) to higher scores on items involving understanding or using information provided by clinicians (Table 3). The Cronbach's α was 0.76.

According to the validated thresholds for the HLS-EU-Q6 [34], 17.2% of respondents in this sample were classified as having inadequate HL, 52.4% as problematic, and 30.4% as sufficient (Fig. 1).

Table 3 Mean and standard deviation for each item of the six-item European Health Literacy Survey Questionnaire among adults in Italy, October 2024–April 2025

Item	HLS-EU-Q6 question	Mean and SD
HLS_1	How easy would you say it is to find information on treatments of illnesses that concern you?	1.94 ± 1.00
HLS_2	How easy would you say it is to understand what your doctor says to you?	2.60 ± 0.99
HLS_3	How easy would you say it is to judge which everyday behaviour is related to your health?	1.69 ± 1.13
HLS_4	How easy would you say it is to judge when you may need to get a second opinion from another doctor?	1.64 ± 1.12
HLS_5	How easy would you say it is to use information the doctor gives you to make decisions about your illness?	2.40 ± 1.06
HLS_6	How easy would you say it is to follow instructions from your doctor or pharmacist?	2.19 ± 1.05
Overall mean HL		**2.07** ± 0.72

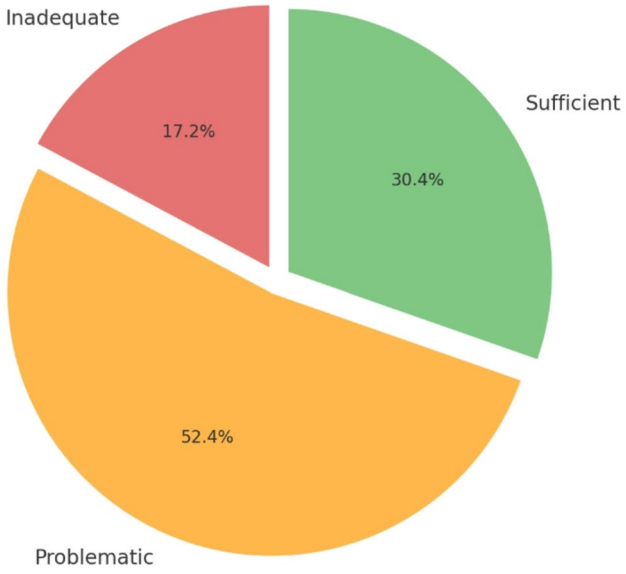

Fig. 1 Distribution of health literacy levels among adults in Italy participating in a national survey on patient information leaflets for medicines, October 2024–April 2025

Regarding FHL in the written domain, 53.7% ($n = 1{,}031$) of the sample reported moderate to extreme difficulty reading written health materials (mean item score: 3.28 ± 1.09), indicating limited HL. The FHL single item correlated moderately with the overall HLS-EU-Q6 score (Spearman's rho = 0.45, $p < 0.0001$).

Sociodemographic and behavioural factors in relation to health literacy

Patterns of HL across sociodemographic and behavioural factors reveal meaningful distinctions in how individuals engage with and comprehend written medicine information (Table 4).

No significant differences in mean HL scores were observed across gender, regions, healthcare background, and frequency of medicine use. For limited FHL, gender and healthcare background likewise showed no differences (both $p > 0.05$), whereas region displayed modest heterogeneity ($p = 0.02$).

In contrast, educational attainment was positively linked to HL. Participants with a university degree had higher mean HL scores (2.09 ± 0.72) than those with lower education (2.02 ± 0.70; $p = 0.042$). A corresponding gradient was observed for limited FHL ($p < 0.0001$).

Engagement with PILs was high upon first use of a medicine: 65.5% of respondents reported "always" reading the PIL for prescription medicines and 71.4% for OTC medicines. HL was closely linked to engagement with PILs. Respondents who reported "always" reading the PIL for prescription medicines had a significantly higher mean HL score (2.11 ± 0.72) than those who reported "never" reading them (1.91 ± 0.79; $p = 0.004$). A graded pattern was also evident for OTC medicines (yes: 2.11 ± 0.71 or "sometimes": 2.04 ± 0.69 compared to "no": 1.82 ± 0.78; $p < 0.0001$;). Limited FHL showed similar results (both $p < 0.0001$).

Emotional and behavioural responses to PILs also differed by HL. Participants reporting none/low anxiety when reading PILs had higher mean HL scores than those with moderate/high anxiety, and those expressing much/very much confidence in medicine use after reading the PIL likewise had higher HL; limited FHL followed the opposite pattern (both $p < 0.0001$). Therapeutic interruption showed a similar though smaller gradient, with slightly higher HL among those who had not discontinued therapy after reading a PIL ($p = 0.02$).

In the drowsiness-warning driving scenario, nearly two-thirds of respondents (64.0%) selected the safest interpretation ("avoid driving for a few hours"), while 26.9% indicated they would assess the degree of drowsiness before deciding, 4.4% endorsed a monitoring strategy ("drive slowly with breaks"), and small minorities chose to counteract drowsiness with caffeine (2.3%) or to dismiss the warning as exaggerated (2.4%) (Data not shown in table).

HL also differed in relation to perceptions of medication risk and commercial interests. In the extract-based risk comparison, participants were presented with two authentic side-effect excerpts, one from an ibuprofen PIL and one from a vaccine PIL, without being told which medicine each referred to. Overall, 55.1% judged the ibuprofen-type statement as riskier, 31.2% judged the vaccine-type statement as riskier, and 13.7% were unsure. Mean HL scores differed significantly across these groups ($p = 0.009$), with higher values among those selecting

Table 4 Mean health literacy scores by sociodemographic and behavioural variables among adults participating in a national survey on patient information leaflets for medicines in Italy, October 2024–April 2025

Variable	Category	*N*	HLS Mean	*p*-value	FHL ≤ 3 *n* (%)	*p*-value
Gender	Male	730	2.08 ± 0.73	> 0.05	394 (54.0)	> 0.05
	Female	1237	2.07 ± 0.71		665 (53.8)	
Education	Low/Medium	525	2.02 ± 0.70	**0.042**	329 (62.7)	**< 0.0001**
	High	1452	2.09 ± 0.72		732 (50.4)	
Region	North	1219	2.08 ± 0.71	> 0.05	663 (54.4)	**0.02**
	Centre	394	2.08 ± 0.72		225 (57.1)	
	South/Islands	364	2.05 ± 0.73		173 (47.5)	
Working in the healthcare field	No	1583	2.07 ± 0.71	> 0.05	859 (54.3)	> 0.05
	Yes	394	2.10 ± 0.76		202 (51.3)	
PIL consultation behaviours						
Frequency of medicine use	≤ once per week	1213	2.07 ± 0.7	> 0.05	645 (53.2)	> 0.05
	≥ once per day or more	764	2.08 ± 0.75		416 (54.5)	
Prescription PIL consultation	Yes	1294	2.11 ± 0.72	**0.004**	602 (46.5)	**< 0.0001**
	No	145	1.91 ± 0.79		109 (75.1)	
	Sometimes	538	2.04 ± 0.68		350 (65.1)	
OTC PIL consultation	Yes	1412	2.11 ± 0.71	**< 0.0001**	692 (49.0)	**< 0.0001**
	No	143	1.82 ± 0.78		104 (72.7)	
	Sometimes	422	2.04 ± 0.69		265 (62.8)	
Emotional and confidence responses						
Anxiety when reading PIL	None/Low	823	2.21 ± 0.72	**< 0.0001**	353 (42.9)	**< 0.0001**
	Moderate/High	1007	1.97 ± 0.70		627 (62.3)	
Confidence after reading PIL	Much/Very much	937	2.22 ± 0.70	**< 0.0001**	378 (40.3)	**< 0.0001**
	None/Moderate	1,040	1.94 ± 0.71		683 (65.7)	
Therapy behaviours						
Therapy interruption after reading PIL	No	1249	2.10 ± 0.71	**0.02**	667 (53.4)	> 0.05
	Yes	728	2.03 ± 0.72		394 (54.1)	
Risk appraisal tasks						
Risk perception	Ibuprofen	1090	2.12 ± 0.72	**0.009**	535 (49.1)	**< 0.0001**
	Vaccine	616	2.02 ± 0.71		368 (59.7)	
	Don't know	271	2.02 ± 0.73		158 (58.3)	
Perception of serious side effects by medicine class (First position) *	Anxiolytic	696	2.07 ± 0.70	**0.008**	361 (51.9)	**< 0.0001**
	Vaccine	495	2.01 ± 0.74		310 (62.6)	
	Antibiotic	353	2.09 ± 0.64		179 (50.7)	
	Antihypertensive	249	2.06 ± 0.75		125 (50.2)	
	Analgesic	184	2.2 ± 0.79		86 (46.7)	
Perceptions of commercial influence						
Perceived commercial influence on PILs	Agree	397	1.92 ± 0.71	**< 0.0001**	263 (66.3)	**< 0.0001**
	Neutral	863	2.04 ± 0.70		492 (57.0)	
	Disagree	717	2.20 ± 0.72		306 (42.7)	

HLS HLS-EU-Q6 mean score (1–4; higher = higher health literacy). FHL ≤ 3 = limited functional health literacy. *p*-values from t-test or ANOVA (HLS) and χ^2 test (FHL ≤ 3), α = 0.05. For rank-order items (*), values reflect first-rank assignments; N and FHL ≤ 3 percentages refer only to that subgroup. Bold values indicate statistically significant results ($p < 0.05$)

the ibuprofen excerpt as riskier (2.12 ± 0.72) compared with those selecting the vaccine excerpt (2.02 ± 0.71) or responding "don't know" (2.02 ± 0.73). FHL was higher among those aligning with the ibuprofen risks (49.1%) than among those selecting the vaccine (59.7%) or "don't know" (58.3%) ($p < 0.0001$). In a separate question on medicine classes, anxiolytics (35.4%) and vaccines (25.0%) were most frequently nominated as carrying the most serious side effects, followed by antibiotics (17.9%), antihypertensives (12.6%), and analgesics (9.3%). HL scores differed significantly across these categories ($p = 0.008$), with the highest values among those indicating analgesics as riskiest (2.24 ± 0.79) and lower values among those nominating vaccines (2.01 ± 0.75). Similarly, limited FHL also differed, ranging from 46.7% among those nominating analgesics to 62.6% among those nominating vaccines ($p < 0.0001$). The ranking of medicine classes did not statistically differ among those who

Table 5 Multivariable logistic regression analysis of predictors of medication risk appraisal among adults in Italy, October 2024–April 2025

Final logistic model	OR	95% CI	*p*
FHL (limited vs. adequate)	1.42	1.18–1.72	**< 0.001**
Anxiety (moderate/high vs. none/low)	0.79	0.65–0.96	**0.015**
Healthcare background	1.29	1.02–1.63	**0.034**
Medicine-use frequency (≥ daily vs. ≤ weekly)	1.25	1.04–1.52	**0.02**

Model statistics: $N = 1,830$; LR $\chi^2 = 32.9$; Pseudo-$R^2 = 0.013$

FLH Functional health literacy, *OR* Odds Ratio, *CI* Confidence Interval

judged the ibuprofen-type statement as riskier, compared to those who judged the vaccine-type statement as riskier, and those who were unsure (Data not shown in the table).

Finally, perceptions of commercial influence in PILs displayed a graded relationship with HL ($p < 0.0001$): mean HL was lowest among those agreeing that PILs are commercially influenced (1.92 ± 0.71), intermediate among neutral respondents (2.04 ± 0.70), and highest among those disagreeing (2.20 ± 0.72). Limited FHL showed the same gradient (66.3%, 57.0%, 42.7%; $p < 0.0001$).

Multivariable analysis of the risk perception

Multivariable logistic regression was carried out to identify independent predictors of risk appraisal. Table 5 shows the predictors statistically significant after backword selection process. In the final model, respondents with limited FHL had higher odds of judging the ibuprofen excerpt as riskier (OR 1.42), whereas those reporting moderate/high anxiety when reading PILs were less likely to select ibuprofen (OR 0.79). Having a healthcare background and more frequent medicine use (≥ daily vs. ≤ weekly) were also positively associated with judging ibuprofen as riskier. Continuous HLS scores were only borderline significant in extended models and were not retained in the final specification. Substituting categorical HL levels (inadequate, problematic, sufficient) produced no substantive differences.

Discussion

This study explored how Italian adults engage with PILs, including perceptions of their clarity, trustworthiness, and risk content, as well as associated behavioural outcomes. HL was considered as a key dimension for interpreting variability in these outcomes, while not being the sole object of investigation. In this nationally distributed sample, overall mean HL was moderate (2.07), with approximately 70% of respondents categorised as having inadequate or problematic HL. This pattern aligns with findings from the European Health Literacy Survey, which documented widespread limitations in HL across participating countries [40], and with Italian studies reporting similarly low levels [35, 41, 42].

The education gradient observed in this study is consistent with previous research identifying educational attainment as one of the most consistent sociodemographic determinants of HL [43]. By contrast, no statistically significant differences were detected by gender, macro-region, or healthcare background. These findings suggest that working or studying in the healthcare field does not necessarily translate into higher HL, supporting evidence that professional context alone does not ensure broader competencies in accessing and applying health information [44].

Beyond sociodemographic characteristics, HL was linked to how participants reported engaging with and experiencing PILs. Frequent PIL readers, both for prescription and OTC medicines, had higher HL than occasional or non-readers. This pattern is consistent with studies indicating that individuals with higher HL are more likely to seek, understand, and use written medicine information [15, 45]. Conversely, lower-HL respondents reported more anxiety when reading PILs, less confidence in subsequent medicine use, and were more likely to report discontinuing therapy after consulting PILs. These differences highlight the importance of HL-sensitive design strategies.

Avoiding PILs was generally linked to substituting written information with interpersonal counselling, rather than to intrinsic distrust. Primary reasons centred on preference for consulting doctors or pharmacists, while format-related difficulties, excessive length, small type, and complex language, appeared lower in the rank order. This pattern suggests both a channel preference and modifiable design barriers, consistent with the observed HL gradients in engagement. Two complementary levers for practice and policy emerge. First, PILs should be positioned as deliberate complements to professional advice. Second, cognitive load should be reduced through HL-sensitive formatting, including brevity, legible type, and plain-language micro-summaries, to lessen avoidant behaviour among readers with lower HL. Section-level patterns may indicate where redesign is likely to yield the greatest gains: "What the medicine is and what it is used for" was both most consulted and most difficult, whereas "Contents of the package and other information" was least consulted and easiest. A clearer architecture could be achieved by front-loading the indication/purpose with a concise plain-language statement, concrete examples, and a "need-to-know" checklist, while relegating ancillary details to layered formats. Such adjustments may better align PILs with real-world use without compromising safety content.

Consistent with our findings, qualitative research has shown that patients often describe PILs as overwhelming

or frightening, particularly when side-effect sections are lengthy and technical, and may respond with avoidance or changes in therapy [15]. Reviews of interventions further indicate that structural and linguistic improvements, such as shorter sections, plain language, and supportive visuals, can reduce comprehension barriers and lower the emotional burden of reading [46].

While causality cannot be inferred, the observed HL gradients in anxiety, confidence, and discontinuation point to the need for experimental evaluation of HL-sensitive redesign strategies that combine clearer organisation of risk information, plainer wording, and supportive visuals. Such adjustments may help reduce anxiety, increase confidence, and limit unnecessary discontinuation among lower-HL readers, thereby promoting more equitable and safer medicine use.

Taken together, our findings also resonate with research on nocebo effects, which demonstrates that poorly quantified or vividly worded risk descriptions exacerbate anxiety and increase therapy discontinuation [17]. This may suggest that lower HL interacts with existing PIL formats to amplify emotional and behavioural barriers to adherence, whereas higher HL mitigates these risks by enabling readers to filter and contextualise information.

To further probe how HL influences the interpretation of risk information, we employed a blinded appraisal task using anonymised excerpts from authentic PILs: one from ibuprofen and one from the Comirnaty (Pfizer–BioNTech) Covid-19 vaccine. The excerpts from the respective PILs consisted solely of brief qualitative descriptions of potential adverse events, articulated through epistemic modality and hedging devices, and did not include numerical incidence data that might be difficult for non-experts to interpret. Nevertheless, the descriptors used in the PILs are grounded in epidemiological evidence, which, for the medicines under consideration, is consistently reported in the literature. For ibuprofen, population-based studies estimate 3–4 cases of upper gastrointestinal bleeding per 1,000 users annually [47], alongside a four- to five-fold increase in ulcer risk with chronic NSAID use [48]. By contrast, observational data indicate that serious allergic reactions following mRNA Covid-19 vaccination are extremely rare, with anaphylaxis estimated at approximately 5 cases per million doses [49].

Despite this disparity in incidence, absent from the PIL excerpts, nearly one third of respondents judged the vaccine excerpt to be riskier, and 13.7% reported uncertainty. HL differentiated performance: respondents who correctly identified the ibuprofen text as riskier had significantly higher HL scores, whereas those selecting the vaccine or "don't know" had lower HL.

Multivariable analysis refined this picture. Anxiety, healthcare background, and frequency of medicine use also showed independent associations, suggesting that risk perception may not be determined by HL alone but shaped by the combined influence of cognitive, emotional, and experiential factors. The divergence between descriptive and adjusted analyses further suggests that apparent group differences in HL may partly reflect variation in emotional state or prior exposure to medicines, which may shape how individuals apply their HL skills when interpreting medicine information in real-world settings.

The distribution of responses across medicine classes suggests that lay perceptions of risk are shaped as much by social narratives as by epidemiological evidence. Anxiolytics emerged as the most frequently identified category, a finding likely reflecting the enduring stigma around psychotropic drugs, where fears of addiction and misuse remain culturally salient [50]. Vaccines followed, consistent with the visibility of vaccine debates and misinformation in public discourse, which may heighten the perceived likelihood of extremely rare adverse events [51]. Antibiotics and antihypertensives occupied intermediate positions, while analgesics were least often judged as risky despite their well-documented association with gastrointestinal and cardiovascular complications.

Mean HL varied significantly across medicine classes ($p = 0.008$), with the highest values observed among those who considered analgesics the riskiest and the lowest among those identifying vaccines. This gradient suggests that higher HL is associated with perceptions more closely aligned with epidemiological evidence, whereas lower HL appears more influenced by social narratives and widely circulating concerns that emphasise rare but emotionally salient outcomes. The findings indicate that the symbolic salience of vaccines may elicit affective responses even among respondents who otherwise demonstrated accurate risk reasoning, underscoring the enduring influence of collective narratives on perception. In this sense, higher HL may support more calibrated risk interpretation, while limited HL may contribute to the overweighting of unlikely scenarios, particularly in relation to vaccines. This interpretation is consistent with international findings that limited HL increases susceptibility to misinformation and vaccine hesitancy [51, 52].

Perceptions of trust further distinguished HL groups. Respondents with lower HL were more likely to agree that PILs are influenced by commercial interests, whereas those with higher HL were more sceptical. This misalignment between regulatory intent and public perception may fuel disengagement among those with limited HL, a pattern consistent with evidence linking lower HL to reduced trust in medical information and heightened perceptions of bias [52]. In this respect, HL-sensitive communication must extend beyond readability to

include trust-building strategies, such as explicitly signalling regulatory authorship and oversight [53].

Taken together, our findings indicate that HL may substantially condition how adults in Italy read, interpret, and act upon PILs. The gradient observed across reading frequency, affective responses (anxiety, confidence), behavioural outcomes (therapy discontinuation), risk appraisal, and trust suggests that PILs are not neutral instruments. Instead, their design can exacerbate inequities by placing disproportionate cognitive and emotional burdens on those with limited HL. This has important implications for public health and regulatory practice. PIL reform should focus on reducing unnecessary complexity and ambiguity while preserving essential safety content [2], drawing on strategies discussed in the literature such as clearer presentation of risk information, improved structuring and layout, use of plain language, and measures to strengthen perceptions of independence and trust [10, 14, 15, 41]. Such reforms would help ensure that PILs support, rather than undermine, informed medicine use across HL levels.

The novelty of this study rests on three contributions. First, to our knowledge, this is the largest Italian dataset to date examining the relationship between HL and multiple dimensions of PIL use, including engagement, emotional response, and behavioural outcomes. Second, the blinded excerpt task provides an innovative and ecologically valid method for examining how HL affects the interpretation of authentic PIL text without the influence of brand cues. Third, by linking engagement, affective response, behaviour, and trust in a single analysis, this study provides insights into how HL may shape interaction with regulatory documents, situating PILs as a crucial intersection of HL, risk communication, and patient safety with direct relevance for public health equity.

Strengths and limitations

Our findings rest on a design with distinctive strengths and recognised limitations. The study benefits from a large sample recruited across multiple regions of Italy, providing broad geographic coverage. Collaboration with general practitioners further strengthened recruitment by reaching older adults and individuals less active online, groups that are often underrepresented in digital surveys. The use of the validated Italian version of the HLS-EU-Q6 allowed assessment of health literacy with an instrument that is widely employed in European and international research and enables direct comparison with existing HL data. In addition, the use of a blinded, authentic-text risk appraisal task extended beyond conventional self-report, offering an ecologically valid assessment of how PIL excerpts are interpreted in practice. To our knowledge, no prior Italian study has investigated PIL engagement, affective responses, therapy behaviours, and risk appraisal in combination at this scale. .

Limitations should also be acknowledged. Recruitment relied on snowball and network-based methods, which inevitably limit representativeness and contributed to an overrepresentation of more educated respondents. However, the distribution of HL categories was similar to that reported in other studies, suggesting that the observed patterns are broadly consistent. Moreover, the persistence of HL-related differences even within this highly educated sample may indicate that such disparities could be even more pronounced in the general population, where lower educational attainment is more prevalent. In addition, the regional distribution of respondents was not fully balanced, with the North more strongly represented than the Centre and South. These patterns reflect structural constraints of voluntary, non-probability survey designs. As a result, the findings should be understood as illustrating patterns within a large, geographically broad adult sample, rather than providing national representativeness. Another limitation concerns the measurement of HL. The HLS-EU-Q6 is a brief self-report instrument; consequently, scores reflect respondents' perceived rather than objectively tested competencies and may be affected by reporting or social desirability bias. Furthermore, outcomes such as reading frequency, anxiety, confidence, and therapy discontinuation were self-reported and therefore vulnerable to similar recall and social desirability bias. The cross-sectional design also precludes causal inference, and reciprocal effects (for example, whether sustained engagement with well-designed PILs could enhance HL over time) remain plausible. Although between-group differences in mean HLS-EU-Q6 scores were numerically modest, they systematically shifted the proportions of respondents classified as having inadequate, problematic, or sufficient HL, indicating meaningful disparities at the population level rather than clinically decisive differences for individual patients. To our knowledge, no minimal clinically important difference has been established for the HLS-EU-Q6, so the observed gradients are interpreted in relative terms, focusing on patterns across sociodemographic and behavioural subgroups rather than on absolute score changes.

Taken together, these strengths and limitations indicate that while the findings are robust in demonstrating HL-related gradients across multiple domains of PIL use, they should be interpreted with caution regarding generalisability and causal direction.

Conclusions

Our study provides new evidence on how Italian adults engage with, interpret, and act upon PILs, highlighting HL as a key dimension contributing to shaping these

differences. Across a large, geographically diverse sample, lower HL was consistently associated with more anxiety, reduced confidence, therapy discontinuation, and less calibrated risk appraisal, while higher HL aligned with more consistent use of PILs, greater confidence, and perceptions closer to epidemiological evidence. These findings underscore that PILs current design may place disproportionate cognitive and emotional demands on readers with limited HL, thereby contributing to inequities in medicine use.

For public health and regulatory practice, the results point to the need for PIL formats that reduce complexity without omitting essential safety content and that explicitly foster trust in their neutrality. Future research should build on existing evidence and standards in risk communication, as well as research on anxiety and nocebo effects, to further explore, through experimental and longitudinal designs, whether HL-sensitive adjustments, such as clearer risk presentation, layered structuring, and transparent authorship cues, can mitigate anxiety, support adherence, and reduce disparities in comprehension. In parallel, more diverse and representative surveys using a broader range of items could establish population benchmarks and monitor inequalities in engagement with written medicine information.

This study identifies PILs as a crucial arena in which HL shapes not only comprehension but also confidence, trust, and treatment behaviour, underscoring the need for public health action to ensure that written medicine information supports safe, equitable, and adherent use across diverse HL levels. Beyond individual outcomes, the observed associations between HL, risk appraisal, anxiety, and vaccine-related perceptions point to broader implications for public trust in vaccination and other preventive measures. In addition, given the links between HL, therapy discontinuation, and confidence in medicine use, PIL design may indirectly affect patient safety and healthcare system efficiency, further reinforcing the importance of HL-sensitive reforms in regulatory communication.

Abbreviations

CI	Confidence Interval
EU	European Union
FHL	Functional Health Literacy
GP	General Practitioner
HL	Health Literacy
HLS	EU–Q6–European Health Literacy Survey Questionnaire, six–item version
NSAID	Nonsteroidal Anti–inflammatory Drug
OR	Odds Ratio
OTC	Over–the–counter (medicine)
PIL	Patient Information Leaflet
SD	Standard Deviation
UK	United Kingdom
WHO	World Health Organization

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13690-026-01901-7.

Supplementary Material 1.

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Authors' contributions
N.P. conceived and designed the study, developed the survey, collected and analysed the data, interpreted the results, and drafted the manuscript. L.C. contributed to the study design, statistical analysis, and reviewed the manuscript. E.C. and A.C. contributed to the project administration, and review of the manuscript. C.M. contributed to data collection and study design. UG contributed to conceptualisation, methodology, and critical review of the manuscript. All authors read and approved the final manuscript.

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Data availability
The datasets generated and/or analysed are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
According to the guidelines of the Ethics Committee of the University of Brescia (DR. 863/2025 prot. n. 307740/2025) and the General Authorisation to Process Personal Data for Scientific Research Purposes issued by the Italian Data Protection Authority (2012), this study fell within a category of anonymous, non-interventional survey research on adults that does not require formal committee approval, as it does not involve the collection of sensitive personal health data. All participants were informed about the study aims and procedures, assured of confidentiality, and provided electronic informed consent prior to participation. Participation was entirely voluntary, and respondents could withdraw at any time without consequence. All procedures were conducted in accordance with the ethical principles of the Declaration of Helsinki and relevant national data protection regulations.

Consent for publication
Not applicable. This manuscript does not contain data from any individual person in any form (including individual details, images, or videos).

Competing interests
The authors declare no competing interests.

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