

Patient satisfaction and adherence to vitamin D supplementation: results from a nationwide survey in Italy

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Abstract

Objective. The objective of the present study was to evaluate patient satisfaction and adherence to different vitamin D formulations and dosing regimens in a large Italian cohort of patients treated for osteoporosis or vitamin D deficiency.

Methods. We did a cross-sectional study; a questionnaire (FEDIOS Survey, version 3.2) was administered across multiple centers under FEDIOS patronage. Questions assessed socio-demographic data, vitamin D treatment characteristics, perceived convenience, tolerability, adherence (Morisky scale), and overall satisfaction.

Results. A total of 658 respondents (mean age 65.5±13.1 years; 86% women) completed the questionnaire. Most participants had a high school diploma (38%), and 96% were currently taking vitamin D, predominantly as liquid formulations (bottles 67%, ampoules 23%). The most frequent dosing was monthly (41%), followed by weekly (37%) and daily (19%). Laboratory confirmation of deficiency was obtained in 83% of cases; 49% were treated for osteoporosis. Only 14% reported difficulties with intake, most commonly problems opening ampoules (36%) or forgetting doses (33%). On a 7-point Likert scale, mean satisfaction scores were 5.74±1.08 for overall treatment satisfaction and 5.81±1.11 for willingness to continue treatment. The Morisky adherence score averaged 1.44 to 1.55 for most formulations, indicating moderate-to-high adherence without significant inter-group differences ($p=0.78$). However, monthly regimens, especially ampoules and bottles, were associated with significantly higher satisfaction for dosing frequency and continuation intention ($p=0.017$ and 0.018 , $\Delta\approx+9\%$). Global satisfaction was highest for monthly ampoules (6.08±0.82) and monthly tablets (6.18±0.91), and lowest for daily tablets (5.69±1.01).

Conclusions. In summary, vitamin D supplementation was generally well accepted among Italian patients, with a preference for monthly liquid formulations, perceived as more convenient and easier to manage. Simplified dosing schedules appear to enhance satisfaction and support sustained adherence.

Key words: vitamin D, adherence, compliance.

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Introduction

Vitamin D plays a central role in calcium homeostasis, skeletal mineralization, and muscle function. Insufficient vitamin D levels are highly prevalent worldwide and have been linked to an increased risk of osteomalacia, osteoporosis, falls, and fractures (1). For these reasons, vitamin D supplementation is a cornerstone in the prevention and management of osteoporosis and other metabolic bone diseases (2). However, despite strong evidence supporting its efficacy, real-world adherence to vitamin D supplementation remains suboptimal (3). The gap between prescription and actual intake limits the effectiveness of preventive strategies and may partly explain why many treated individuals still present with persistently low serum 25-hydroxyvitamin D [25(OH)D] concentrations (4, 5). Multiple factors contribute to poor adherence to vitamin D supplementation. In addition to forgetfulness and limited patient awareness, the formulation and frequency of administration play a crucial role. In Italy, vitamin D is available in a variety of pharmaceutical forms, liquid ampoules, oral solutions (bottles), softgel capsules, tablets, or drops, with schedules ranging from daily to monthly dosing. While pharmacokinetic studies indicate that inter-

mittent high-dose and daily low-dose regimens achieve similar steady-state concentrations (6), the real-world experience of patients may differ substantially depending on the convenience and perceived tolerability of the formulation used. In practice, patients are often not systematically asked about their preferences, and clinicians may rely on availability or habit rather than evidence-based considerations of adherence and satisfaction. From a patient-centered perspective, satisfaction with treatment is an important determinant of adherence and long-term persistence. In the context of vitamin D supplementation, understanding patient perceptions and practical barriers is therefore essential for optimizing public health interventions and clinical recommendations. Yet, despite the widespread use of vitamin D across Italy, comprehensive data on patient satisfaction, preference for formulation, and perceived efficacy are scarce. The Italian Federation of Osteoporosis and Skeletal Diseases (FEDIOS) recognized this unmet need and promoted a nationwide survey to investigate how formulation type and dosing frequency influence adherence and satisfaction in patients receiving vitamin D supplementation. The underlying hypothesis was that simpler regimens, particularly monthly or liquid formulations, may improve patient experience and adherence compared with more frequent or complex schedules.

Materials and Methods

This was a cross-sectional, multicenter survey conducted under the patronage of FEDIOS between 2023 and 2024. The initiative was designed to capture patient-reported data on satisfaction, adherence, and perceived convenience of vitamin D supplementation in everyday clinical practice across Italy. Participating physicians distributed paper-based questionnaires to adult outpatients who were currently receiving or had recently received vitamin D supplementation for osteoporosis or vitamin D deficiency. Participation was voluntary and anonymous. Patients provided informed consent prior to completing the survey, and data were collected and analyzed in accordance with the principles of the Declaration of Helsinki.

Questionnaire and measures

The FEDIOS Vitamin D Satisfaction Questionnaire (Version 3.2) was developed by an expert panel comprising clinicians and patient representatives. The full Italian questionnaire is provided in the *Supplementary Material*.

The questionnaire covered: i) sociodemographic characteristics, including age, sex, educational level, and menopausal age (for women); ii) treatment details, including current use of vitamin D, type of formulation (ampoule, bottle, tablet, capsule, or drops), and dosing frequency (daily, weekly, biweekly, monthly, or other); iii) self-management and adherence behaviors, such as who manages the medication, frequency of missed doses, and whether doses were ever skipped, reduced, or stopped without medical advice; iv) knowledge and perception of formulations, including awareness of alternative forms and whether the prescribing physician asked for the patient's preference; v) perceived convenience, tolerability, and satisfaction, assessed through a series of 7-point Likert-scale items ranging from 1 ("very dissatisfied") to 7 ("very satisfied") and the following aspects were evaluated: frequency of intake, convenience, ease of intake, ease of remembering, ability to integrate vitamin D with other therapies, time required for administration, trust in treatment efficacy, trust in physical well-being, overall satisfaction, and willingness to continue treatment; vi) adherence assessment, based on the Morisky Medication Adherence Scale (MMAS-4) (7), consisting of four yes/no questions about forgetfulness, carelessness, stopping medication when feeling better, and stopping when feeling worse. Scores ranged from 0 (high adherence) to ≥ 2 (low adherence).

Additionally, respondents were asked whether they had undergone laboratory assessment for vitamin D deficiency, whether the treatment was reimbursed through the national health system, and whether they experienced any difficulties related to the mode of administration (e.g., opening ampoules, counting drops, swallowing tablets). The FEDIOS Vitamin D Satisfaction Questionnaire, version 3.2, was developed specifically for this survey by an expert panel with experience in osteoporosis and metabolic bone diseases. The instrument was designed to capture patient-reported information on vitamin D treatment characteristics, practical barriers to intake, formulation awareness, adherence-related behaviors, and satisfaction with treatment. The questionnaire was intended as a pragmatic, disease-specific survey tool for real-world clinical practice rather than as a formally psychometrically validated instrument.

Data handling and grouping

For comparative analysis, patients were categorized according to both formulation (ampoule, bottle, tablet, or drops) and dosing

frequency (daily, weekly, or monthly). Participants reporting no current supplementation were excluded from satisfaction and adherence analyses. All data were anonymized and entered into a centralized database.

Statistical analysis

Descriptive statistics were calculated for all variables and are presented as mean $\pm$ standard deviation for continuous data and as frequency (%) for categorical variables. Between-group differences in satisfaction and adherence were evaluated using one-way analysis of variance (ANOVA), followed by pairwise comparisons with Bonferroni correction for multiple testing. For categorical comparisons (e.g., presence of difficulties, physician consultation about preferences), χ^2 tests were applied. Statistical significance was set at $p < 0.05$. All analyses were performed using GraphPad Prism 10 and SPSS Ver 26.

Results

Study population

A total of 661 questionnaires were collected by 10 general practitioners and 5 specialists (2 rheumatologists, 2 endocrinologists, and 1 orthopedic). Among these, 658 were complete and eligible for analysis. The mean age of respondents was 65.5 ± 13.1 years, and the majority were women (86% female, 14% male) with a mean menopausal age of 49.9 ± 3.9 years. Educational attainment was distributed as follows: 18% elementary school, 26% middle school, 38% high school diploma, and 18% university degree. The main indications for vitamin D supplementation were laboratory-detected vitamin D deficiency and osteoporosis. Because this questionnaire item allowed multiple responses, these categories were not mutually exclusive. Overall, 398 patients (60.5% of the total cohort) reported both osteoporosis and laboratory-detected vitamin D deficiency as indications for treatment. Table 1 shows the demographic and educational characteristics of the sample.

Patterns of vitamin D supplementation

Nearly all respondents (96%) reported current vitamin D use. The most frequent formulations were bottles (67%), followed by ampoules (23%) and tablets (9%); drops were used only occasionally ($< 1\%$). No participant reported using soft gel capsules.

The preferred dosing schedule was monthly (41%), followed by weekly (37%) and daily (19%) regimens. Most respondents (83%) reported that they self-managed their supplementation. Laboratory confirmation of vitamin D deficiency before starting therapy had been performed in 83%, and nearly two-thirds (65%) obtained their prescription under the National Health Service reimbursement scheme.

The main indications were osteoporosis (49%) and vitamin D deficiency (53%), with some overlap between the two categories; 13% cited other conditions such as chronic pain or fatigue.

Difficulties and adherence behaviors

Overall, 14% of participants reported some difficulty with intake. The most frequent issues were opening or emptying ampoules (36%), forgetting to take doses (33%), and difficulty counting drops (25%). More than half of the sample (54%) admitted that they had at least occasionally forgotten a dose, 26% had skipped vitamin D within the previous two weeks, and 26% reported having stopped or reduced supplementation without medical

advice. When assessed using MMAS-4, adherence was generally moderate to high, with mean scores between 1.42 and 1.75 across formulation groups (lower scores indicate better adherence). The overall ANOVA p-value was 0.778, indicating no significant differences in adherence across formulation types. The lowest (best) adherence scores were observed with monthly ampoules (1.47 ± 0.64) and monthly bottles (1.44 ± 0.56), while the highest (worst) adherence corresponded to daily tablets (1.75 ± 0.45). Results of the Morisky scale are shown in Figure 1.

Knowledge and communication with healthcare providers

Awareness of the existence of different vitamin D formulations was limited: only 53% of respondents declared they were aware of all available options, while 27% knew only some and 20% were unaware. When asked whether their physician discussed formulation preferences, 41% reported that the doctor never asked, 45% said the question was asked only at treatment initiation, and only 14% were routinely consulted about their preferred formulation.

Patient satisfaction

Patients expressed high overall satisfaction with vitamin D supplementation. On a 7-point Likert scale (1 = very dissatisfied, 7 = very satisfied), the mean score for overall satisfaction was 5.74 ± 1.08 , and for willingness to continue therapy, it was 5.81 ± 1.11 . Satisfaction was highest for trust in efficacy (5.73 ± 1.02) and trust in physical well-being (5.85 ± 1.00) and lowest for ease of remembering intake (5.25 ± 1.36). When analyzed by formulation, satisfaction differences emerged despite the overall high baseline. The monthly ampoule and monthly bottle groups achieved the most favorable mean scores across most domains, while daily tablets consistently ranked lower. For the item “overall satisfaction with current therapy”, monthly ampoules (mean 6.08 ± 0.82) and monthly tablets (6.18 ± 0.91) scored significantly higher than monthly bottles (5.57 ± 0.97 ; $p=0.031$). Similarly, for “willingness to continue treatment”, the monthly ampoule group (6.17 ± 0.88) reported greater

satisfaction compared with monthly bottles (5.65 ± 1.01 ; $p=0.018$). Figure 2 shows satisfaction toward different formulations of vitamin D.

Regarding dosing frequency, a strong positive association was observed between lower dosing frequency and higher satisfaction. The perception of dosing frequency (“how satisfied are you with the frequency of intake?”) differed significantly across groups ($p<0.001$), with monthly regimens scoring higher than daily or weekly ones. In particular, monthly ampoules vs. daily tablets showed a 27.6% higher satisfaction score ($p=0.008$). In contrast,

Table 1. Characteristics of the study population.

Variable	n (%) or mean $\pm$ standard deviation
Total participants	658 (100)
Macroregion of Italy	
Nord	342 (52)
Center	112 (17)
South	204 (31)
Age (years)	65.5 ± 13.1
Sex	
Female	568 (86.3)
Male	90 (13.7)
Menopausal age (women only, years)	49.9 ± 3.9
Educational level	
Elementary school	118 (17.9)
Middle school	168 (25.5)
High-school diploma	252 (38.3)
University degree	120 (18.2)
Currently taking vitamin D	635 (96.1)
Formulation type	
Bottle (oral solution)	413 (66.9)
Ampoule	141 (22.9)
Tablet	57 (9.2)
Drops	6 (0.9)
Capsule	0 (0)
Dosing frequency	
Daily	121 (19.2)
Weekly	234 (37.2)
Every 2 weeks	11 (1.8)
Every 3 weeks	1 (0.2)
Monthly	261 (41.5)
Every 45 days	1 (0.2)
Self-management of therapy	
Manages alone	539 (83.3)
Always assisted	67 (10.4)
Occasionally assisted	41 (6.3)
Laboratory test for vitamin D deficiency performed	529 (83.4)
Reason for prescription	
Osteoporosis	321 (49.5)
Laboratory-detected deficiency	351 (53.2)
Other indications	84 (12.7)
Prescription reimbursed (national health system)	417 (65.0)
Difficulty in intake (any)	92 (14.3)
Most frequent difficulties (among those reporting)	
Opening/emptying ampoules	33 (35.9)
Forgetting to take dose	30 (32.6)
Counting drops	23 (25.0)
Swallowing	11 (12.0)
Other reasons	3 (3.3)

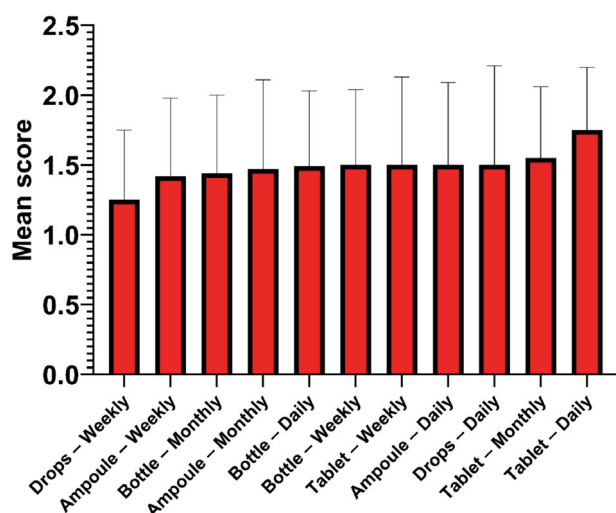


Figure 1. Morisky scale results for different dose, time and route of vitamin D supplements.

satisfaction related to ease of remembering, time required, or integration with other therapies did not differ significantly across formulation types, indicating that the overall convenience was generally well perceived irrespective of form.

Perception of formulation effectiveness and tolerability

When asked which formulation they believed to be most practical, 28% chose liquid (ampoule or bottle), 27% tablets, and 36% were unsure. Regarding perceived efficacy, 18% indicated liquids, 11% tablets, and 67% reported they “did not know”. Similar distributions were observed for perceived tolerability, with 21% favoring liquids, 14% tablets, and 59% uncertain.

Influence of co-administration and timing

Most participants (48%) did not consider taking vitamin D with food to be problematic, while 23% rated it “slightly” and only 3% “very” problematic.

When asked about the time burden associated with the mode of intake, 53% reported that the difference between taking vitamin D in a bottle and in a tablet/capsule was irrelevant, and 33% considered it slightly relevant. Only 2% deemed it critical.

In an exploratory analysis, patients receiving monthly regimens were numerically older than those receiving daily regimens, although the difference was not statistically significant (66.1 ± 12.8 vs. 64.3 ± 13.4 years; $p=0.21$). The mean age among patients receiving weekly regimens was 65.5 ± 13.1 years, with no significant overall difference across dosing-frequency groups.

Discussion and Conclusions

This survey conducted under the auspices of FEDIOS provides a comprehensive overview of patient experiences with vitamin D supplementation in Italy. The findings reveal that vitamin D therapy is generally well accepted, with high levels of satisfaction and moderate-to-high adherence across formulations. Importantly, dosing frequency and formulation type emerged as key drivers of patient satisfaction: monthly administration and liquid formulations, particularly ampoules and bottles, were consistently associated with greater perceived convenience and higher satisfaction scores, while adherence as measured by the Morisky scale was largely stable across groups. Together, these results underscore the value of patient-centered strategies that prioritize simplicity, practicality, and shared decision-making in vitamin D replacement therapy. Adherence to chronic preventive medications, including vitamin D, is a well-recognized challenge in real-world practice. Estimates from large observational studies suggest that up to 40% of individuals prescribed vitamin D discontinue treatment within the first year, and many others take it irregularly (3, 8, 9). In our cohort, self-reported forgetfulness and practical barriers, such as difficulty opening ampoules or counting drops, were the most common reasons for nonadherence. Nevertheless, the average Morisky score of approximately 1.5 across formulations indicates an acceptable adherence level, comparable to or slightly better than that reported for other preventive agents such as bisphosphonates or antihypertensive drugs. The absence of major differences among formulations suggests that overall compliance is more influenced by regimen simplicity than by the physical form of medication. A particularly consistent finding in our study was the clear preference for a monthly regimen, which scored significantly higher than daily or

weekly ones for satisfaction with frequency of intake (10). This echoes the broader principle observed across many chronic conditions: patients favor treatments requiring less frequent administration, provided they are perceived as effective and easy to remember (11). Monthly vitamin D dosing simplifies routines, minimizes the cognitive burden of daily intake, and may be easier to align with other scheduled health-related activities. Previous studies have demonstrated comparable efficacy between daily and intermittent vitamin D regimens in maintaining serum 25(OH)D concentrations, which supports the clinical safety of less frequent dosing (6). Liquid preparations were the most commonly used formulations in this survey, reflecting Italian prescribing habits and market availability. These forms were not only predominant but also associated with greater patient satisfaction compared with solid oral forms. Several factors may explain this preference. First, liquids eliminate the need for swallowing large tablets, which some older adults find difficult. Second, visual confirmation of intake (emptying an ampoule or measuring a dose) may enhance the perception of adherence and efficacy. Finally, liquid formulations often come in premeasured doses that are convenient for monthly administration. The few respondents who reported difficulties, mainly related to opening glass ampoules, represent a small but notable subset that could benefit from improved packaging or alternative delivery devices.

In contrast, tablets and capsules, while practical in other therapeutic contexts, were less favored here. Interestingly, despite slightly lower satisfaction scores, adherence did not significantly differ, suggesting that dissatisfaction alone may not translate directly into noncompliance but could affect long-term persistence. The preference for monthly regimens may also be partly related to the older age profile of the study population and the need for simplified therapeutic routines. In our exploratory analysis, patients receiving monthly vitamin D were numerically older than those receiving daily regimens, although this difference was not statistically significant. Therefore, age may contribute to the observed preference for less frequent dosing, but it does not appear to fully account for the higher satisfaction associated with monthly regimens.

An unexpected yet important finding was the limited patient awareness of formulation options and the relative lack of dialogue with healthcare providers regarding preferences. Only about half of respondents were aware that multiple forms of vitamin D existed, and fewer than 15% reported that their physician routinely discussed these options. This observation highlights a potential area

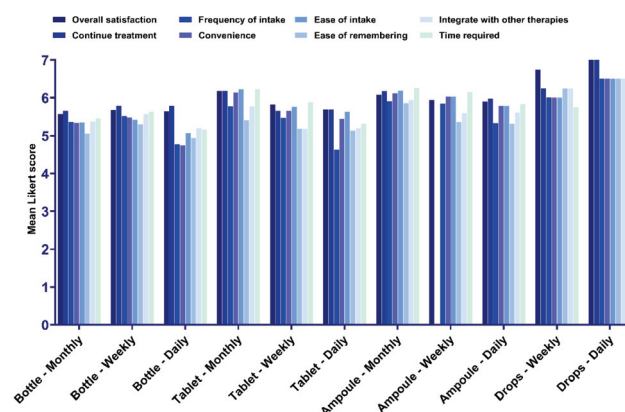


Figure 2. Satisfaction toward different dose, time and route of vitamin D supplements.

for improvement in clinical communication. Evidence from other therapeutic areas showed that limited communication about medication formulations can undermine both adherence and patient satisfaction. Studies have demonstrated that when clinicians actively engage patients in decisions about how treatment is administered, whether by discussing formulation, dosing frequency, or mode of intake, patients report greater trust, empowerment, and long-term persistence (12, 13). Therefore, incorporating a brief, structured conversation about formulation preference into routine clinical practice could represent a simple yet effective strategy to enhance both adherence and the overall quality of care. Encouraging shared decision-making and offering choices tailored to patient lifestyles may further enhance satisfaction and engagement.

The overall pattern emerging from this survey supports a pragmatic approach to vitamin D supplementation: favoring simple, infrequent, and well-tolerated regimens while ensuring patients are informed and involved in the decision process. Monthly ampoules or bottles appear to offer an optimal combination of convenience and acceptability, which may be especially valuable in older populations or those with polypharmacy. From a health-system perspective, improving adherence to vitamin D therapy could yield meaningful reductions in fracture risk and healthcare costs, given the established benefits of maintaining adequate vitamin D levels for bone and muscle health. Our findings may also be interpreted in the broader context of emerging evidence on potential extraskelatal effects of vitamin D. Fassio *et al.* reported that cholecalciferol supplementation in vitamin D-deficient healthy subjects was associated with a reduction in serum interleukin (IL)-6 and IL-17A concentrations, without marked differences among daily, weekly, and biweekly regimens (14). Although our study did not assess inflammatory markers or extraskelatal endpoints, these observations suggest that achieving and maintaining adequate vitamin D exposure may be relevant beyond skeletal outcomes. From this perspective, formulation and dosing frequency may matter not only pharmacologically but also behaviorally by improving acceptability, regular intake, and long-term persistence. Prospective studies combining patient-reported outcomes with biochemical and clinical endpoints are needed to test this hypothesis.

The strengths of this study include its large sample size, real-world design, and broad inclusion across multiple centers. The use of a validated adherence scale (MMAS-4) and multiple Likert items allowed a multidimensional assessment of patient experience. However, certain limitations should be acknowledged. The survey was cross-sectional and based on self-reported data, which are susceptible to recall and social desirability biases. Serum 25(OH)D levels were not systematically collected, precluding correlation between adherence and biochemical outcomes. Additionally, the predominance of female and elderly respondents may limit generalizability to younger populations or men. Geographic variations in prescribing practices or socioeconomic factors were not analyzed. Finally, although the questionnaire explored the perceived ease of integrating vitamin D with concomitant therapies, it did not quantify comorbidity burden or the exact number of ongoing medications. Therefore, the potential role of polypharmacy in shaping preferences for monthly dosing should be specifically investigated in future studies.

In summary, this survey demonstrates that vitamin D supplementation is broadly accepted and well-integrated into patients' daily lives in Italy. Adherence is generally good, and satisfaction is particularly high with monthly liquid formulations, which combine convenience, ease of use, and perceived effectiveness. Simplifying administration schedules and involving patients in treatment choices

appear to be key determinants of successful long-term supplementation. These insights should inform both clinicians and policy-makers aiming to improve the effectiveness of preventive vitamin D strategies within real-world healthcare settings.

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Online supplementary material

Supplementary Material. Full Italian translation of the FEDIOS Vitamin D Satisfaction Questionnaire (Version 3.2). Reproduced with permission from FEDIOS.

Received: 10 November 2025; Accepted: 13 July 2026.

Contributions: Giovanni Adami, Stefano Negri: conceptualization, investigation, supervision, validation, writing – original draft, review and editing. Giovanni Adami: data curation, formal analysis, project administration.

Conflict of interest: Giovanni Adami has received advisory board honoraria, consultancy fees and/or speaker fees from Theramex, UCB, Lilly, Galapagos, Fresenius Kabi, Amgen, BMS, Abiogen and Pfizer. Stefano Negri has nothing to disclose.

Ethics approval and consent to participate: the study was conducted according to the protocol 1483CESC approved by the Ethics Committee of Verona, in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent: informed consent was collected for each participant.

Patient consent for publication: patients provided consent for publication of anonymized data.

Availability of data and materials: data of the analysis are available upon reasonable request.

Declaration of generative artificial intelligence and artificial intelligence-assisted technologies in the writing process: no AI or AI-assisted technologies have been used during the writing process.

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