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From conventional to living guidelines – faster updates for better informed guidance? A scoping review

Von der konventionellen Leitlinie zur Living Guideline – häufigere Aktualisierungen zur besseren Orientierung? Ein Scoping Review

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ABSTRACT

Objective: The goal of living guidelines is keeping recommendations in guidelines up-to-date as new evidence becomes available. This review aims at scoping the prevalence and formal characteristics of living guidelines in the field of medicine and explore differences between formats.

Methods: A selective search of living guidelines in MEDLINE via PubMed, Google Scholar and six relevant online repositories for guidelines (MAGICApp, AWMF, GIN, NICE, WHO-Iris, BIGG) was conducted. Authors and editors were contacted to receive previous non-living guideline versions. Living guidelines were subsequently analyzed according to pre-defined methodological criteria as described below *(inter-comparison)*. Differences between living and their conventional (non-living) versions were assessed *(intra-comparison)*.

Results: 83 living guidelines were identified and selected for further screening, out of which 26 were eligible for analysis. 61.5% were new publications *(de-novo* guidelines) and 38.5% updates of pre-existing guidelines. There are some concepts defining, for example, the update cycle (AWMF, maximum of 12 months) but not all living guidelines follow or refer to existing concepts. The analysis shows that living guidelines in line with the established standards for (non-living) clinical guidelines involve an evidence standard, an extensive consensus process (often in the form of a Delphi process), and the inclusion of stakeholders (patients/relatives) in the development process, despite the high frequency of updates. When comparing living and conventional guidelines with the descriptive approach changes were found in update frequency (being more frequent with living guidelines, annually at the latest) and publication format (towards more digital) and public consultation (living guidelines offered more possibilities), no substantial methodological differences were observed in the description of consensus processes, changes in number of recommendations, inclusion of patient representatives. Given the small number of comparable pairs, the results reflect a tendency in the analyzed sample.

Conclusions: The definition and development of living guidelines varied. Standardization (i. e. in the form of a checklist, procedure template) is needed to assess quality of the living process.

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ZUSAMMENFASSUNG

Hintergrund: Living Guidelines zielen darauf ab, Empfehlungen klinischer Leitlinien stets aktuell zu halten, indem diese überarbeitet werden, sobald neue Erkenntnisse vorliegen. Ziel dieser Arbeit ist es, eine Übersicht über die Verbreitung, die formalen Charakteristika und Unterschiede zwischen den Formaten von Living Guidelines im Bereich der Medizin zu schaffen.
Methode: Eine selektive Literaturrecherche in MEDLINE via PubMed, Google Scholar und sechs relevanten digital verfügbaren Registern für Leitlinien (MAGICApp, AWMF, GIN, NICE, WHO-Iris, BIGG) wurde durchgeführt. Autor*innen und Herausgebende wurden kontaktiert und um Zusendung vorausgehender Versionen im konventionellen, Non-Living-Format gebeten. Living Guidelines wurden anhand a priori festgelegter Kriterien *(inter-comparison)* sowie hinsichtlich der Unterschiede zwischen non-Living und Living Formaten (*intra-comparison*) analysiert (für eine genaue Beschreibung der Kriterien wird auf die Beschreibung im Text verwiesen).
Ergebnisse: Es wurden 83 Living Guidelines für das Screening ausgewählt und 26 davon als passend für die Analyse identifiziert. 61,5% waren neue Publikationen (De-novo-Leitlinien) und 38,5% revidierte Aktualisierungen bereits bestehender Leitlinien. Es existieren Konzepte, die feste Kriterien für Living Guidelines, z. B. im Hinblick auf Aktualisierungsintervalle, festsetzen (AWMF, max. 12 Monate). Nicht alle Living Guidelines beziehen sich auf bestehende Konzepte zum Living-Prozess.

Die Analyse zeigt, dass Living Guidelines im Einklang mit den etablierten Standards für (Non-Living-) klinische Leitlinien einen Evidenzstandard, einen umfassenden Konsensprozess (oft in Form eines Delphi-Prozesses) und die Einbeziehung von Interessenvertreter*innen (Betroffene/Angehörige) in den Entwicklungsprozess beinhalten, trotz der hohen Aktualisierungsfrequenz. Beim Vergleich von Living Guidelines und konventionellen Leitlinien wurden mit dem deskriptiven Ansatz Veränderungen in der Aktualisierungshäufigkeit (Living Guidelines werden häufiger, spätestens jährlich, aktualisiert) und im Publikationsformat (hin zu mehr digitalen Formaten) sowie in der öffentlichen Konsultation (häufiger bei Living Guidelines) festgestellt, während bei der Beschreibung der Konsensprozesse, den Veränderungen in der Anzahl der Empfehlungen und der Einbeziehung von Betroffenen oder deren Interessensvertreter*innen keine wesentlichen methodischen Unterschiede beobachtet wurden. Angesichts der geringen Anzahl vergleichbarer Paare sind die Ergebnisse als Tendenz zu interpretieren.
Schlussfolgerung: Die Definition und Schritte in der Entwicklung der analysierten Living Guidelines variierten. Eine weitere Standardisierung (z. B. in Form einer Checkliste oder eines Manuals) zur Beurteilung der Güte und Qualität des *Living*-Prozesses erscheint erforderlich.

Introduction

Clinical practice guidelines support physicians, patients and other stakeholders to make decisions that are relevant to individual patient care in a broad body of scientific evidence [1]. The Institute of Medicine (2011) defines clinical practice guidelines as "statements that include recommendations intended to optimize patient care. These statements are informed by a systematic review of evidence and an assessment of the benefits and costs of alternative care options." [1]. The development of a guideline is extensive in terms of time and costs. Multiple experts, professions and associated stakeholders are involved and have to agree on the certainty of the relevant evidence and reach consent on recommendations. To ensure the high quality of a clinical guideline a number of standards have been established [2,3]. The development takes its time and due to an exponential growth in scientific evidence, clinical guidelines are often no longer up-to-date at the time of their publication [4]. This poses specific problems, since - as the COVID19-pandemic has shown – a rapidly changing evidence base should trigger frequent updating of recommendations. In this context, a recent study on the validity of recommendations in clinical guidelines showed that 92 percent (95% confidence interval 86.9–97.0) of the recommendations were valid 1 year after their development. This probability decreased at 2 (85.7%), 3 (81.3%) and 4 years (77.8%) [4]. The Association of the Scientific Medical Societies in Germany's guideline register requires to update a guideline at least after 5 years [2]. This finding demonstrates a potential gap between growing scientific knowledge and its implementation in the clinical work with patients.

The concept of *living guidelines* represents one approach to close the gap [5]. "Living guidelines aim to provide timely advice for decision makers by optimizing the guideline development process [...] to allow updating individual recommendations as soon as new relevant evidence becomes available" [5].

This goal can be achieved, for example, by publishing and managing the guidelines online, updating only individual recommendations in a living format and/or recruiting a living guideline panel, in the form of a committee, which commits to being available in the shortest possible time [5]. One platform that supports the development and publication of living guidelines is MAGICApp (https://app.magicapp.org). However, also other digital, web based and cross-platform tools as well as repositories of guideline creation and dissemination are required which, through continuous updating, allow a higher level of usage to be expected. Examples can be found on the websites of AWMF (Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V.), International Database of GRADE guidelines (BIGG), Guidelines International Network (GIN), National Institute for Health and Care Excellence (NICE), World Health Organization (WHO-Iris).

In a systematic review of methodological handbooks (2014), which analyzed 35 handbooks, the problem was identified that there is no guidance described on how to conduct a living process, nor is there a consistent understanding of when a guideline is dynamic or can be considered a living guideline [6]. There was no further research after this systematic review, which was published in 2014 and may therefore no longer be up to date [6]. According to the study protocol, a systematic review on the guideline update process is already being planned, but has not yet been published [7]. The aim of this review is therefore to evaluate the current scientific landscape of living guidelines in the field of medicine and to identify the state-of-the-art by analyzing existing living guidelines and comparing them with their previous non-living guidelines. For this, criteria were analyzed to find out whether one of the established guideline processes is changed due to frequent updating.

The criteria were defined by the working group. Since this is an initial schematic analysis, the criteria are based on methodological papers on living guidelines and the AWMF regulations [2,5,8].

The following questions are addressed:Question A: What are the characteristics of published living guidelines regarding the following criteria: Screening and update frequency, use of living systematic reviews (LSR), standard for quality of evidence and strength of recommendations, consensus process, involvement of stakeholders (e.g. patient, caregiver or other third party representatives) in the development process and publication format?

Question B: Is there a difference between living and non-living guidelines regarding the following criteria: Screening frequency, publication format, consensus process, consensus-based and evidence-based recommendations, public consultation of the guideline prior to publication, and involvement of non-medical stakeholders in the development process?

Thus, the overall aim of this review is to provide a deeper insight into the living concept and exploring the differences and similarities of living and non-living formats.

Methods

Search strategy

Selective searches were conducted on 29th July 2021. The publications indexed in MEDLINE via PubMed and Google Scholar using the search terms "living AND guideline" OR "living AND evidence" OR "living AND recommendation" were extracted. The abstracts and titles of articles identified through electronic searches were independently screened by two reviewers (ES-H, MS). MEDLINE via PubMed is one of the leading databases in the national library of medicine and focuses on biomedical and health articles. Publications about living guidelines from the medical field should be found here. In addition, Google Scholar was chosen to broaden the search radius and directly include published living guidelines. A search exclusively via scientific databases causes the risk of finding guidelines only if additional publications were published.

After this initial first search and a first analysis of the retrieved literature, six online repositories for guidelines (MAGICApp, AWMF, GIN, NICE, WHO-Iris, BIGG) were identified. These six guideline repositories were identified through the broad search in MEDLINE via PubMed and Google Scholar and were known to the guideline experts in our working group as common databases for guidelines. These repositories were screened independently (ES-H, MS) in a second search approach for published guidelines in a living format, using again the before mentioned keywords. Rayyan was used as software to collect, rate and extract the data (https://www.rayyan.ai/) [9]. Since the platform MAGICApp is designed to be specifically a living evidence ecosystem where all uploaded recommendations can potentially be modified by the authors, the used search strategy included all available publications covering the terms "guideline" or "recommendation" (so without necessarily naming it "living"). The search term was broadened here to ensure no living format is missed.

An aimed registration of the systematic reviews' protocol at PROSPERO was submitted on 25th July 2021 but declined (reason: no direct health-related outcome reported), hence the systematic review was not registered.

Inclusion criteria

A publication was eligible for inclusion if: (a) it represents a published living guideline or it covered methodological aspects of a (living) guideline process or if it could be seen as a complementary document to an existing living guideline, (b) the publication language was English or German, (c) its focus was on clinical issues (diagnosis and treatment) with a broad definition in the health care sector, (d) it was not considered grey literature or short articles/announcement, (e) it was published within the last five years until the end of August 2021 and (f) information about the period of updating was available, without such information it is not clear whether the guideline can be considered actually living.

Data extraction/analysis

To allow comparison on a descriptive level without considering the actual clinical content, all detected living guidelines were subsequently analyzed and information was extracted independently by four reviewers (ES-H, MS, CP, MF) with regard to the following a-priori defined criteria which were considered key by the working group. The use of standardized assessment tools (e.g. AGREE II) were considered but for the aim of the scoping review the following general characteristics were chosen: publication country, year (version), professional society, format of publication, field, screening and update frequency, platforms, reporting of standards for quality of evidence and recommendations, number of recommendations, use of living systematic reviews, reporting of consensus processes and involvement of non-medical stakeholders and public consultation prior to publication.

Comparison with non-living guidelines

To compare differences between current living and previous non-living guidelines, the authors and editors of all 26 included living guidelines were systematically contacted via e-mail in the period from 18th October to 22nd November 2021. In case of non-response, the respective authors and editors were contacted again. The request towards the editors and authors comprised three questions: 1) to grant access to previously published versions of the guideline in a non-living format, 2) to share their considerations for choosing the current living format and 3) to describe the main difference they personally perceive between living and non-living guideline approaches. The aim of this comparison was to investigate observed similarities and differences from the perspective of editors and authors regarding the practical use of living guidelines. The non-living guidelines were analyzed according to the same scheme as the living guidelines to ensure a systematic approach.

Results

In the following sections the identification, systematic analysis, and two separate comparisons between the guidelines are presented. Section Overview provides an overview of the selected living guidelines (and their main characteristics). All selected living guidelines are presented in Table 1. Section inter-guideline comparison gives a more detailed overview of the living guidelines and describes the comparison between the selected living guidelines further referred to as the *inter-guideline* comparison. Section intra-guideline comparison describes the comparison between living guidelines and their (if existing) previous non-living format version further referred to as the *intra-guideline* comparison.

Overview of retrieved living guidelines (descriptive criteria)

Figure 1 (PRISMA) summarizes the identification and selection of the living guidelines. The flow diagram shows the identification and selection process of the available literature according to the PRISMA statement [10]. The initial list of 83 living guidelines was retrieved from the before mentioned internet-based platforms and databases. Out of these, five were excluded since they had not been published yet. Another 12 guidelines turned out to be guidelines in a non-living format or considered non-living according

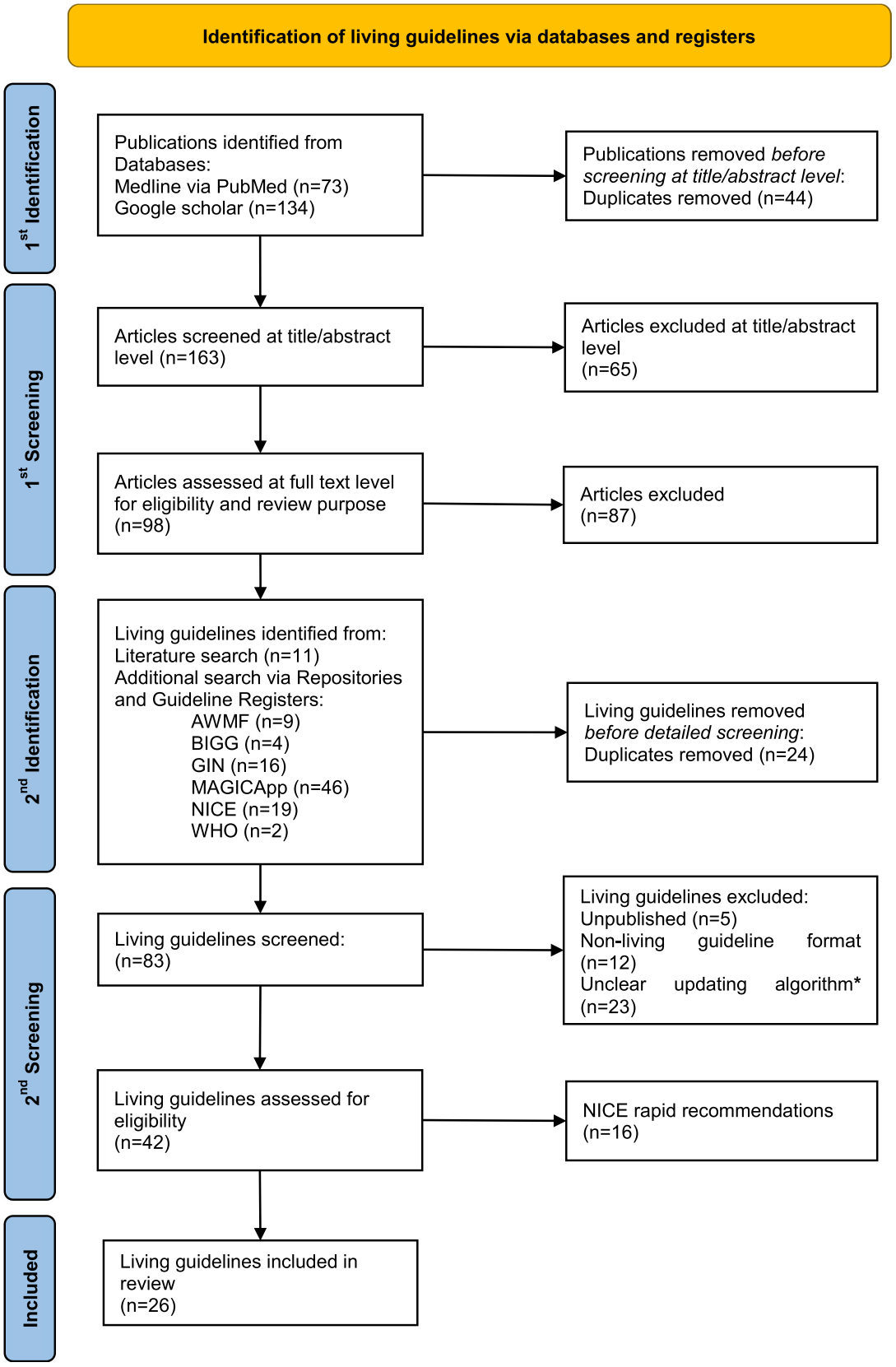

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram. First approach identifying relevant publications and published living guidelines via databases. Second approach to identify further living guidelines via repositories and registers. Abbreviations: n: number of guidelines and publications; AWMF: Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V., BIGG: International Database of GRADE guidelines, GIN: Guidelines International Network, MAGICApp: a digital authoring and publication platform for the evidence ecosystem, NICE: National Institute for Health and Care Excellence, WHO: World Health Organization.*missing information about updating interval or unspecified updating depending on new evidence. Adapted from: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

to the authors. 23 publications were excluded from analyses since update/revision was not clearly stated. One guideline could not be analyzed since it was only available in Japanese.

As a consequence of the current COVID-19 pandemic, almost half of the included living guidelines were related to COVID-19 (n = 12, 46.2%) [11–22] and many COVID-19 guidelines defined as *rapid-guidelines* were published by NICE. Three of these COVID-19 *rapid guidelines* could also be detected in MAGICApp [14–16]. The structure of these three guidelines is like other included guidelines in terms of both template and scope and were therefore added to the analyses. The other 16 NICE COVID-19 *rapid guidelines* were excluded from this review due to their limited scope (e.g. restricted to single recommendations, such as 1.3 "Do not offer a vitamin D supplement to people solely to treat COVID-19, except as part of a clinical trial", [23]). Finally, 26 living guidelines were included in the review analysis [11–22,24–38] (see Table 1). As mentioned almost half of the included living guidelines were related to COVID-19, the other remaining 13 (50.1%) guidelines relate to other medical topics (e.g. Oncology, Gastroenterology, see column 'Field' in Table 1).

To allow the comparison on an intra-guideline and inter-guideline level it was of interest whether the living guidelines were newly created guidelines (*de-novo*) or updated versions of already published guidelines in a previous non-living format. Over half of the retrieved living guidelines are *de-novo* (n = 16, 61, 5%) [11–15,17–20,22,24,27,29,32,35,36], subsequently ten guidelines (38.5%) are updates of existing guidelines [16,21,25,26,28,30,31,33,34,38] (see Table 1).

Regarding the country of publication, nine living guidelines were published in Germany [11,12,24–30], four in the United Kingdom [13–16], four in Switzerland [17–19,34], one in the USA [20], six in Australia [21,22,31–33,36] and one in Canada [38]. Another living guideline was classified as "international" since different countries were involved in the publication [35] (see Table 1).

Inter-guideline comparison – the living process

In the following section the results of the comparison between the 26 selected living guidelines are reported. Criteria to characterize the methodological process of guideline development were defined a priori by the working group and all identified guidelines were analyzed according to these criteria.

The criterion "screening frequency" defines in which interval searches for new evidence are performed. The living guidelines were divided into three subcategories: the first category included *short-term screening interval* guidelines (n = 13, 50%), where new evidence was searched either daily, weekly, monthly or up to an interval of every 3 months [11,14,16–22,32,33,36,38]. The second category (n = 3, 11.5%) – *mid-term screening interval*- included guidelines which screened either after three months, three times a year or up to every six months [12,29,31]. The third category (n = 10, 38.5%) – *long-term screening interval* – included all guidelines which stated either an annual screening (n = 4) [24–26,30], or did not precisely define a screening interval (n = 6) [13,15,27,28,34,35] but reported that an updated version will be published latest after 12 months. Therefore, it was assumed that the screening process itself would be performed at least once a year. Consecutive criterion is "updating frequency". Following the screening of new evidence most guidelines decide whether the newly identified data is sufficient for updating the living guideline, hence the majority of the analyzed living guidelines report such an update interval *depending on screening* (n = 15, 57.7%), but latest at the end of 12 months [13,15,16,24,33–36,38]. Further seven living guidelines (26.9%) reported that an update is triggered on an annual basis [25–30,32] and a smaller fraction of four living guidelines (15.4%) reported that an update is triggered in shorter time intervals (two on a weekly basis [19,21,22], one on a monthly basis [19] and one every 2–3 months [11]).

The "use of living systematic reviews or living meta-analysis" was a further criterion. Seven living guidelines (26.9%) reported the use of such dynamic living reviews (LSR) or meta-analyses where newly identified evidence is included [11,17–22]. These seven living guidelines all belong to the *short-term screening interval* category. No mid- or long-term screening living guideline included LSR or living meta-analyses.

Other criteria of interest were the "reported standards for quality of evidence and strength of recommendations". In total, 25 living guidelines (96.2%) reported that systematic standards were applied, most frequently GRADE [39] (n = 17, 65.4%) [11–22,31–34,36]. All short- and mid-term screening interval living guidelines reported any standard for rating quality of evidence and defining the strength of recommendations (e.g., OCEBM, customized standards) and most long-term interval living guidelines (90%).

Furthermore, the "reporting of how consensus was reached" between the guideline members, was investigated. Out of all analyzed living guidelines, 20 (76.9%) reported the process or applied standards (e.g. Delphi-Method) of reaching consensus [12,13,16,18–22,24–30,32–35,38]. More specifically, this was reflected in 69.2% of the short-term, 66.7% of the mid-term and 90% of the long-term screening interval living guidelines. Other sources included for reaching consensus were an independent expert advisory board, a clinical expert review or a steering committee.

Another criterion was the "reported involvement of other stakeholders" (e.g. patients, caregivers). 19 out of 26 living guidelines (73.1%) reported such an involvement (69.2% of short-term, 66.7% of mid-term, 80% long-term screening interval guidelines) [12–21,25,26,28,30,31,33–36].

As "publication format", most frequently a static PDF version is used. Except for one guideline [31], all living guidelines (n = 25, 96.2%) are available as PDF documents. The second most frequently used format is MAGICApp, which is an online platform for guidelines and evidence summaries. Out of the retrieved living guidelines for this review nearly half of them (n = 14, 53.9%) are available on MAGICApp [11,14–19,21,22,32–36]. The third most frequently used dissemination format is granting free access to an online version mostly on the webpages of related professional societies. Nine living guidelines were published in an online/web-based format (guideline being directly embedded in the website) [14–18,20,21,31,38].

Intra-guideline comparison living vs. non-living guidelines

Intra refers to the comparison of living guidelines with their respective previous versions in a non-living format. 16 living guidelines were created *de-novo* and therefore no comparison with a previous non-living version was possible. After contacting all editors of the selected 26 guidelines via e-mail, 15 responses were received. Considering the responses, three guidelines had to be removed since they were incorrectly labeled as living guidelines by the review group (the editors themselves do not define their guideline as a living guideline) [40–42]. In total, seven guidelines in non-living formats were received and therefore comparable to the updated versions in a living format [43–49] (see Table 2).

Six non-living guidelines are updated at a frequency of three up to five years, whereas for all seven living guidelines, screening for new evidence is performed at least annually (see the analysis in results section inter-guideline comparison). One of the non-living guidelines was regularly reviewed and electronically updated on the publishers' website [47]. Four living guidelines [30,31,33,38] differ in publication format from their respective versions, with the living formats being available on the MAGICApp website, as a mobile application, or online on the publishers' website. All guidelines, whether living or non-living are available as PDF.

Regarding the consensus process criterion, the analysis showed that all seven non-living guidelines describe a consensus process.

Table 1
Table of all living guidelines included in the review with their descriptive criteria.

Publication Country	Year (version)	Professional society	Title	Reference	Format of publication	Field	Screening frequency	Update frequency	Platforms	Applied standard for equality of evidence and recommendations	Use of living systematic reviews	Reporting of process of consensus	Involvement of patients, caregivers or third-parties
Germany	2021 (v3.0)	DEGAM	Schutz vor Über- und Unterversorgung – gemeinsam entscheiden	[21]	PDF	General medicine	annually	depending on screening, at least every 3 years	AWMF, Website of professional society, published in journal	yes	no	yes	no
	2021 (v6.0)	DGVS	S3 – Leitlinie Colitis ulcerosa	[22]	PDF	Gastroenterology	annually	annually	AWMF, Website of professional society, published in journal	yes	no	yes	yes
	2020 (v5.0)	DGGG, DKG	Gestationelle und nichtgestationelle Trophoblasterkrankungen	[23]	PDF	Gynaecology	annually	annually	AWMF, Website of professional society	no	no	yes	yes
	2021 (v5.0)	DGIIN, DIVI, DGP, DGI	S3-Leitlinie Empfehlungen zur stationären Therapie von Patienten mit COVID-19	[8]	PDF, Videos, MAGICApp	COVID-19	weekly	every 2-3 months	AWMF, Website of professional society	yes	yes	no	no
	2021 (v2.0)	DGZMK	Umgang mit zahnmedizinischen Patienten bei Belastung mit Aerosol-übertragbaren Erregern	[24]	PDF	Dentistry	no info	annually	AWMF, Website of professional society	yes	no	yes	no
	2021 (v5.1)	DGN	Diagnose und Therapie der Multiplen Sklerose, Neuromyelitis-Optica-Spektrum-Erkrankungen und MOG-IgG-assoziierte Erkrankungen	[25]	PDF	Neurology	no info	annually	AWMF, Website of professional society	yes	no	yes	yes
	2021 (v2.0)	DGP	Häusliche Versorgung, soziale Teilhabe und Lebensqualität bei Menschen mit Pflegebedarf im Kontext ambulanter Pflege unter den Bedingungen der COVID-19 Pandemie	[26]	PDF	Home Care	every 6 months	annual at the latest	AWMF, Website of professional society, published in journal	yes	no	yes	no
	2020 (v4.0)	DGGG	Diagnostik, Therapie und Nachsorge maligner Ovarialtumoren	[27]	PDF, App	Oncology	annually	annually	AWMF, Website of professional society, OnkologieApp	yes	no	yes	yes
	2021 (v1.0)	DGEpi, DGPH, DGKJ, DGPI	Maßnahmen zur Prävention und Kontrolle der SARS-CoV-2 Übertragung in Schulen	[9]	PDF	COVID-19	3 months	no info	GIN, AWMF	yes	no	yes	yes
United Kingdom	2021 (v1.0)	ERS	Management of hospitalised adults with coronavirus disease-19 (COVID-19): A European Respiratory Society living guideline	[10]	Free PMC article	COVID-19	no info	regualry	BIGG, PubMed	yes	no	yes	yes
	2020 (v1.0)	NICE	covid19-rapid-guideline: managing the long-term effects of COVID-19	[11]	Online version, PDF, MAGICApp	COVID-19	weeky	no info	MagicApp, NICE, GIN, PubMed	yes	no	no	yes
	2021 (v11.0)	NICE	covid19-rapid-guideline: managing COVID-19	[12]	Online version, PDF, MAGICApp	COVID-19	no info	regulary	NICE, MAGICApp, PubMed	yes	no	no	yes
	2021 (v4.0)	NICE	covid19-rapid-guideline: vaccine-induced immune thrombocytopenia and thrombosis	[13]	Online version, PDF, MAGICApp	COVID-19	weekly	depending on screening	NICE, MAGICApp, PubMed	yes	no	yes	yes
Switzerland	2021 (v5.0)	WHO	Therapeutics and COVID-19	[14]	PDF, MAGICApp, WHO App, BMJ	COVID-19	daily	depending on screening	WHO Website, BIGG, MAGICApp, PubMed	yes	yes	no	yes
	2021 (v3.1)	WHO	A living WHO guideline on drugs to prevent COVID-19	[15]	PDF	COVID-19	daily	depending on screening	WHO website, BIGG, MAGICApp, PubMed	yes	yes	yes	yes
	2021 (v1.4)	WHO	COVID-19 clinical management: living guidance	[16]	PDF	COVID-19	monthly	monthly	WHO website	yes	yes	yes	yes
	2021 (v2.3)	WHO	WHO Guidelines for Malaria	[31]	MAGICApp, PDF	Malaria	no info	when new evidence is available	WHO website, BIGG	yes	no	yes	yes
Canada	2021 (March)	Ontario Neurotrauma Foundation	Living guideline for pediatric concussion care	[35]	Web-version, PDF, Community Handouts, family version	Neurology	monthly	no info	Website	yes	no	yes	no
USA	2021 (v1.0)	American Society of Hematology	American Society of Hematology 2021 guidelines on the use of anticoagulation for thrombophylaxis	[17]	Online version, PDF	Medicine, COVID-19	monthly	no info	GIN, PubMed, NICE	yes	yes	yes	yes

(*continued on next page*)

Table 1 (*continued*)

Publication Country	Year (version)	Professional society	Title	Reference	Format of publication	Field	Screening frequency	Update frequency	Platforms	Applied standard for equality of evidence and recommendations	Use of living systematic reviews	Reporting of process of consensus	Involvement of patients, caregivers or third-parties
			in patients with COVID-19										
Australia	2021 (January)	ATAGI	Australian Immunisation Handbook	[28]	Online version, mobile App	Vaccination	3 times per year	depending on screening	GIN	yes	no	no	yes
	2021 (v1.2)	ANZMUSC, Clinical Trials Network, ARA, Cochrane Musculoskeletal, NPS MedicineWise consortium	An Australian Living Guideline for the Pharmacological Management of Inflammatory Arthritis	[29]	MAGICApp, PDF	Rheumatology	every 3 months	annually	MAGICApp	yes	no	yes	no
	2021 (versions different for each chapter)	Stroke Foundation	(Australian and New Zealand) Clinical Guidelines for Stroke Management	[30]	MAGICApp, PDF	Neurology	prioritised topics are under monthly surveillance, others 6-12 months	no info	MAGICApp	yes	no	yes	yes
	2021 (v42.0)	National COVID-19 Clinical Evidence Taskforce	Australian guidelines for the clinical care of people with COVID-19	[18]	MAGICApp, online version, PDF	COVID-19	weekly	weekly, when new evidences becomes available	MAGICApp	yes	yes	yes	yes
	2021 (v1.0)	National COVID-19 Clinical Evidence Taskforce	Australian Guidelines for SARS-CoV-2 infection prevention and control of COVID-19 in healthcare workers	[19]	MAGICApp, PDF	COVID-19	weekly	when new evidence becomes available	MAGICApp	yes	yes	yes	no
	2020 (v1.2)	NHMRC	Australian Evidence-Based Clinical Guidelines for Diabetes	[33]	MAGICApp, PDF	Diabetes	monthly	depending on screening	MAGICApp	yes	no	no	yes
International	2021 (v2.3)	WHO	WHO Guideline on self-care interventions for health and well-being	[32]	MAGICApp, PDF	General health and well-being	when new evidence becomes available	when new evidence becomes available	MAGICApp, WHO website, BIGG, PubMed	yes	no	yes	yes

Note. DEGAM = Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin e.V., DGVS = Deutsche Gesellschaft für Gastroenterologie, Verdauungs- und Stoffwechselkrankheiten, DGGG = Interdisziplinäre Leitlinie der Deutschen Gesellschaft für Gynäkologie und Geburtshilfe, DKG = Deutsche Krebsgesellschaft e.V., DGIIN = Deutsche Gesellschaft für Internistische Intensivmedizin und Notfallmedizin, DIVI = Deutsche Interdisziplinäre Vereinigung für Intensiv- und Notfallmedizin, DGP = Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin, DGI = Deutsche Gesellschaft für Infektiologie, DGZMK = Deutsche Gesellschaft für Zahn-, Mund- und Kieferheilkunde, DGN = Deutsche Gesellschaft für Neurologie, DGP = Deutsche Gesellschaft für Pflegewissenschaft e.V., DGEpi = Deutsche Gesellschaft für Epidemiologie, DGPH = Deutsche Gesellschaft für Public Health, DGKJ = Deutsche Gesellschaft für Kinder- und Jugendmedizin, DGPI = Deutsche Gesellschaft für Pädiatrische Infektiologie, ERS = European Respiratory Society, NICE = National Institute for Health and Care Excellence, WHO-Iris = World Health Organization, Institutional Respository for Information, ATAGI = Sharing, National Health and Medical Research Council, Australian Technical Advisory Group on Immunisation, ANZMUSC = Australia and New Zealand Musculoskeletal, ARA = Australian Rheumatology Association, NHMRC = National Health and Medical Research Council, MAGICApp = Making GRADE the Irresistible Choice, AWMF = Arbeitsgesellschaft der Wissenschaftlichen Medizinischen Fachgesellschaften, GIN = The Guidelines International Network, BIGG = The International Database of GRADE Guidelines.

Table 2
Table of the living guidelines compared to their preceded versions.

Title	Reference	Format	Format of publication	Screening Frequency	Update Frequency	Number of evidence-based recommendations	Number of consensus-based recommendations	Description of consensus-process	Involvement of patients, caregivers or third-parties	Public consultation before publication
S3 – Leitlinie Colitis ulcerosa	[22]	living guideline	PDF	annually	annually	96 (63**)	57 (37**)	yes	yes	yes
S3 – Leitlinie Colitis ulcerosa	[40]	non-living guideline	PDF	no info	after 4 years	99 (64**)	55 (36**)	yes	yes	no
Gestationelle und nichtgestationelle Trophoblasterkrankungen	[23]	living guideline	PDF	annually	annually	none (S2k)	73 (100**)	yes	yes	no
Gestationelle und nichtgestationelle Trophoblasterkrankungen	[41]	non-living guideline	PDF	no info	at least after 5 years	none (S2k)	71 (100**)	yes	yes	no
Diagnose und Therapie der Multiplen Sklerose, Neuromyelitis Optica Spektrum und MOG-IgG-assoziierte Erkrankungen	[25]	living guideline	PDF	no info	annually	none (S2k)	223 (100**)	yes	yes	yes
Diagnose und Therapie der Multiplen Sklerose	[42]	non-living guideline	PDF	no info	after 3 years	*not quantifiable	none (S2e)	yes	no	no
S3-Leitlinie Diagnostik, Therapie und Nachsorge maligner Ovarialtumoren	[27]	living guideline	PDF, App	annually	annually	52 (51**)	49 (49**)	yes	yes	yes
S3-Leitlinie Diagnostik, Therapie und Nachsorge maligner Ovarialtumoren	[43]	non-living guideline	PDF	no info	after 3 years	45 (52**)	41 (48**)	yes	yes	no
Australian Immunisation Handbook	[28]	living guideline	PDF, Website, App	3 times per year	depending on screening	not defined	not defined	no	yes	no
Australian Immunisation Handbook	[44]	non-living guideline	PDF	regularly	no info	not defined	not defined	yes	yes	yes
(Australian and New Zealand) Clinical Guidelines for Stroke Management	[30]	living guideline	PDF, MAGICApp	monthly	depending on screening	191 (71**)	79 (29**)	yes	yes	yes
(Australian and New Zealand) Clinical Guidelines for Stroke Management	[45]	non-living guideline	PDF	no info	every 3-5 years	214 (64**)	121 (36**)	yes	yes	yes
Living guideline for peiatric concussion care	[35]	living guideline	PDF, Webversion	monthly	depending on screening	59 (51**)	56 (49**)	yes	no	no
Guidelines for diagnosing and managing pediatric concussion	[46]	non-living guideline	PDF	no info	after 3 years	60 (77**)	18 (23**)	yes	yes	no

Note. LG = living guideline, non-LG = non-living guideline, S2e and S2k, as well as S3-Guidelines are classifications of different Guideline-development levels, defined by AWMF. S2e-Guidelines only contain evidence-based recommendations. S2k-Guidelines only contain consensus-based recommendations. S3-Guidelines are the union of these two levels. The Stroke living guidelines can be found in MAGICApp divided by chapters. These numbers are a total sum of all chapters. *Recommendations not quantifiable; according to authors former guideline does not meet the requirements for guideline standards according to AWMF. **Relative numbers.

In comparison, six living guidelines reported a consensus process, with one not doing so [31].

As described in Table 2, two pairs had no quantifiable or no defined number of recommendations. The number of recommendations in the Australian Immunisation Handbook was not defined and the comparison between the versions of the multiple sclerosis guideline was not included since the classification changed from formerly evidence based to now consensus-based in the living format [28,31,45,47]. Considering the relative numbers of evidence-based recommendations, a paired two-sample t-test between five guideline pairs showed no significant difference in the *evidence*-based recommendations between living guidelines and their non-living versions ($t_{(4)} = 0.74$, $p = .50$). Additionally, another paired two-sample t-test equally did not show a significant difference between the *consensus*-based recommendations in the living and the preceded non-living guidelines ($t_{(4)} = 0.74$, $p = .50$).

Five out of the seven non-living guidelines did not carry out a public consultation. Two non-living guidelines stated that a public consultation was conducted [47,48]. Four living guidelines reported to have posted a version of the guideline online for public comment [25,28,30,33]. In addition, six living and non-living guidelines, with the exception of one living guideline [38] and one non-living guideline [28], involved non-medical stakeholders in the development process.

With reference to the three questions mentioned above (see comparison with non-living guidelines under methods), the authors and editors stated that regular and rapid updates are the key argument in deciding for the living format. According to the editors, published high-quality studies can be integrated into the guideline in a timely manner, which is not feasible in a non-living format. The living format is perceived as a continuation of the process of guideline optimization. It allows a rapid further development of the evidence situation and topicality about methodological knowledge, which is important for patient care. In addition, the large number of publications on COVID-19 makes it necessary to update this topic repeatedly in short intervals, according to the editors. An overview of the editors' and authors' responses can be found in the Table 3.

Discussion

This review aims to best of our knowledge for the first time at assessing the prevalence and formal characteristics of living guidelines in the field of medicine. The "evidence-practice" or "know-do" gap [50] has been described for many years. The concept of living guidelines [51] might contribute to close this gap. Therefore, a selective search of literature and guideline repositories was conducted yielding in a total of 83 living guidelines. Applying stricter definitions of a living process (update within one year) which is described in the literature [2], only 26 living guidelines could be considered for further analyses. Of note, out of the initially identified n = 83 living guidelines, n = 23 had to be excluded due to missing information regarding specified update interval and thus could not be characterized as genuinely living approaches. This result shows very impressively the lack of an overarching understanding of *Living* and in particular the updating process. As already showed in the introduction according to Akl et al. (2017), the updating process of a living guideline is particularly characteristic [5]. The rapid increase in Living Guidelines in the Covid-19 pandemic illustrates the importance of rapid recommendations as new evidence becomes available.

It can be speculated that this finding reflects the need to increase flexibility and release new versions depending on new evidence in the field of medicine. This flexibility in not defining a periodicity might be to the advantage of the real clinical needs [52].

Even though availability of living guidelines could be observed in the last five years by 83 (respectively 26) identified publications, almost half of these guidelines were related to COVID-19. It can be

Table 3
Responses from authors and editors of the included living guidelines.

Responses	Considerations for choosing a living format	Essential difference between non-living and living format
Response 1	no info	■ main difference: methods for searching for new evidence to update the guidelines ■ living guideines: monthly search for new publications, historically: search for new literature every 3-7 years ■ content updates only in response to relevant new evidence
Response 2	■ rapid further development of the evidence base ■ dynamic evolution of infection incidence ■ it is timely in light of methodological findings and on principle within the COVID-19 evidence ecosystem and its focus at living reviews and living guidelines	no info
Response 3	■ always intended to create a living guideline ■ expected a rapid evolution of evidence that would be important for patient care	no info
Response 4	■ to keep the guideline continuously up to date	■ Essential difference: The administration of maintaining and updating the living guideline
Response 5	■ decision by professional society to change several guidelines with the aim of achieving greater topicality	■ shorter update cycle, thus also less extensive research ■ to improve quality through higher topicality
Response 6	■the flood of publications on COVID-19 necessitated several updates on this topic	■ Normal guidelines are updated only every 4-5 years; high-quality studies published in the meantime cannot be integrated into the guideline in a timely manner ■ living guideline has clear advantages, but is more costly in terms of continuous updating
Response 7	■did not really change the guideline to the "living guideline" principle ■ while creating the current guideline, they looked for a concept that would allow regular and rapid updating: the "living guideline" principle came in handy	■old updating principle is burdensome and lengthy (because it is always a partial restart) ■ the "living guideline" principle keeps the guideline always fresh, is expectable (namely at least 1x / year) and never lets the process of guideline optimization come to a standstill (in a positive sense) ■ It is also a good tool to quickly address problems and criticisms that arise in the implementation and/or everyday use in the guideline
Response 8	■ New therapy trends arise during the year, which affects only a few recommendations but is relevant for therapists and payers	■ To increase applicability/usability through timeliness (Guideline will not be used if it is revised only after 3-5 years)

Note. N = 8, in order to preserve the anonymity of the authors and editors, their names are not mentioned.

speculated that the needs and circumstances of the pandemic (to deliver new evidence on time) might have served as an acceleration for the development and use of living guidelines. In order to implement up-to-date recommendations, platforms are needed that enable rapid publication. It was observed on MAGICApp that a fraction of the online entries comprised only a few single recommendations to a specific clinical question. Maybe web-based tools will make it easier in the future to address distinct clinical questions and their corresponding recommendation without being part of a larger, more comprehensive guideline. This aspect accounts for the flexibility of a living guideline in terms of adapting its content.

Another aspect is the flexibility in terms of formal appearance and publication format. Except for one, all evaluated living guidelines still use a static PDF version, so PDF is still the most common format, complemented in half of the cases by online tools such as MAGICApp or in fewer cases customized web-based versions and specifically developed apps which may increase the use of the guideline at point of care. It might be of further interest to investigate the impact the publication format has on the implementation and use of living guidelines.

The majority of available living guidelines screen for new evidence in short-term intervals (within the next three months). This tendency towards very short intervals is presumably related to the need for timely new advice during the COVID-19 pandemic (9 out of 13 living guidelines using short-term intervals were related to COVID-19). In general, screening and updating of the guideline may fit the need of the area of interest and the expected amount of new evidence and should be clearly stated by the authors when describing the process of updating.

Akl et al. [5] proposed in their series of articles that living systematic reviews (LSR) serve as a basis for translating new evidence into clinical practice recommendations. Roughly one quarter of the selected living guidelines reported the use of such LSRs all of which belonged to the short-term screening category. This point may be interpreted that the use of LSR is yet not fully an integral part of living guidelines and may be suitable especially for guidelines with more frequent screening and updating cycles.

To evaluate potential differences to previous non-living versions, seven matching predecessor versions were identified and used for head-to-head comparisons between guidelines. According to the editors, the main difference from a previous non-living version appears is rooted in the methodology of the respective guidelines regarding the process of identifying new evidence to update existing recommendations. However, the living format is more complex due to a continuous update process of its recommendations. Furthermore, the benefit of the MAGICApp was underlined as a guideline development and publication platform, integrating the GRADE methodology with its update capacity. Transparent reporting of applied standards (reaching consensus, grading of evidence, strength of recommendations) and involvement of third parties and public consultations before publication were applied by most (5 out of 7) living- and non-living guidelines in the intra-comparison. Given the limited number of guidelines in the intra-guideline comparison, this finding must remain purely descriptive. Nevertheless, no evidence was found that living-formats necessarily lack the participation of patients and/or care-givers or are less open to external contributions. By comparing the number of recommendations no statistically significant differences could be observed between living and non-living versions. This might imply, that living guidelines do not have to be necessarily shortened (regarding the extent of recommendations) to ensure efficient and more frequent updating. However, the results must be interpreted with caution due to a limited amount of data and therefore must be considered exploratory.

The synopsis of all included guidelines displays that living guidelines might not be considered as a novel approach, but rather as an optimization of standard procedures [53]. Previous reviews [5,6] could not find systematic standards for living guidelines in methodological manuals, the practical implementation analyzed in this review concludes also no generic concept of living guidelines.

In the methodological chapters of guidelines or supplementary methodological publications guideline's editors describe the process of development. Who was involved, which work groups were formed and performed which tasks in the development and how consent was reached. Considering the described processes (which varied in the degree of structure, e.g. how many groups were defined, how consensus was reached) and from the perspective of this review's authors Figure 2 demonstrates necessary steps to ensure a standardized development and therefore also the quality of a living guideline. The update of living guidelines is a recurrent process always following the same procedure. The GRADE approach provides a framework, supporting and guiding the iterative process of evaluating available evidence, implementing, and developing evidence-based recommendations as well as administrating every step.

A limitation of this review could be that even by using the term "living" as a search string, not all existing living guidelines were identified. On the one hand, it turned out that some guidelines were declared as "living", which after the queries were not defined as a living guideline by the respective editors and authors. One of the a-priori defined criterion was an update interval within 12 months. A discussed advantage of living guidelines is the independence of fixed time intervals for updating and only to revise on demand if new evidence is sufficient for triggering an update [52]. Therefore, some actual living guidelines might have been excluded, which formally could have been considered *living*. On the other hand, the question arises as to whether guidelines exist that follow the formal criteria of a living process but are not labeled as living guideline. The current COVID-19 pandemic and its need for timely evidence-based recommendations might have accelerated the use of living formats. By almost half of the selected guidelines being related to COVID-19 there is a clear bias towards this topic in the results of this scoping review. Due to the non-exhaustive search strategy, the present review makes no claim to completeness of all available living guidelines. Nevertheless, to elicit a broad spectrum of living guidelines, generic keywords were used. The number of duplicates (roughly a fifth part of the total amount of findings) indicates that published living guidelines are disseminated on multiple platforms and the applied search method might have covered the majority of the currently available living guidelines in English and German language at the time of search. In this context the possibility of bias by selection of German as second language should also be mentioned. Since the present review is a first selective analysis, very broad criteria were chosen. For future work, established criteria for assessing the quality of a guideline (e.g. the AGREE II tool) should be used as a standardized procedure. The lacking systematic quality evaluation should be considered as a potential limitation of our work.

The fact that there is no uniformity between the living guidelines indicates how important a standard procedure is. A checklist supporting the development of a living guideline and generating a uniform standard would substantially contribute to a homogenization of living concepts (in areas where it serves ensuring the quality of the guideline). By screening the structure and the procedure of the living guidelines and partly their previous versions, criteria of a living process could be elaborated.

Conclusion

It can be concluded that the development and therefore availability of living guidelines is on the rise. Recently published living guidelines varied in the range of extensive and comprehensive versions similar to previous non-living formats to short and single-

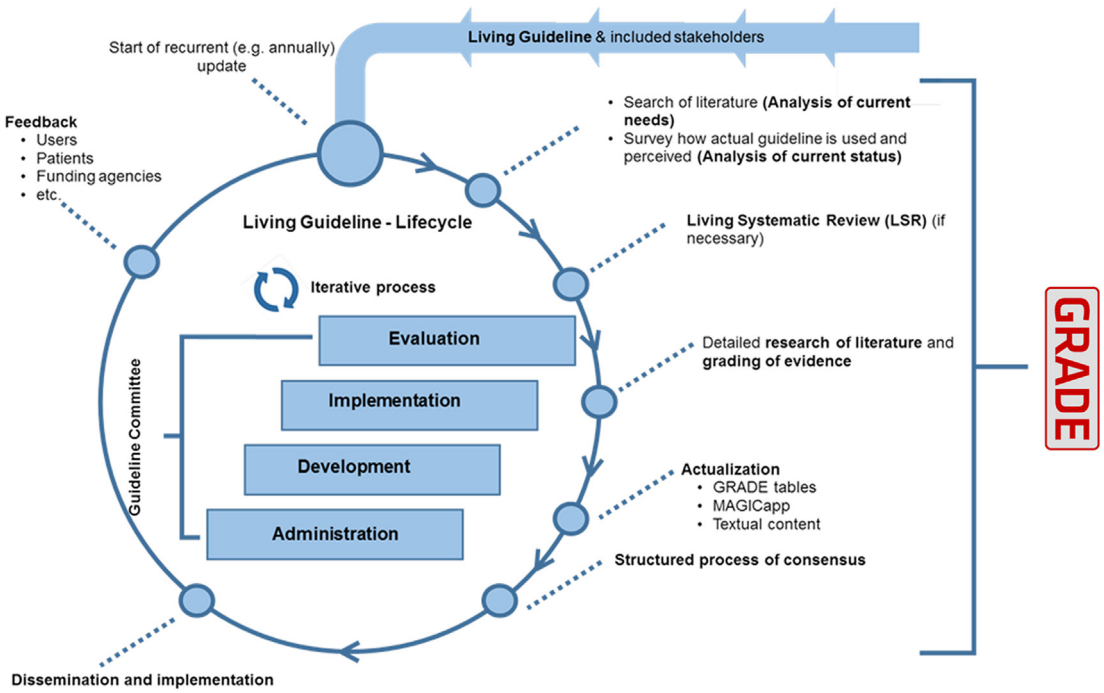

Figure 2. The iterative process of the living guideline following the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach.

recommendation guidelines focusing on specific clinical questions. A clear trend towards shortening the living guidelines when adapting from non-living to living could not be observed. To ensure the guideline's quality, tools tailored to assess the development and especially the update process could be a useful and necessary part in the trend towards faster updates and therefore better-informed guidance.

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