



Conversational agents for pharmaceutical use: insights from the eCCo database

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Abstract

Conversational agents are computer programmes designed to replicate bidirectional human conversation through spoken or written language, potentially supplemented with nonverbal features. The eCCo database is a searchable repository of primary studies on conversational agents in health and well-being. It catalogs 657 papers currently, published between 1991 and 2022; 51 address the use of medicines. Most of these papers focus on usability rather than rigorous effectiveness or implementation research, underscoring a need for more robust evaluation. The largest category of conversational agents for pharmaceutical use consists of non-embodied agents ($n = 24$), followed by virtual embodiment only ($n = 19$), most using virtual humans ($n = 16$). This database facilitates the comparison and appraisal of existing research in this field, while contributing to a more nuanced understanding of this technology through multidimensional attributes. We aim to enhance the database accuracy and expand its completeness beyond 2022 with the support of the global research community.

Keywords Artificial intelligence · Conversational agents · Digital health · Medication adherence · Self-management · Virtual humans

The evolution of conversational agents: from disembodied rule-based systems to virtual humans with advanced capabilities

Conversational agents are computer programmes that replicate bidirectional human conversation through spoken or written language, potentially supplemented with nonverbal features [1].

ELIZA, developed at MIT in the mid-1960s, is credited as the first computer programme to simulate a conversation by adopting the role of a psychotherapist. ELIZA was disembodied, as it lacked any virtual or physical persona; it was delivered solely through a computer interface, users typed their questions or statements, and the programme responded in text form [2].

In simpler models, such as ELIZA, the dialogue engine is rule-based. This means that the system component that controls the flow of conversation is based on rules and scripts that provide a predefined set of responses to user inputs. When using free text, user input is recognised only if it matches keywords, and the system's outputs are limited to question-and-answer pairs. These systems can incorporate synthetic voice output, allowing them to "speak" their responses aloud using text-to-speech software. Rule-based conversational agents are unable to grasp the nuances of human conversation and lack the ability to adapt to new situations. However, they can still be chosen due to easier deployment and scalability. In some cases, they can operate on relatively simple devices and function without a constant internet connection, making them particularly suitable for low-resource settings or areas with limited access to high-speed internet. An example of these scalability features is the

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prototype of a conversational agent to support medication adherence as part of a multi-behaviour intervention for older people with type 2 diabetes [3].

Powered by advances in artificial intelligence (AI), contemporary conversational agents often leverage natural language processing to understand textual user input, without being constrained by keyword matching with a predefined database. Additionally, deep learning algorithms, a subset of machine learning, have significantly improved the accuracy and efficiency of speech recognition. Another notable advancement are natural language generation algorithms, which enable agents to produce human-like responses to user inputs, resulting in more natural and engaging interactions. Currently, one of the most powerful natural language generation algorithms is Generative Pretrained Transformer 4 (GPT-4).

The integration of speech recognition and natural language generation with a human representation, on screen or in the form of humanoid robots, is the ultimate evolution. This integration, combined with non-verbal language, such as gestures and facial expressions, has created more empathetic interactions, bridging the gap between technology and emotional connection. One example is the World Health Organization's Smart AI Resource Assistant for Health (SARAH), a prototype of a digital health promoter, available in 8 languages [4].

The promise of conversational agents in care provided by pharmacists

In a narrative review on the use of chatbots in pharmacy practice and education, Ramadhani highlighted several roles for this digital technology, from providing educational content about medication, offering personalised reminders and tailored medication adherence support, to streamlining pharmacists' workflows by automating routine tasks, such as processing refill requests or triaging patient queries [5]. However, the review's scope is broader than its title suggests, as many of the references in its extensive list do not cover the pharmacy-specific use of conversational agents.

Jongen & Rijcken [6] referred to digital pharmacists as virtual humans developed to simulate pharmaceutical care through AI, interacting with users via text or speech. They suggested that within blended approaches, digital pharmacists may assist with medication supply, educate persons about their medicines, support medication adherence, and take on a coaching role [6]. By handling more straightforward queries, they could allow pharmacists to focus on complex cases, which benefit more from human intervention. This aspect is of particular importance given the shortage of pharmacists, particularly in low-income countries [7], and the increasing demands of an ageing population. Jongen and

Rijcken [6] showed optimism about the impact of conversational agents on the 5 components of pharmaceutical care defined by the American Pharmacists Association. These include strengthening the professional relationship between pharmacists and patients, collecting and recording health data, and reviewing health data to shape pharmaceutical care plans through the analysis of interactions with conversational agents.

The eCCo database of conversational agents: insights for medication use and beyond

As part of the project "Harnessing the Power of Conversational e-Coaches for Health and Well-being Through Swiss-Portuguese Collaboration" (eCCo; <https://ecco.esel.pt>), we conducted a literature search for an evidence map on conversational agents in health and well-being [1]. Our search, which covered papers published until 2022, indicates a long-term growth in published papers, with distinct phases: a slow growth phase until the early 2000s, with minimal increases over time; a gradual increase phase starting in the early 2000s, with a relatively moderate growth rate; and a steep surge beginning around 2020, in what appears to be an exponential increase until 2022. This pattern is common in emerging trends, which shift from niche to mainstream, as illustrated by the number of publications in the field of AI [8].

One of the planned outputs of our evidence map was an open, searchable database on conversational agents for health and well-being, which is expected to foster collaboration, by pinpointing expertise across international centres, and avoid unnecessary duplication of efforts by building upon existing work.

This database was populated by eligible primary studies from the search conducted as part of our evidence map [1] and is available at <https://ecco.humantech.institute/>. It includes filters to support topic-specific exploration, such as publication and study type, plus a free-text search bar in article titles.

The eCCo database catalogs currently a total of 657 papers, published between 1991 and 2022. Given the substantial number of eligible papers, we were unable to conduct independent double extraction of data, as originally planned in the evidence map protocol [1]. As quality control we conducted iterative independent checks on random subsets of the extracted data, followed by formative feedback to the team. In addition to bibliographic data for each paper, we extracted data on other attributes, such as the nature of the health intervention, based on the international Classification of Health Interventions (ICHI) [9]. According to ICHI, the intervention target represents the entity receiving the health intervention, with pharmaceutical use classified as an intervention target that captures behaviours on medicine use.

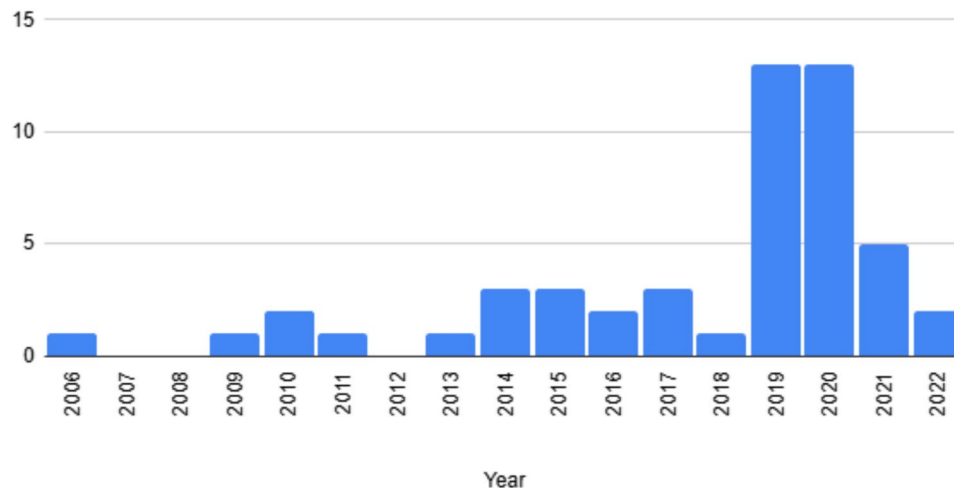


Fig. 1 Yearly distribution of papers on conversational agents targeting pharmaceutical use in the eCCo database

A total of 51 papers on conversational agents addressing pharmaceutical use are part of the eCCo database, covering the period from 2006 to 2022. While the yearly counts shown in Fig. 1 are relatively small and should be interpreted with caution, they highlight an overall growth trend in these publications, suggesting increasing interest in this intervention target.

Table 1 depicts key findings of the 51 papers on conversational agents addressing pharmaceutical use. The predominance of usability evaluation studies, combined with the lower number of randomised controlled trials (RCTs), suggests that research on conversational agents for pharmaceutical use is still in an exploratory or developmental phase.

The fact that 14 papers included external human intervention by health professionals, including pharmacists or pharmacy staff, aligns with blended care models. Under this umbrella, possibilities include conversational agents referring cases to pharmacists or other healthcare professionals and integrating the digital tool into their workflow (for example, for data collection on behaviour such as physical activity or medication-taking).

The largest category of conversational agents for pharmaceutical use consists of non-embodied agents (24 papers), followed by virtual embodiment only (19 papers). This preference may be driven by practicality, scalability, and lower development costs compared to physical embodiments. Among the studies with embodied agents, most used virtual humans (16 papers). Taken together these data show that conversational agents can have a role in supporting medication use regardless of their embodiment and persona.

Thirteen papers featured conversational agents with proactivity, that we defined as the agent's ability to provide relevant information or perform appropriate actions without explicit user requests. This category was not included in

a more recent classification of healthcare conversational agents [10]. However, proactivity can add value by anticipating and addressing user needs, thereby enhancing personalisation and engagement.

Papers in our database support the roles posited by Jongen and Rijcken [6] for conversational agents: assisting with medication supply [11], educating persons about their medicines [12], supporting medication adherence [13], and taking on a coaching role [14]. However, included papers do not necessarily support these roles as part of blended care delivered by pharmacists or through conversational agents embodying the role of a pharmacist. Instead, embodied conversational agents often take on the role of a virtual human coach rather than explicitly representing a pharmacist [15].

Concluding remarks

The eCCo database provides a searchable repository of primary studies on conversational agents in health and well-being, including those addressing pharmaceutical use, making it easier to locate, compare, and critically evaluate existing research in this field. To our knowledge, there are currently no other databases offering this level of thematic specificity and structured access to primary evidence in this rapidly evolving field. By cataloging multidimensional attributes of conversational agents, the database contributes to a more nuanced understanding of this technology.

We expect the database to evolve into a dynamic tool, disseminated to the research community, updated with its contributions, and curated by our research team. One limitation of the database is that data extraction was performed by single researchers. Contributions from the research community may help mitigate this limitation by identifying

Table 1 Summary of key findings on conversational agents for pharmaceutical use in the eCCo database

Category	Attribute	Findings (<i>N</i> =51 articles*)
Nature of literature on conversational agents	Country of the study (corresponding author)	USA (17); Australia (5); Portugal (5); France (3); Taiwan (2); The Netherlands (2); New Zealand (2); UK (2); Switzerland (2); Macedonia (2); Japan (2); India (2); Others (6)
	Study types	Usability evaluation (37); RCT (9); Other longitudinal study designs (7)
Characteristics of health interventions using conversational agents	Additional end-users	Family or caregivers (13); External human intervention; such as pharmacists; physicians or nurses (14)
	Specific patient conditions	Diabetes (3); Urinary Incontinence (2); Schizophrenia (2); Others (10)
	Intervention Actions	Assessment (21); Education (30); Social Support (15); Behaviour change (20)
	Intervention target (in addition to pharmaceutical use)	Physical activity (16); Eating (14); Symptoms management (21); Alcohol consumption (4); Tobacco (3); Hygiene (3); Sleep and rest (2); Sexual and reproductive behaviour (2)
Characteristics of the automated conversations conducted in health interventions	Input modalities of the conversational agent	User inputs: Predefined options (28); Voice (24); Free text (21); still images (2); Both voice and free text (9) Indirect inputs: from external devices (e.g., smartwatches)(13); from computer vision (4)
	Output modalities of the conversational agent	Voice (36); Text (35); Both voice and text (20); Other modalities (e.g., gestures, facial expressions) (17)
	Embodiment of the conversational agent	Type of embodiment: Only Virtual (19); Only physical (5); Physical + Virtual (1); No Embodiment (24) Form of the embodiment: Virtual humanoid (16); Physical non-humanoid robot (4); Physical non-humanoid (e.g., pet) (3); Virtual non-humanoid (e.g. pet, 2); Virtual non-humanoidrobot (1); Physical humanoid robot (1)
Characteristics of the agents used in health interventions	Delivery channel	Mobile application (20); Existing messaging app (e.g., Telegram, Facebook Messenger, 10); Website Application (9); Standalone device with dedicated software (6); Mobile robot (4); Desktop application (4)
	Other characteristics	Conversational agent emotions (14); Proactivity (13); User's sentiment detection (3); Conversational agent personality (2)

*Some attributes are not mutually exclusive

potential inaccuracies. Additionally, expert review cycles will be conducted, allowing domain specialists to assess data accuracy, identify inconsistencies, and refine classification criteria. User feedback mechanisms will be integrated, enabling continuous improvements based on insights from researchers and practitioners. Furthermore, we plan to strengthen completeness of our database beyond 2022, by testing AI-assisted tools to support and streamline data extraction and classification.

Studies in the eCCo database showed a preference for anthropomorphic designs in agents supporting medication use: of the 19 papers featuring virtual embodied agents, 16

used virtual humans. This aligns with findings in the literature [16], which suggest that realistic, human-like representations are often perceived as more trustworthy than other representations.

There is a need for rigorous research examining the effectiveness of conversational agents in pharmaceutical use and their implementation in real-world settings, to strengthen their claimed benefits. For example, Bramanti et al. consider voice assistants as a category of conversational agents capable of engaging in interactive dialogue [17]. Their systematic review on the use of this technology for managing noncommunicable diseases included 8 studies; of these, only

2 were RCTs and a third was referred to as a “semi-RCT”, a designation that is not standard. The use of effectiveness-implementation hybrid studies [18] may shorten the timeline between evidence generation and adoption and scale-up of this technology by simultaneously addressing the effectiveness of conversational agent interventions and their implementation in real-world settings. A relevant example is the My Diabetes Coach trial, a mobile app-based conversational agent designed to support self-management in persons with type 2 diabetes, including medication-taking [15]. This hybrid study assessed both effectiveness (glycated hemoglobin and health-related quality of life) and implementation outcomes, such as engagement patterns. This dual focus helps accelerate the transition from research to practice and supports healthcare systems and policymakers in making more informed decisions.

Furthermore, the market penetration of conversational agents for pharmaceutical use featured in the eCCo database remains uncertain; it is likely that a significant gap exists between prototypes or pilot studies and broader market access. The evaluation of these digital health technologies through assessment frameworks is expected to address concerns regarding accuracy, privacy, and security, fostering trust among pharmacists and primary users, encouraging adoption in the future. While a diversity of frameworks for digital health technology assessment exists, both in the academic literature [19] and through private initiatives [20], authorities in several countries have also taken steps to develop and implement regulatory approaches, such as the UK's Digital Technology Assessment Criteria for Health and Social Care (DTAC) [21], and the French standard for the assessment of digital services in the mHealth sector [22].

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Conflicts of interest The authors declare that they have no conflicts of interest.

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