Bibliographic Analysis of Medication Adherence and Use of Reminders

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ABSTRACT

The study aimed to highlight the work of different researchers and publication platforms in disseminating knowledge about medication adherence and the use of reminders. The trend of publication, prominent contributors, funders, countries, and shift in the use of reminders was encompassed based on bibliographic and text analysis. Articles published in the last 10 years between 2011 to 2020 were extracted from the Scopus database. Data of 1007 articles were analysed in VOS viewer to obtain graphs and network diagrams. Most of the research was done in the United States (526 documents). The research conducted by Harvard Medical School had the maximum number of publications (42). In recent years there has been active publication from the countries like Norway, France, Singapore, and China. It was also found that studies at the beginning of the decade were mainly focused on SMS and mobile phone interventions. The trend has shifted towards intentions like mobile applications, and the term "mhealth" is used more in the current years.

KEYWORDS

Bibliographic Analysis, Medication Adherence, Medication Compliance, Reminder, VOS Viewer

INTRODUCTION

The fluid nature of medication-taking behaviour has been a subject of study for many years. Scientists, researchers and scholars have tried to solve the problem of medication non-adherence but have failed to reach a consensus. What kinds of reminders are effective for various diseases and varied patient types? and what is the improvement in adherence rate sustained over time? (Singh & Varshney, 2019a) remains a baffling question to the researchers. Medication non-adherence is a significant impediment to attaining optimum results in chronic illness (Saha et al., 2021b). Adherence to medication therapy is a dynamic process. There are various stages like initiation, maintenance, and discontinuation. The process is influenced by numerous factors like the type of disease, patient, regime, treatment, health care system, socioeconomics etc. (Brown & Bussell, 2011). Non-adherence to the prescribed medication is caused due to several factors: patients' beliefs, poor communication from service providers, depression, medication dose frequency etc. (Saha et al., 2021a). It has been postulated that support and continuous behavioural intervention are essential to have adherence over some time. A network meta-analysis study conducted by Wiecek et al. (2019) identified multicomponent

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interventions like rewards, attitude, education and technology to improve adherence over some time. According to the authors, attitude dealt with a change of behavioural purpose constructed on the "Theory of Planned Behaviour". Education dealt with information shared by healthcare professionals. Technology dealt with systems/instruments/interventions that helped take the medication, and it worked best in an association of reward with it.

The large number of studies conducted on medication adherence and means to increase adherence indicate the importance of this problem. There is a lack of literature based on the bibliographic analysis of medication adherence and reminders used to improve adherence. This study tries to highlight the work done by different researchers and the publication platforms (journals) in disseminating the knowledge to the readers at large. This study attempts to encompass the trend of publication, the prominent contributors, funders, countries and shift in the direction of reminders used, based on bibliographic and text analysis.

BACKGROUND

Medication adherence is the process by which patients take the correct dose of medication at the right time as prescribed by their physician (Vrijens et al., 2012). Medication non-adherence is a global public health challenge (M et al., 2021). Studies on diabetic patients show that nearly 33% of oral medications and 38% of insulin for type 2 diabetes are not adhered to (Krass et al., 2015). A clinical trial using electronic monitoring devices on Children's Oncology Group found that the adherence rate was less than 95% for 44% of the patients (Bhatia et al., 2015).

Studies confirm that reminders for medication adherence are desirable (Tran et al., 2013) and to increase the adherence rates, different types of reminders may be used (Singh & Varshney, 2019b). The percentage of patients who wish to receive such reminders are estimated to be more than 80 (Piette et al., 2010). The type of reminders may vary from simple and static reminders for a single dose to active complex reminder systems that remind patients to take the medication until it is still safe to consume it (Varshney & Singh, 2020). Advanced technological devices like smartphones and electronic pillboxes are used as reminders to increase adherence (Basit et al., 2020). Reminders through mobile applications have improved adherence in patients suffering from cancer, diabetes, HIV, hypertension, and other chronic diseases (Beauchemin et al., 2019; Graetz et al., 2018; Huang et al., 2019; Ricci et al., 2020). For an electronic intervention to be successful, access, engagement and connectivity are essential. Technology provides an innovative approach to realizing behavioural intervention (B et al., 2021).

According to a study in Singapore, mobile phones have had a penetration rate of more than 100% since the last decade (*Mobile Penetration Rate-Data.Gov.Sg*, n.d.) which provides an opportunity to use computer-automated short message service (SMS) reminders to optimize adherence (E. H. Tan et al., 2020). According to the Pew Research Institute survey report, mobile phones are possessed by 96% of adult U.S. residents, and 81% have a smartphone (*Demographics of Mobile Device Ownership and Adoption in the United States | Pew Research Center*, n.d.). 95% of teenagers between the age group of 13 to 17 years was reported to possess a smartphone and nearly 50% was reported "being online constantly".

Bibliometric analysis is one of the emerging methods to understand the trend of publications in a given field of research (Cooper et al., 2021). In bibliometric analysis, researchers have considered vital elements like the citation of articles, institutions, countries, authors and keywords which are contributing to the field of research and provide an overview of the publication pattern (Liang et al., 2021; Pitt et al., 2021; Sattari et al., 2021; Zhang et al., 2021). The VOS viewer programme used to create graphical diagrams of the bibliometric maps was developed by Van Eck & Waltman. The software enables users to develop bibliographic coupling, bibliographic co-occurrence, comparison of co-citations, text data visualization etc. (Guleria & Kaur, 2021; Orduña-Malea & Costas, 2021; Rajeswari et al., 2021; Sood et al., 2021). This study encompasses indicators like term co-occurrence,

publications with more extraordinary citation, co-authorship, bibliographic coupling etc., to analyze the bibliographic data of medication adherence and reminder.

METHODOLOGY

This study emphasizes the articles published in the last ten years between 2011 to 2020 and indexed in the Scopus database. The keywords ("medication adherence" AND "reminder") OR ("medication compliance" AND "reminder") were used to retrieve the metadata of the published articles. A total of 1,103 documents were obtained based on the search criteria. Articles published in the English language were only considered for the study. Further filtration was done based on the document type. Only articles and review papers were included in the search criteria. The final result-set consisted of 1007 articles. In the first part of the study, the top five authors with the highest number of publications, top five Universities and top five funding sponsors have been identified and detailed with their number of publications. The descriptive analysis of the published articles has been presented in year-wise publications, top 10 journals contributing to this field of research, and a ranking table has been prepared for the top 10 most cited publications based on their average citation per year. A matrix for year wise publications and citations has also been prepared. In the second part of the study, a bibliographic analysis of the articles considered for the study has been done. VOS viewer software has been used to perform the analysis and generation of the graphs and network diagrams. Cluster colouring has been done based on years (as given in the legend at the bottom of each graph) to differentiate and understand the evolution of different parameters considered in the study over the years.

RESULTS AND DISCUSSION

The top five authors with the highest number of publications in the period considered for this study are: i) Haberer, J.E. with fifteen articles, ii) Car, J. with ten articles, iii) Bouvy, M.L. with nine articles, iv) Feldman, S.R. with eight articles and v) Redfern, J. with eight articles. The top five Universities contributing to this field of research are: i) Harvard Medical School with 42 publications, ii) The University of Sydney with 32 publications, iii) Massachusetts General Hospital with 28 publications, iv) V.A. Medical Center with 27 publications, and v) University of Pennsylvania Perelman School of Medicine with 25 publications. The top five funding sponsors towards this field of research are i) U.S. Department of Health and Human Services which sponsored 240 publications, ii) National Institutes of Health, which sponsored 236 publications, iii) National Institute of Mental Health which sponsored 57 publications, iv) National Institute of Allergy and Infectious Diseases which sponsored 44 publications and v) National Institute on Drug Abuse which sponsored 38 publications.

Descriptive Analysis

In the past decade, the number of articles published with the terms "medication adherence" or "medication compliance" and "reminder" has increased considerably. A yearly increase in the number of publications indicates the importance of this field of research. Figure 1 presents a graphical view of the year-wise publication of articles. In a decade, the number of yearly publications increased from 40 in 2011 to 149 in 2020, increasing 272.5%.

Journals are one of the best platforms to disseminate the knowledge and findings of any research. The 1007 articles published with the keywords used for this study was published in 479 different, highly cited journals. This indicates the importance of medication adherence and the use of reminders. The high number of platforms also demonstrate the importance of adherence and reminder in different types of diseases. The top 10 journals with their number of publications are depicted in table 1. JMIR mHealth and uHealth, published the highest number of articles (32), followed by Patient Preference and Adherence (31).

Citations are an essential rhetorical device used in academic research to acknowledge and evaluate the works of researchers. It helps to substantiate authors' arguments and endorse their work

Figure 1. Year-wise publication of articles
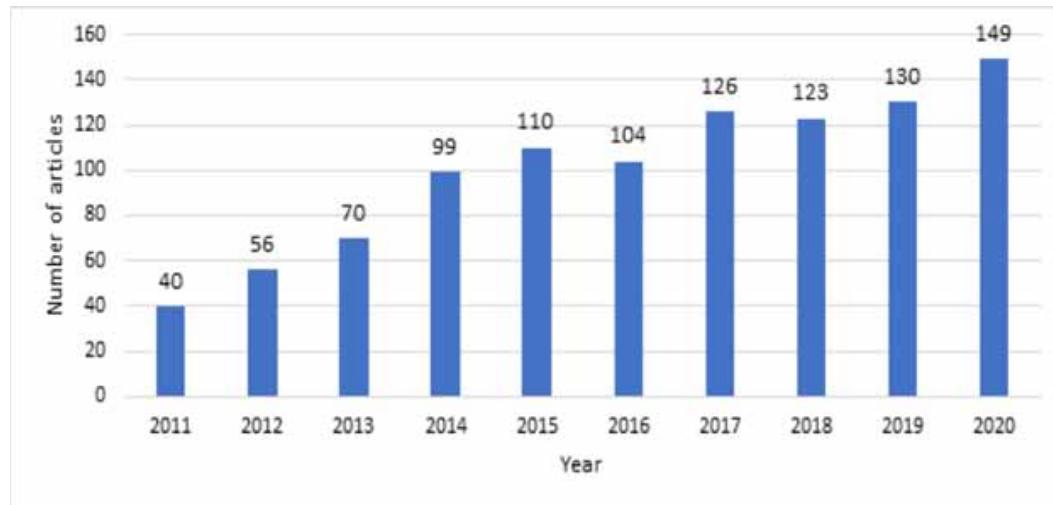
Table 1. Top 10 Journals with the highest number of publications

Sl.No	Journal	Total
1	JMIR mHealth and uHealth	32
2	Patient Preference and Adherence	31
3	PLoS ONE	29
4	AIDS and Behavior	26
5	BMJ Open	25
6	Trials	20
7	AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV	19
8	Cochrane Database of Systematic Reviews	18
9	Journal of Medical Internet Research	15
10	International Journal of Medical Informatics	11

and knowledge claims (Karamina & Wachidah, 2021). Hence, the parameter of citation of articles was used in this research. Table 2 shows the yearly citation structure of the 1007 articles used for this study. It includes various thresholds (greater than or equal to 100 citations, greater than or equal to 50 citations, etc.). Papers published between the years 2012 and 2017 has received a high number of citations (greater than 2000), the year 2014 being the highest (3198). The highest average citation was achieved in 2012, in which there were 52.9 citations per paper. Eight papers published this year received more than 100 citations. It is interesting to see that 80.34% of the publications received one or more citations.

According to the Scopus database, the top 10 most cited articles published with the keywords "medication adherence" or "medication compliance" and "reminder" are listed in Table 3. To compare the articles, we have considered citation per year (citation/age of article). The paper titled "Mobile telephone text messaging for medication adherence in chronic disease a meta-analysis" written by Thakkar et al. (2016) has received the highest number of citations per year (57). The paper titled

Table 2 Yearly citation structure

Year	TP	TC	TC/TP	≥100	≥50	≥25	≥10	≥5	≥1	0
2011	40	1299	32.5	2	7	10	9	5	6	1
2012	56	2965	52.9	8	11	13	15	6	2	1
2013	70	2740	39.1	4	13	14	23	9	4	3
2014	99	3198	32.3	6	8	26	34	13	8	4
2015	110	2619	23.8	2	11	23	42	15	11	6
2016	104	2374	22.8	2	9	20	35	21	11	6
2017	126	2111	16.8	1	6	17	53	25	15	9
2018	123	1246	10.1		4	4	33	36	31	15
2019	130	536	4.1			1	14	28	42	45
2020	149	197	1.3					12	29	108
Total	**1007**	**19285**		**25**	**69**	**128**	**258**	**170**	**159**	**198**

TP = Total number of papers, TC = Total number of citations

Table 3. Top 10 most cited documents

Rank	Title	Citation	Year	TC	AG	TC/AG
1	"Mobile telephone text messaging for medication adherence in chronic disease a meta-analysis."	(Thakkar et al., 2016)	2016	285	5	57.0
2	"Adherence and health care costs"	(Iuga & McGuire, 2014)	2014	325	7	46.4
3	"Adherence to therapies in patients with type 2 diabetes"	(Garc\'\ia-Pérez et al., 2013)	2013	333	8	41.6
4	"Mobile phone messaging for facilitating self-management of long-term illnesses."	(De Jongh et al., 2012)	2012	310	9	34.4
5	"What is the economic evidence for mHealth? A systematic review of economic evaluations of mHealth solutions."	(Iribarren et al., 2017)	2017	130	4	32.5
6	"Smartphone medication adherence apps: Potential benefits to patients and providers"	(Dayer et al., 2013)	2013	240	8	30.0
7	"The effectiveness of interventions using electronic reminders to improve adherence to chronic medication: A systematic review of the literature."	(Vervloet et al., 2012)	2012	254	9	28.2
8	"Interventions to Improve Medication Adherence: A Review"	(Kini & Ho, 2018)	2018	79	3	26.3
9	"Association of a smartphone application with medication adherence and blood pressure control: The MedISAFE-BP randomized clinical trial."	(Morawski et al., 2018)	2018	74	3	24.7
10	"The use of mobile apps and SMS messaging as physical and mental health interventions: Systematic review"	(Leigh & Prescott, 2017)	2017	98	4	24.5

TC = Total number of citations, A.G. = Age of the article as of 2021, TC/AG = Average citation per year

"Adherence and health care costs", written by Iuga & McGuire (2014), has received the second-highest number of citations (325) with an average citation of 40.6 per year. The paper focuses on the costs related to medication non-adherence based on diseases like HIV/AIDS, diabetes, depression, asthma, chronic obstructive pulmonary disease (COPD), and cardiovascular diseases. The article "Adherence to therapies in patients with type 2 diabetes" written by Garc\'\ia-Pérez et al. (2013) has received the highest number of citations (333) with an average citation of 41.6 per year. This indicates that medication adherence in patients with type 2 diabetes is of great concern, and research on reminders to enhance researchers is considering the adherence rates. Articles written by De Jongh et al. (2012), Thakkar et al. (2016), Dayer et al. (2013) and others have focused on the use of mobile phones, text messages and smartphone apps to overcome the problem of medication non-adherence. These papers have also received a high number of citations over the years, with average citations being 38.8, 35.6 and 30.0, respectively, indicating that technology is being used to overcome this problem.

Bibliometric Analysis

In this section, with the help of VOS viewer software, a graphical overview of the papers selected for this study is presented. The size of circles symbolizes the importance of the items. Different colours and distances between the circles are used to identify various clusters. Bibliometric analysis helps identify the most active research areas, their sub-disciplinary structure, the most critical topics, forms of interrelationship, and transformative discoveries (Díez-Martín et al., 2021). Figure 2 represents the co-citations based on cited authors. For generating this diagram, a complete counting method was used with a minimum number of citations of an author as 100. Out of 57218 authors, only 30 authors met the threshold criteria. The diagram depicts two clusters. The most influential authors in cluster 1 are Hynes, R.B., Osterberg, I. and Van Dijk, I. In cluster 2 the most influential authors are Bangsberg, D.R., Mills, E.J. and Lester, R.T.

When two publications reference a third common publication in their bibliographies, bibliographic coupling occurs (L. P. Tan, 2021). The similarity between publications is established using both bibliographic coupling and co-citation. Figure 3 represents a graphical representation of bibliographic coupling based on authors. For generating the diagram, the minimum number of documents for an author was set to 6. Out of 5101 authors, only 24 met the threshold criteria. The author Redfern J. with eight documents, had the highest link strength (1578), which Thiagalingam A. followed with

**Figure 2. Co-citation based on cited authors**
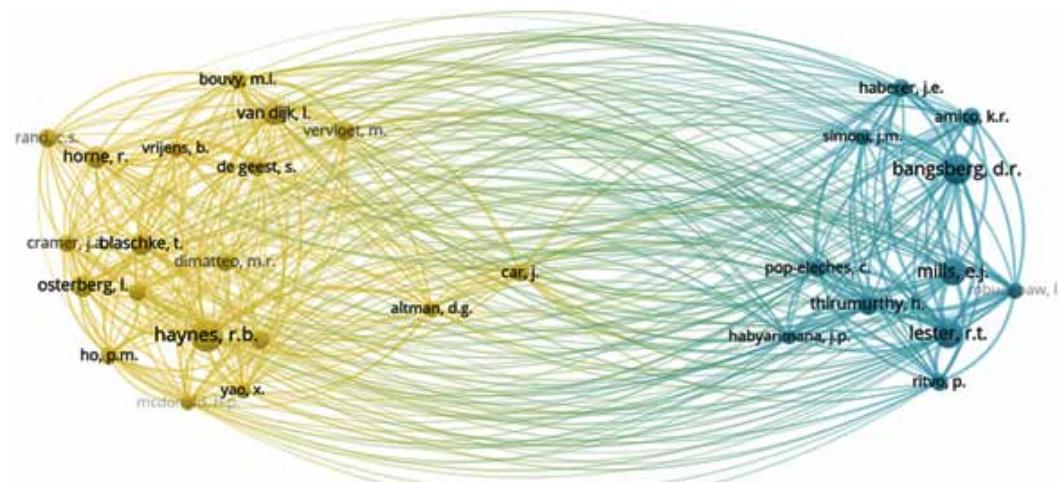
Figure 3. Bibliographic coupling based on the author
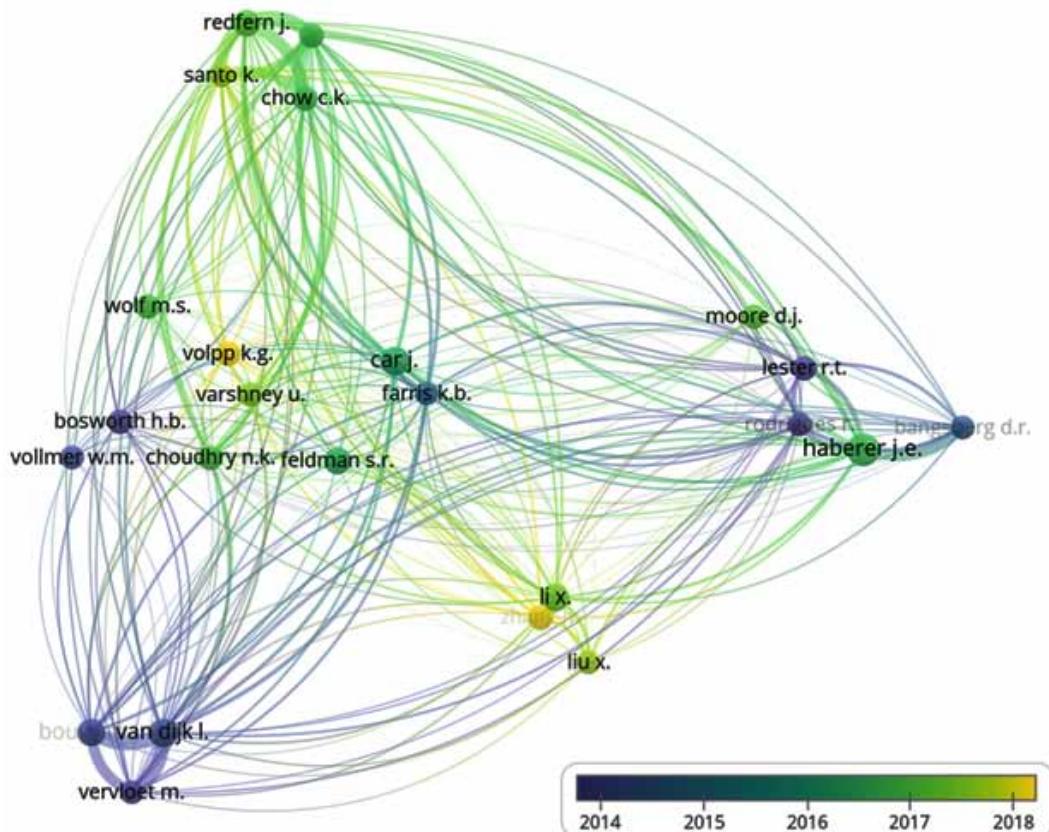
seven documents and a link strength of 1493. It is interesting to note that the works of Redfern J., Santo K., Volpp K.G, Varshney U. and Li X. and Liu X. are of the most recent origin.

Figure 4 represents bibliographic coupling based on country. For generating the visualization diagram, the minimum number of documents for a country was set to 5. Out of 101 countries, only 40 met the threshold. Table 4 lists the top 10 countries with the highest link strength. The United States tops the list with 526 documents, 10950 citations and 81060 as the link strength. The United Kingdom follows it with 117 documents, 2983 citations and 36918 link strength. On examining figure 4, it can be seen that the studies in Singapore, Thailand, China, Russia, France, Iran, and Indonesia are of recent origin, indicating that researchers from these countries have also started working in medication adherence and reminders.

As shown in Figure 5, the term co-occurrence was analyzed based on text data. The text was extracted from titles and abstracts. The full counting method was used. The minimum number of occurrences of a term was fixed to 50. Out of 21692 items, 182 met the threshold. The figure consists of four clusters. Cluster 1 has 31items like "article", "bias", diabetes", "medicine", "meta-analysis", "non-adherence", "patient adherence" and "patient education" etc. Cluster 2 consists of 28 items like "arm", "blood pressure", "china", "hypertension", "month", "SMS", "SMS reminder", "text message" etc. Cluster 3 has 28 items like "adolescent", "art", "art adherence", "caregiver", "factor", "HIV", "individual", "text", text message reminder", "text messaging" etc. The 4th cluster has 22 items like "acceptability", "app", "application", "asthma", "management", "medication reminder", "mhealth", "mhealth intervention", "smartphone", etc.

Figure 4. Bibliographic coupling based on country
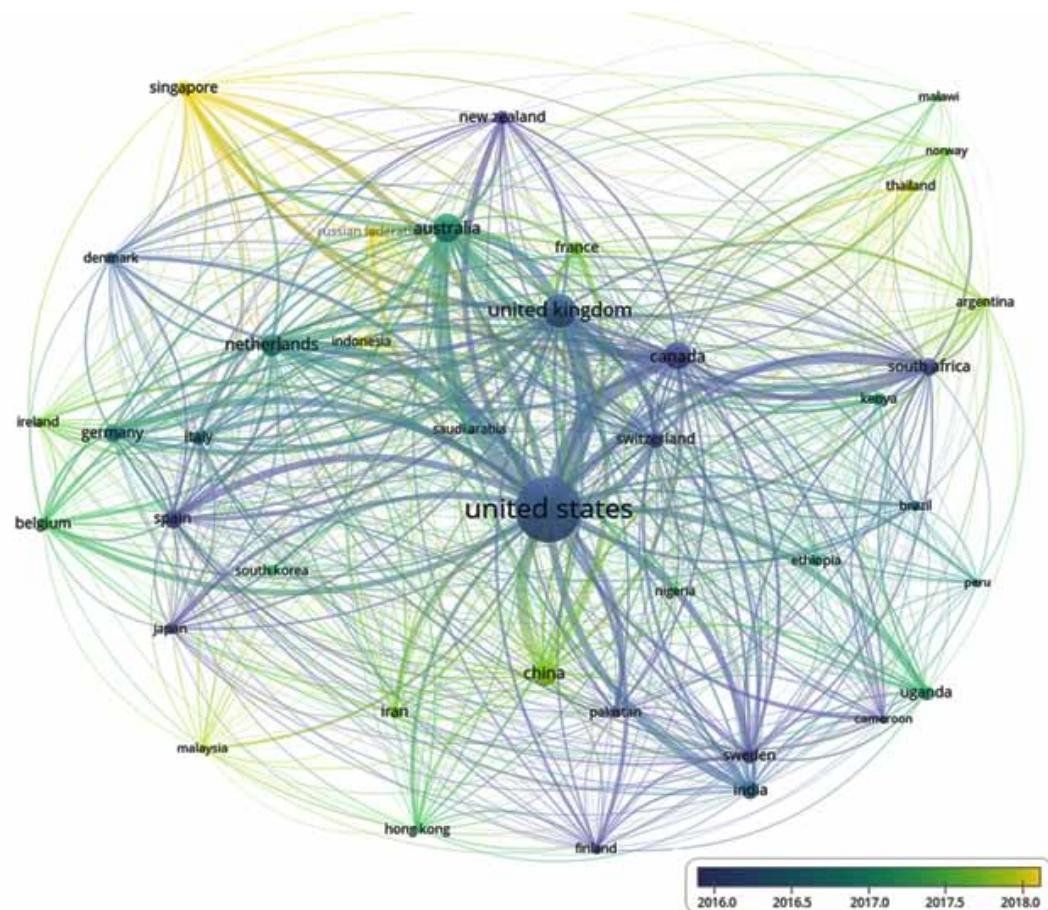
Table 4. List of top 10 countries with the highest link strength

Sl.No	Country	Documents	Citations	Total Link Strength
1	United States	526	10950	81060
2	United Kingdom	117	2983	36918
3	Australia	80	1915	27079
4	Canada	73	1447	25145
5	Netherlands	46	1594	16326
6	China	55	611	13128
7	South Africa	27	602	10622
8	Switzerland	23	825	9987
9	Singapore	16	151	8238
10	Germany	27	298	8098

Figure 5. Term co-occurrence based on text data
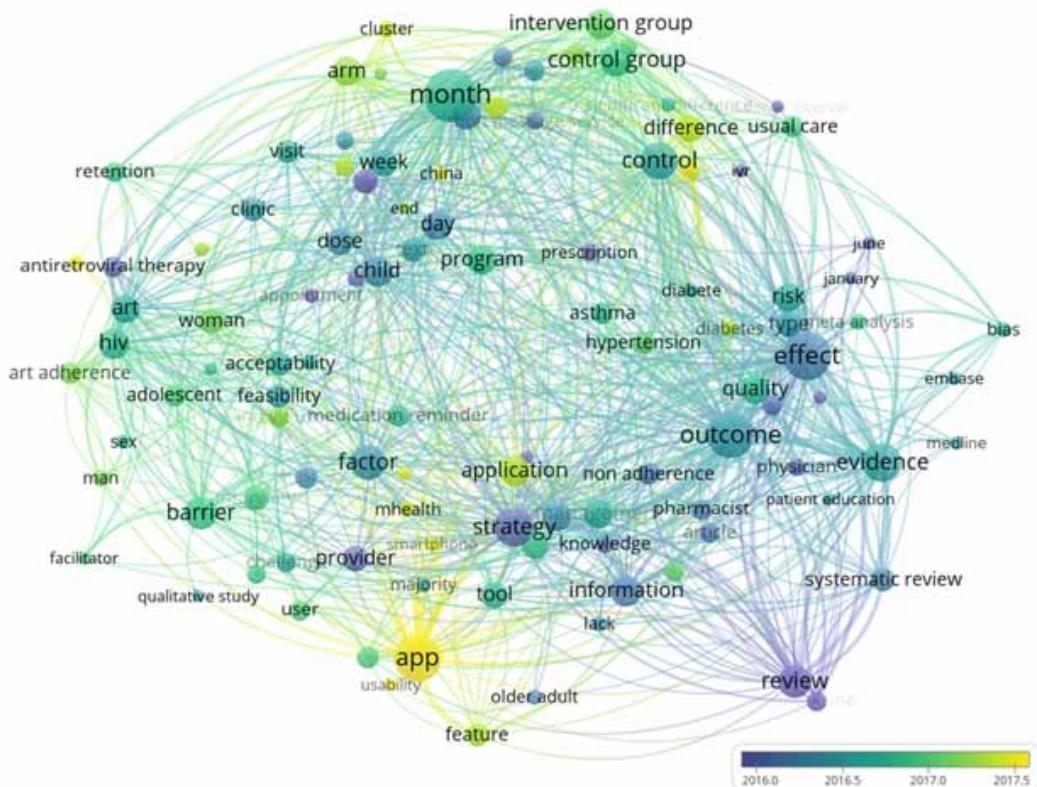
Figure 6 gives a graphical representation of the highlights of term co-occurrence based on clusters. It consists of 6 diagrams obtained from the consolidated diagram, as shown in Figure 5. Figure 6 (A) represents the co-occurrence of terms with focal point "review". It has strong co-occurrence with the terms "app", "strategy", "outcome", "effect", "evidence", etc. Figure 6 (B) represents the co-occurrence of terms with focal point "effect". It has strong co-occurrence with the terms "outcome", "evidence", "month", "factor", "barrier", etc. Figure 6 (C) represents the co-occurrence of terms with the focal point "month". It has strong co-occurrence with the terms "week", "HIV", "art", "program", "factor", "control", etc. Figure 6 (D) represents the co-occurrence of terms with focal point "barrier". It has strong co-occurrence with the terms "user", "interview", "qualitative study", etc. Figure 6 (E) represents the co-occurrence of terms with focal point "app". It has strong co-occurrence with the terms "application", "user", "feature", "development", "diabetes", "mhealth", etc. Figure 6 (F) represents the co-occurrence of terms with focal point "application". It has strong co-occurrence with the terms "smartphone", "difference", "control", "hypertension", etc. The terms "app", "youth" "arm", "feature", "application" and "pregnancy" are of more recent origin than the others like "phone", medicine", "interview", "HIV", "mhealth", "smartphone" etc. The text data analysis indicates the development that has taken place in this field of research in the past decade.

CONCLUSION

The study aimed to highlight the work of different researchers and publication platforms (journals) in disseminating knowledge about medication adherence and the use of reminders. The trend of publication, prominent contributors, funders, countries, and shift in the use of reminders was

Figure 6. Highlights of term co-occurrence based on clusters
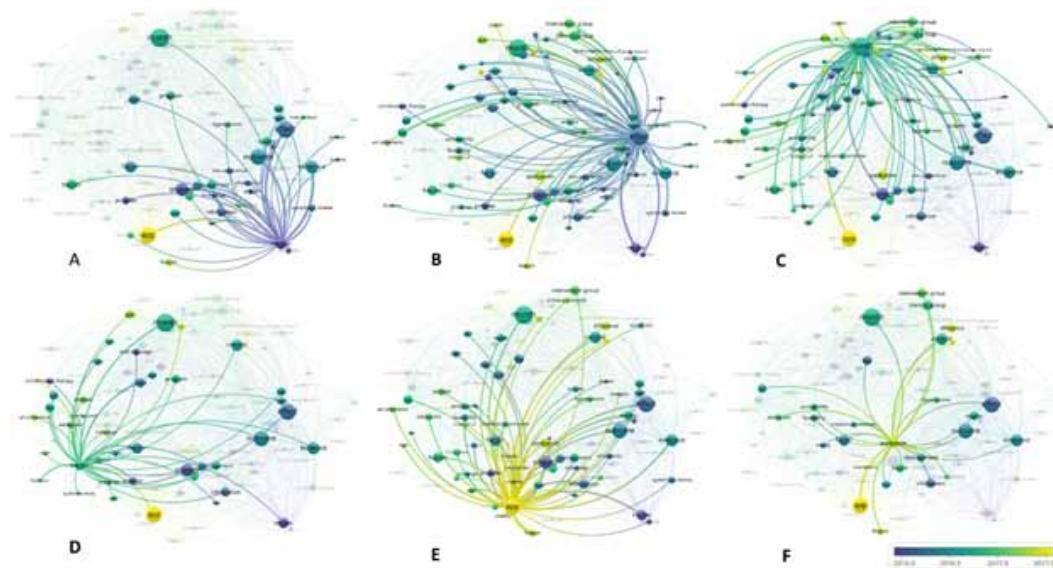
encompassed based on bibliographic and text analysis. Articles published in the last ten years between 2011 to 2020 indexed in the Scopus database were used for the analysis. Data of 1007 articles were analyzed in VOS viewer to obtain graphs and network diagrams. The paper titled "Adherence to therapies in patients with type 2 diabetes" (Garc\'\ia-Pérez et al., 2013), published in 2013, received the highest number of citations (333). Most research was done in the United States (526 documents), followed by the United Kingdom (117 documents). In recent years there has been active publication from the countries like Norway, France, Singapore and China. It was also found that studies at the beginning of the decade were mainly focused on SMS and mobile phone interventions. The trend has shifted towards intentions like mobile applications, and the term "mhealth" is used more in the current years.

Until the widespread use of smartphones and quality mobile apps, SMS was the preferred mode of sending reminders to patients. With smart mobile apps and the use of the internet, sharing information to patients in real-time has increased the possibility of better adherence. Researchers from different countries are participating in this field of research. They are trying to find better intervention techniques aiming to change the behaviour of patients and ultimately increase medication adherence behaviour. The research conducted by (2016) shows that the odds of medication adherence in chronic diseases are doubled using reminders through SMS. Park et al. (2014) proposed that two-way communication act as a better intervention technique.

The research was limited to the keywords "Medication Adherence", Medication Compliance", and "Reminder", and the studies conducted in the past decade. Future studies can be conducted on specific intervention techniques and specific diseases to find the different impact metrics and the contributors.

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