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Computer and Mobile Technology Interventions to Promote Medication Adherence and Disease Management in People with Sickle Cell Disease: A Systematic Review

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Joyce Joseph[1], Asha P Shetty[2*], Athar Javeth[3], Suvashri Sashmal[3], Kuruvepatta Helaimani[4]. Computer and Mobile Technology Interventions to Promote Medication Adherence and Disease Management in People with Sickle Cell Disease: A Systematic Review. JCS

Abstract

Introduction: Sickle Cell Disease (SCD) is a chronic genetic disorder requiring complex management needs. Poor medication adherence and limited self-management are frequent challenges. The increasing use of digital health technologies offers opportunities to enhance adherence, self-care, and patient engagement in SCD management, however, evidence regarding their effectiveness remains fragmented. Therefore, this systematic review aimed to evaluate the effectiveness of computer- and mobile-based technology interventions in promoting medication adherence and disease management among individuals with SCD.

Methods: This systematic review was conducted in accordance with PRISMA guidelines and registered in PROSPERO (CRD42025639596). Comprehensive searches of PubMed, EMBASE, Scopus, Web of Science, Cochrane Library, Ovid, Clinical Key, and Google Scholar identified studies published from January 2000 to February 2025. Eligible studies included randomized controlled trials, quasi-experimental, cohort, and cross-sectional designs evaluating digital interventions aimed at improving medication adherence or disease management in SCD. Study quality was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklists.

Results: Twenty-three studies involving 1,841 participants met the inclusion criteria. Interventions included mobile applications, SMS reminders, web-based platforms, and telehealth tools. Most

reported improvements in medication adherence, disease knowledge, self-efficacy, and pain management. However, studies were generally small, short-term, and of moderate-to-high risk of bias, with user engagement declining over time.

Conclusion: Digital health interventions show encouraging potential to support self-management in SCD, particularly through mobile and cognitive behavioral therapy–based tools. Nevertheless, larger, theory-based, and longer-term trials are needed to confirm their effectiveness, sustainability, and accessibility in lower-resource contexts.

Keywords: Sickle Cell Disease; Medication Adherence; Digital Health; Self-Management; Patient Compliance.

Introduction

Managing Sickle Cell Disease (SCD) poses significant challenges for individuals living with the condition and their families.[1] Studies indicate a high prevalence of poor self-management and non-adherence to treatment regimens among both children and adults with SCD, similar to other chronic health conditions.[2,3] However, effective self-management is critical to optimizing treatment efficacy, improving clinical outcomes, and reducing unnecessary healthcare utilization and costs.[4] In SCD, self-management involves several key aspects, including pain management, adequate hydration, balanced nutrition, clinic attendance, and adherence to prescribed medications. These challenges become even more pronounced during the transition from pediatric to adult care, where a decline in adherence and disease management is often observed.[4]

In addition to the complexity of managing the condition, disparities in access to care and resources, especially in industrialized countries where SCD predominantly affects ethnic minority populations, can further hinder effective disease management.[5] Digital health technologies, including computer- and mobile-based interventions (eHealth) such as mobile apps, web-based platforms, and telehealth solutions, offer promising strategies to enhance self-management, medication adherence, and patient-provider communication. Given the widespread adoption of smartphones, internet access, and social networking among individuals with SCD and their families, leveraging these technologies could improve disease management across diverse age groups and socioeconomic backgrounds.[6]

Although some systematic reviews have explored the impact of such interventions, evidence regarding their effectiveness remains unclear.[7] To our knowledge, no prior review has comprehensively evaluated the impact of computer- and mobile-based technologies on both medication adherence and disease management in SCD. The present review is novel in three key ways: it synthesizes evidence from diverse digital modalities; including mobile applications, SMS reminders, web-based platforms, wearable devices, and telehealth; published up to February 2025; it applies a rigorous methodological appraisal using Joanna Briggs Institute (JBI) tools across multiple study designs; and it uniquely examines age-specific variations and intervention design features that influence user engagement and outcomes. By clarifying these aspects, this review addresses important gaps in the literature and provides insights for optimizing digital interventions in SCD management.

The primary objective of this systematic review is to assess the effects of computer- and mobile-based technology interventions in promoting medication adherence and disease management among individuals with SCD.

Materials and Methods

This systematic review was conducted according to PRISMA guidelines and registered in PROSPERO (CRD42025639596)**,** with searches that covered studies published from January 2000 to February 2025 across all databases. The review had minor protocol deviations including the addition of Google Scholar, expanded outcomes (self-efficacy and disease knowledge), and use of narrative synthesis due to heterogeneity. We searched PubMed, EMBASE, Scopus, Web of Science, Cochrane Library, Ovid, Clinical Key, and Google Scholar using combinations of keywords and MeSH terms related to sickle cell disease, digital health interventions, medication adherence, and disease management. Full database-specific search strategies are provided in Table 1 (Supplementary Data). No language restrictions were applied.

Table 1. Search strategy

No	Database	Search String
1	PubMed (Searched February 2025)	("sickle cell disease"[MeSH Terms] OR "sickle cell"[Title/Abstract]) AND ("mobile health"[Title/Abstract] OR "mHealth" OR "digital health" OR "telemedicine" OR "mobile application"[Title/Abstract] OR "eHealth") AND ("adherence"[Title/Abstract] OR "medication adherence"[MeSH Terms] OR "self-management"[Title/Abstract] OR "disease management"[MeSH Terms]) Filters: Humans, English, 2010–2025
2	Embase	'Sickle cell disease'/exp AND ('mobile health' OR mHealth OR 'digital health' OR telemedicine OR 'mobile application' OR eHealth).ab,ti. AND ('medication adherence'/exp OR 'self-management'/exp OR 'disease management'/exp) Limits: English, Humans, 2010–2025
3	Scopus	TITLE-ABS-KEY ("sickle cell" AND ("mobile health" OR mHealth OR "digital health" OR telemedicine OR "mobile app*" OR eHealth) AND ("medication adherence" OR "self-management" OR "disease management")) AND PUBYEAR > 2009 AND (LIMIT-TO (LANGUAGE, "English"))
4	Web of Science	TS= ("sickle cell") AND TS=("mobile health" OR mHealth OR "digital health" OR telemedicine OR "mobile app*" OR eHealth) AND TS=("medication adherence" OR "self-management" OR "disease management") Timespan: 2010–2025. Languages: English.
5	Cochrane Library	("sickle cell" in Title Abstract Keyword) AND ("mobile health" OR mHealth OR "digital health" OR telemedicine OR "mobile app*" OR eHealth) AND ("medication adherence" OR "self-management" OR "disease management") Publication years: 2010–2025; English only
6	Ovid	Exp sickle cell anemia/ AND (mobile health OR mHealth OR digital health OR telemedicine OR mobile application OR eHealth).tw. AND (medication adherence OR self-management OR disease management).tw. Limit to English, Humans, 2010–2025
7	Clinical Key	"sickle cell" AND ("mobile health" OR mHealth OR "digital health" OR telemedicine OR "mobile app*" OR eHealth) AND ("medication adherence" OR "self-management" OR "disease management") Filters: 2010–2025, English only
8	Google Scholar	allintitle: "sickle cell" ("mobile health" OR mHealth OR "digital health" OR telemedicine OR "mobile app*" OR eHealth) ("medication adherence" OR "self-management" OR "disease management") Time filter: 2010–2025

Inclusion and Exclusion Criteria

Studies were included if they evaluated digital health interventions delivered via mobile phones, the Internet, or other mobile technology devices, including Web-based and Web 2.0 interventions designed to improve medication adherence or disease management in individuals with SCD. Eligible technologies included personal computers, mobile applications, tablets (iOS/iPads, Android devices, smartphones), and self-administered or user-centered interventions tailored to user needs. The target population comprised children, adolescents, and adults with SCD, as well as parents or caregivers involved in disease management. Studies could include comparators such as standard care, educational materials (digital or hard copy), self-management tools, face-to-face support, placebo, or alternative digital interventions.

Studies were excluded if they did not involve digital interventions (e.g., only face-to-face therapy or printed materials), focused on populations without confirmed SCD, or addressed only general health promotion without targeting adherence or disease management. Interventions designed exclusively for healthcare professionals were also excluded. Non-empirical studies (commentaries, editorials, narrative reviews), case reports or series, studies with fewer than five participants, posters, systematic reviews, protocols without results, and studies published in languages other than English or without full-text availability were excluded. Abstract-only conference proceedings and studies published before 2000 were also excluded, unless providing relevant technological insights.

Study Selection and Quality Appraisal

The systematic review followed PRISMA guidelines (Diagram 1) to ensure transparency and reproducibility. Four authors (JJ, AJ, SS, and KH), working in pairs, independently screened titles and abstracts, reviewed full texts, and extracted relevant data using a standardized form. Disagreements were resolved through discussion or consultation with a third reviewer. Reviewer agreement exceeded 85% during title and abstract screening, confirming strong consistency. Eligible studies were classified by design: Randomized Controlled Trials (RCTs) with random allocation, quasi-experimental studies including pre-post or non-equivalent control designs, cohort studies assessing outcomes over time, and cross-sectional studies capturing single time-point data. Pilot or feasibility studies with random allocation were treated as RCTs, and single-group pre-post studies were considered quasi-experimental.

All 23 included studies were appraised using the Joanna Briggs Institute (JBI) Critical Appraisal Checklists, 2020 version, customized for each design type (randomized controlled trials, quasi-experimental, cohort, and cross-sectional).[8] RCTs were assessed for randomization, allocation concealment, blinding, follow-up completeness, and selective reporting, while quasi-experimental studies were evaluated for clarity of intervention, group comparability, outcome measurement, and statistical analysis. Each criterion was scored as "Yes" (1) or "No/Unclear" (0), and studies were categorized as low, moderate, or high risk of bias based on the proportion of criteria met.

Data extraction was conducted using a standardized form, capturing the following details: first author's name, publication year, country, study design, setting, sample size, population (age group), intervention duration (weeks/months), aim/objective, intervention modality (e.g., mobile app, SMS reminders, web-based intervention), comparator (e.g., control group, standard care, placebo), outcome measures (e.g., medication adherence, disease management, quality of life), and key findings.

Due to heterogeneity in interventions, populations, outcomes, and follow-up durations, meta-analysis was not feasible; a narrative synthesis summarized the direction of effect for each outcome. The narrative synthesis involved several stages. First, the included studies were categorized according to the type of digital health intervention (e.g., mobile applications, text messaging interventions, web-based platforms, and telehealth approaches). Second, studies were compared based on their objectives, participant characteristics, intervention components, duration

of follow-up, and outcome measures. Third, findings were systematically examined to identify recurring patterns, similarities, and differences across studies. The results were then synthesized thematically according to major outcome domains, including medication adherence, disease self-management, disease knowledge, health-related quality of life, patient engagement, and clinical outcomes. Finally, the strength and consistency of evidence across studies were evaluated to provide an overall interpretation of the effectiveness of digital health interventions in supporting the management of sickle cell disease.

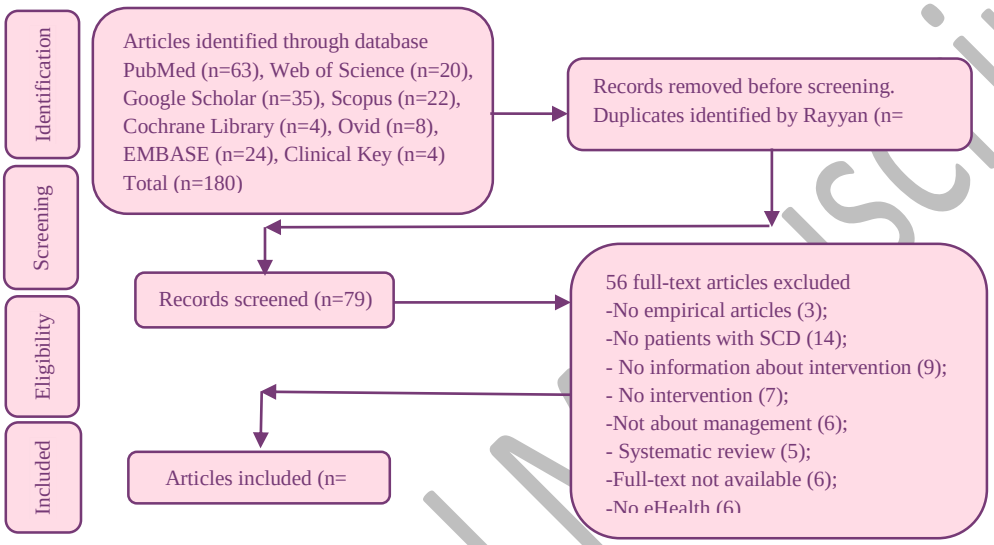

Diagram 1. PRISMA flow diagram PRISMA: Preferred reporting items for systematic reviews and meta-analyses

Results

From 180 records initially identified through a systematic search across multiple databases, 101 duplicates were removed using the Rayyan software, 79 studies were screened, and 23 studies comprising 1,841 participants, met inclusion criteria. The PRISMA diagram (Diagram 1) details this selection process.

The **table 2** summarizes the key characteristics of the 23 included studies. The studies encompassed diverse age groups, from children and adolescents to adults with sickle cell disease, and examined a wide range of digital tools, including mobile health applications, cognitive behavioral therapy modules, text messaging systems, and wearable technologies. Collectively, these studies highlight the heterogeneity of methods, intervention types, and measured outcomes in the field of digital health for sickle cell disease management.

Table 2. Main features of the included studies

Author, (Year)	Country	Design	Sample	Population	Intervention	Main Outcomes	Key Findings
Curtis K et al[6] (2019)	UK	Cross sectional	10	Adolescents with SCD (11-17 y)	Adherence support development	Medication adherence	Identified adherence barriers and support needs.
Hankins JS et al[9] (2023)	USA	Quasi experimental	235	SCD patients (15-45 y)	Multilevel mHealth intervention. App: 6 months + Toolbox: 9 months	Hydroxyurea adherence	Improved hydroxyurea adherence.
Crosbi et al[10] (2020)	USA	RCT	53	Adolescents and young adults aged (13-21 y) with SCD	SCThrive + iManage app	Self-management, disease knowledge	Improved self-management and disease knowledge.
Jonassaint et al[11] (2020)	USA	RCT	359	Adults with SCD (18-65 y)	Digital CBT	Pain, mental health	Improved pain coping and mental health outcomes.
Lalloo et al[12] (2022)	USA/ Canada	RCT	46 dyads	Youth (12-18 y) with SCD and their caregivers	iCanCope app	User engagement	Higher engagement associated with greater satisfaction.
Dyal et al [13] (2020)	USA	RCT	228	Adults (18–74 y) with SCD	PAINUCope intervention	Pain, adherence	Improved analgesic adherence but not pain outcomes.
Pernell et al[14] (2017)	USA	RCT	47	Individuals with SCD and asthma	Two-way SMS reminder	Medication adherence	Significant improvement in medication adherence.
Parchuri et al [15] (2023)	USA	RCT	21	Individuals with SCD, (16–35 y)	Adapted CBT mobile app	Depression, pain, self-efficacy	Improved depression, pain, and self-efficacy.
Phillips et al[16] (2021)	USA	Quasi experimental	60 dyads	Children and adolescents with SCD (0-17 y)	Self-management mHealth app	Adherence, satisfaction	High initial engagement that declined over time.
Saulsberry et al[17] (2020)	USA	Cohort study	183	Adolescents with SCD (12-15 y)	STEP web-based program	Disease knowledge	Improved disease knowledge
Palermo et al[18] (2024)	USA/ Canada	RCT	137	Adolescents with SCD (12-18 y)	iCanCope-SCD CBT	Pain, coping	Reduced pain and improved coping.
Schatz J et al[19] (2015)	USA	RCT	46	Children and adolescents with SCD (8-21 y)	Smartphone CBT	Pain, coping	Improved coping and reduced pain intensity.
Johnson et al[20] (2019)	USA	Cross sectional	27	Adults with SCD having acute pain	Wearable device + mHealth app	Pain monitoring	Machine-learning models successfully predicted pain scores.
Hood et al[21] (2021)	USA	RCT	26	Adolescents and young adults with SCD (13-21 y)	iManage for SCD	Self-management, self-efficacy	Greater app use associated with improved outcomes.
Palermo et al[22] (2019)	USA	Quasi experimental	48	Adolescents and parents	Web-MAP CBT	Feasibility, engagement	Feasible and acceptable pain-management intervention.
Anderson et al [23] (2018)	USA	Quasi experimental	32	Youths, (7–18 y)	Intensive Training Program app	Adherence, knowledge	Improved adherence and disease knowledge.
Creary et al[24] (2019)	USA	Quasi experimental	55	Patients with SCD on hydroxyurea (≤19 y)	Mobile DOT	Hydroxyurea adherence	Increased adherence with positive clinical trends.
Cronin et al[25] (2023)	USA	Quasi experimental	67	SCD patients (18 - 70 y)	mHealth app + guideline booklet	Knowledge, hospitalization	Improved knowledge and possible reduction in hospitalization.
Estepp et al[26] (2014)	USA	Quasi experimental	83	Children/ adolescents with SCD	Text-message reminders	Hydroxyurea adherence	Improved laboratory indicators of adherence.
Shah et al[27] (2014)	USA	Cross sectional	117	Adults with SCD (18-50 y)	Mobile application assessment	Technology acceptance	High willingness to use mobile applications.
Anderson et al[28] (2016)	UK	Cross sectional	46	Children with SCD (8-18 y)	Adherence assessment	Quality of life	Better adherence associated with improved quality of life
Jonassaint et al[29] (2023)	USA	RCT	359	Adults with SCD	Digital CBT chatbot	Pain interference	Both CBT and education improved pain-related outcomes.
Ezenwa et al[30] (2016)	USA	RCT	28	Adults with SCD	Audio-visual relaxation intervention	Stress, pain	Reduced pain intensity following intervention.

Impact of Computer- and Mobile-Based Technology Interventions on SCD Management

Digital interventions show promise in supporting the management of SCD, with most evidence focusing on medication adherence, self-management behaviors, and patient-reported outcomes. Mobile health (mHealth) applications such as InCharge Health and SCThrive, along with SMS-based tools including Mobile DOT and the SIMON system, were associated with improved hydroxyurea adherence; for example, two-way SMS reminders produced statistically significant gains in adherence scores (P= 0.01).[9,10,14] Self-management interventions such as SCThrive and iManage reported improvements in self-efficacy, symptom tracking, and disease knowledge, while web-based platforms like the STEP program primarily enhanced knowledge but had limited impact on self-management confidence. Digital cognitive behavioral therapy (CBT) programs; including iCanCope and Beating the Blues; demonstrated reductions in pain intensity and better coping, although engagement varied and long-term sustainability remains uncertain.[18,21] Some blended approaches, such as an mHealth app combined with a booklet, suggested potential reductions in hospital visits, but results were inconsistent and often underpowered.[25] Overall, while these interventions were generally associated with short-term improvements in adherence, knowledge, and psychosocial outcomes, the evidence base is heterogeneous, and conclusions about long-term clinical benefit should be drawn cautiously.

Effectiveness of Different Digital Interventions

Different types of digital interventions have shown varying degrees of effectiveness in managing SCD. Mobile applications (apps) are widely used due to their features such as symptom tracking, goal setting, reminders, and self-monitoring. Apps like iManage, iCanCope, and adapted CBT-based interventions have demonstrated positive effects on pain management, self-efficacy, and mental health.[18,21,29] However, a common challenge with mobile apps is low user engagement over time, which limits their long-term effectiveness. SMS reminders have proven to be effective in improving medication adherence, but they have had a limited impact on sustained engagement beyond adherence support.[14,26] Web-based platforms, such as the STEP program, have successfully enhanced disease knowledge, although their effectiveness in improving self-management behaviors has been inconsistent.[17,22] Telehealth interventions remain underexplored in SCD management, but some studies indicate that they can increase patient-provider communication and improve medication adherence, suggesting their potential as a complementary tool in digital health interventions.[19]

Age-Specific Variations in Intervention Effectiveness

Age-specific variations in the effectiveness of digital interventions for SCD management highlight differences in engagement and outcomes across different life stages. Children (0-12 years) were the least directly targeted by interventions, with most studies focusing on caregiver engagement, particularly in parent-child dyads using mHealth tools.[12,22] In contrast, adolescents showed the highest responsiveness to self-management apps, peer-support interventions, and educational platforms.[22,26,28] Among this group, digital cognitive behavioral therapy (CBT) interventions were particularly effective in pain management and improving self-efficacy.[18,19] Adults were more

inclined to engage with self-monitoring tools and telehealth interventions, benefiting from increased patient-provider communication. However, they also faced barriers in maintaining long-term engagement with mobile applications.[27,29] Despite this, digital CBT and mobile health interventions significantly improved mental health and medication adherence among adults, underscoring the need for tailored engagement strategies for each age group.

Role of Intervention Design

The design of digital interventions plays a crucial role in their effectiveness, particularly in engagement and outcomes for individuals with SCD. Blended approaches, combining eHealth with face-to-face interaction, have shown higher engagement and effectiveness.[9,25] Hybrid interventions such as SCThrive and iManage, which integrate group sessions with digital tools, demonstrated better user participation and outcomes.[10] Studies highlighted that digital interventions were more effective when combined with provider support, reinforcing the importance of human interaction in digital health strategies.[18,25,30] Theoretical models were commonly applied in intervention design, particularly Cognitive Behavioral Therapy (CBT) frameworks in pain management interventions, while behavioral activation and motivational strategies were frequently used in self-management programs.[15,18,22,29] However, a notable limitation was that many studies did not explicitly state their theoretical foundation, making it difficult to compare the effectiveness of different models. User engagement and acceptability were also key factors, with many interventions experiencing high initial engagement but a decline over time. To enhance long-term adherence, studies suggested incorporating personalization, gamification, and interactive features to sustain user interest and participation.

Risk of Bias Assessment

Among the 11 randomized controlled trials, six were rated moderate and five high risk of bias, primarily due to inadequate blinding, unclear allocation concealment, and incomplete intention-to-treat analyses, suggesting possible overestimation of benefits. Of the seven quasi-experimental studies, six were low risk and one moderate, though most lacked control groups and had potential confounding. The single cohort study was high risk (3/11), reflecting poor group comparability and limited follow-up. Among the four cross-sectional studies, one was low risk and three moderate, mainly due to unadjusted confounding and limited sampling details.

Overall, study quality was variable, with many randomized trials judged at moderate to high risk. These findings underscore that, while digital interventions for SCD show promise, the evidence should be interpreted cautiously. Larger, methodologically rigorous trials with adequate follow-up are required to confirm their effectiveness. A summary of classifications and main sources of bias is presented with detailed appraisals in **Tables 3a and 3b**.

Table 3 a. Risk of bias summary

JBI CRITERIA QUASI EXPERIMENTAL	1	8	14	15	16	17	18
Is it clear in the study what is the 'cause' and what is the 'effect' (i.e., there is no confusion about which variable comes first)?	Y	Y	Y	Y	Y	Y	Y
Were the participants included in any comparisons similar?	Y	N	Y	N	U	Y	U
Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Y	N	U	N	U	Y	U
Was there a control group?	N	N	Y	N	U	N	N
Were multiple measurements of the outcome pre- and post-intervention/exposure taken?	Y	Y	Y	Y	Y	Y	Y
Was follow-up complete, and if not, were differences between groups adequately described and analyzed?	Y	Y	U	Y	Y	Y	Y
Were outcomes measured in the same way for the groups being compared?	Y	Y	Y	Y	Y	Y	Y
Were outcomes measured in a reliable way?	Y	Y	Y	Y	Y	Y	Y
Was appropriate statistical analysis used?	Y	Y	Y	Y	Y	Y	Y
Was there any confounding factor accounted for in the design or analysis?	U	U	Y	Y	Y	Y	Y
SCORE	8/10	6/10	8/10	7/10	7/10	9/10	7/10

JBI CRITERIA RCT	**2**	**3**	**4**	**5**	**6**	**7**	**10**	**11**	**13**	**22**	**23**
Was true randomization used for assignment of participants to treatment groups?	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y
Was allocation to treatment groups concealed?	U	U	U	Y	U	U	Y	Y	U	Y	U
Were treatment groups similar at baseline?	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y
Were participants blind to treatment assignment?	N	N	N	N	N	N	U	U	U	N	N
Were those delivering treatment blind to treatment assignment?	N	N	N	N	U	U	U	U	U	N	N
Were outcome assessors blind to treatment assignment?	U	Y	U	Y	U	U	U	U	U	U	Y
Were treatment groups treated identically other than the intervention?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was follow-up complete, and if not, were differences between groups adequately described and analyzed?	Y	Y	Y	Y	N	N	Y	Y	U	Y	Y
Were participants analyzed in the groups to which they were randomized (intention-to-treat analysis)?	U	U	U	U	U	U	Y	Y	U	U	U
Were outcomes measured in the same way for both treatment groups?	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y
Were outcomes measured reliably?	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y
Was appropriate statistical analysis used?	Y	Y	Y	Y	Y	Y	N	Y	N	Y	Y
Was the trial design appropriate, considering the topic?	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y
SCORE	**8/13**	**9/13**	**8/13**	**10/13**	**6/13**	**6/13**	**9/13**	**10/13**	**2/13**	**9/13**	**9/13**

JBI CRITERIA Cohort Studies	**9**
Were the two groups similar and recruited from the same population?	U
Were the exposures measured similarly to assign people to both exposed and unexposed groups?	Y
Was the exposure measured in a valid and reliable way?	Y
Were confounding factors identified?	U
Were strategies to deal with confounding factors stated?	U
Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	N
Were the outcomes measured in a valid and reliable way?	Y
Was the follow up time reported and sufficient to be long enough for outcomes to occur?	U
Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	U
Were strategies to address incomplete follow up utilized?	U
Was appropriate statistical analysis used?	U
SCORE	**3/11**

JBI CRITERIA Cross Sectional Studies	**12**	**19**	20	21
Were the criteria for inclusion in the sample clearly defined?	U	Y	Y	Y
Were the study subjects and the setting described in detail?	U	U	Y	U
Was the exposure measured in a valid and reliable way?	Y	Y	Y	Y
Were objective, standard criteria used for measurement of the condition?	Y	Y	Y	Y
Were confounding factors identified?	U	U	U	U
Were strategies to deal with confounding factors stated?	U	U	U	U
Were the outcomes measured in a valid and reliable way?	Y	Y	Y	Y
Was appropriate statistical analysis used?	Y	Y	Y	Y
SCORE	**4/8**	**5/8**	**6/8**	**5/8**

Note: For a succinct assessment of the general quality of the included studies, these were categorized as follows: (1) low risk of bias (studies that met at least 75% of the standards for quality), (2) studies with a moderate risk of bias (compliant with 50–74% of the quality standards), and (3) studies with a high risk of bias (those that only complied with less than 49% of the standards for quality). (Pink- low risk, green-moderate risk, white- high risk)

Table 3 b. Summary of risk of bias assessment across included studies

Study ID	Study Design	JBI Score	Risk Level	Main Sources of Bias
1	Quasi-Experimental	8/10	Low	No control group; confounders not addressed
2	RCT	8/13	High	No blinding; unclear allocation concealment; intention-to-treat analysis unclear
3	RCT	9/13	Moderate	No blinding; unclear allocation
4	RCT	8/13	High	No blinding; unclear Intention-to-treat analysis; unclear allocation concealment
5	RCT	10/13	Moderate	Unclear intention-to-treat analysis
6	RCT	6/13	High	No blinding; unclear allocation concealment; intention-to-treat analysis unclear
7	RCT	6/13	High	No blinding; unclear allocation concealment; intention-to-treat analysis unclear; low outcome reliability
8	Quasi-Experimental	6/10	Moderate	Minor differences in treatment comparability, confounding factor unclear
9	Cohort	3/11	High	Unclear about two groups, Poor follow-up; confounders unaddressed, unclear statistical tests
10	RCT	9/13	Moderate	Partial blinding, statistical test unclear
11	RCT	10/13	Moderate	improper blinding
12	Cross-sectional	4/8	Moderate	Sampling method not clear; confounders unreported
13	RCT	2/13	High	Trial design, randomization, blinding, treatment concealment, follow up everything unclear
14	Quasi-Experimental	8/10	Low	Follow up unclear, treatment variability
15	Quasi-Experimental	7/10	Low	Participant variability; no control group
16	Quasi-Experimental	7/10	Low	Treatment variability; unclear comparability
17	Quasi-Experimental	9/10	Low	Missing data points on control group
18	Quasi-Experimental	7/10	Low	No control group; unclear confounding factors
19	Cross-sectional	5/8	Moderate	Study setting and Confounding not addressed
20	Cross-sectional	6/8	Low	Well-measured exposure; some confounding gaps
21	Cross-sectional	5/8	Moderate	Minimal detail on setting and confounding factors
22	RCT	9/13	Moderate	Unclear blinding and intention-to-treat- analysis
23	RCT	9/13	Moderate	Issues with concealment and intention-to-treat analysis

Note: Low risk= ≥75% JBI criteria met; Moderate= 50–74%; High= <50%.

Outcome harmonization

Table 4. Outcome harmonization

Outcome domain	No. of studies reporting	Favors intervention	Favors control	Null / mixed	Typical follow-up range	Risk of bias profile
Medication adherence	11	8	0	3	4 weeks – 12 months	Mostly quasi-experimental; moderate RoB; few high
Disease knowledge	6	4	0	2	6 weeks – 12 months	Mixed: some low risk (quasi-experimental), some moderate
Self-efficacy	5	3	0	2	6 weeks – 6 months	Mostly RCTs; moderate–high RoB
Pain outcomes	9	5	1	3	2 weeks – 18 months	Primarily RCTs; moderate–high RoB
Healthcare utilization	4	2	0	2	6–12 months	Underpowered studies; mostly high RoB

Table 4 illustrates, medication adherence emerged as the most consistently positive outcome, with the majority of interventions (8 of 11 studies) demonstrating improvements, although evidence was mainly from quasi-experimental designs with moderate risk of bias. Disease knowledge and self-efficacy showed benefits in several studies but were not universally improved, reflecting variability across interventions and populations. Pain-related outcomes were mixed; while five of nine studies favored the intervention, one favored control, and three reported null or inconsistent effects, often in the context of randomized controlled trials judged at moderate to high risk of bias. Healthcare utilization outcomes were the least conclusive, with only two of four studies showing reductions in hospitalizations or related events, and these were underpowered and at high risk of bias. Across domains, follow-up periods were generally short (≤12 months), limiting conclusions about the long-term sustainability of intervention effects.

Summary of Key Findings

Risk of bias influenced our certainty in the findings. Adherence outcomes were the most consistently positive; however, much of the supporting evidence came from quasi-experimental designs lacking robust control groups, which limits confidence in the strength of these findings. Pain and psychosocial outcomes were evaluated primarily in randomized trials, but most were judged at moderate to high risk of bias due to methodological limitations such as lack of blinding and incomplete follow-up, making these results promising but provisional. Evidence on healthcare utilization outcomes, such as hospitalizations, came from a small number of underpowered or high-risk studies, providing only limited support for firm conclusions.

Discussion

Digital health interventions are increasingly recognized as promising strategies to address the challenges of medication adherence and self-management in Sickle Cell Disease. The present review synthesized evidence from 23 empirical studies, revealing positive but preliminary results across various digital modalities. To enhance clarity findings are discussed below according to intervention type.

Mobile Applications and SMS-Based Interventions

Mobile health (mHealth) apps and short message service (SMS) reminders were the most frequently studied digital tools. Applications such as InCharge Health and HU Toolbox demonstrated measurable improvements in hydroxyurea adherence, while two-way SMS reminders in the study by Pernell et al achieved significant adherence gains.[9,14] Similarly, Mobile DOT and the SIMON messaging system enhanced medication possession ratios and hematologic parameters.[24-26] Mobile and text-based interventions appeared to have favorable effects on adherence-related outcomes in several studies. However, variations in study design, intervention characteristics, and follow-up duration limit firm conclusions regarding their effectiveness, particularly over the long term.

Web-Based and Educational Platforms

Web-based programs and digital education tools primarily targeted disease knowledge and transition readiness among adolescents with SCD. The STEP e-learning program improved disease knowledge and awareness but had limited effects on self-management behaviors or confidence.[17] Other web-based interventions offered structured learning modules and quizzes but lacked interactive or feedback components, which may have limited behavioral change.[23] Although educational platforms appeared to improve disease knowledge in several studies, their influence on self-care behaviors was less evident.

Cognitive Behavioural Therapy and Psychosocial Digital Tools

Cognitive behavioural therapy (CBT)–based and psychosocial digital interventions showed consistent benefits for pain reduction, coping, and mental health outcomes. Programs such as iCanCope, Beating the Blues, and guided relaxation modules produced moderate improvements in pain intensity, coping skills, and emotional well-being among adolescents and adults.[18, 29,30] These findings are broadly consistent with existing evidence supporting CBT-based approaches for chronic pain management.[3]

Telehealth and Hybrid Models

Telehealth and blended approaches that combined digital platforms with clinician or peer interaction demonstrated higher engagement and acceptability. Interventions like SCThrive integrated online group sessions with mobile self-management tools, leading to improvements in self-efficacy and motivation.[10] Similarly, mHealth apps combined with provider toolkits or patient-facing guidelines facilitated better communication and showed trends toward reduced hospitalizations, although statistical significance was rarely achieved.[25] These hybrid approaches highlight the value of human interaction and multidisciplinary support in reinforcing digital self-care efforts.

Cross-Cutting Issues: Engagement and Theory

Across intervention types, sustained engagement emerged as a persistent challenge. Most studies reported high initial participation that declined over time, particularly in app-based interventions.[16,30] Only a few interventions explicitly referenced behavior change models such as

Social Cognitive Theory or the Health Belief Model, limiting understanding of mechanisms underlying observed improvements.[10,21] Overall, variability in user engagement and the limited use of explicit theoretical frameworks may have contributed to differences in intervention outcomes across studies.

Areas for Future Research

Future research should prioritize larger, methodologically rigorous studies with longer follow-up periods to evaluate the long-term effectiveness and sustainability of digital interventions for SCD. Further investigation is needed to determine the effectiveness of personalized, culturally appropriate, and age-specific interventions, as well as blended care models that integrate digital technologies with routine clinical care. Future studies should incorporate theoretically informed frameworks, report intervention fidelity consistently, and examine strategies to sustain user engagement over time. Research conducted in low- and middle-income settings is also needed to improve understanding of the feasibility, accessibility, and equity of digital health interventions across diverse populations.

Strengths and Limitations

This systematic review provides a comprehensive synthesis of digital interventions for SCD, encompassing 23 empirical studies evaluating a broad range of technologies, including mobile applications, SMS-based interventions, web-based platforms, and telehealth approaches. A key strength of the review is its examination of multiple outcome domains, including medication adherence, self-management, pain management, quality of life, and healthcare utilization, providing a holistic assessment of intervention effectiveness. The inclusion of studies involving children, adolescents, and adults also enabled exploration of age-specific differences in intervention engagement and outcomes.

Several limitations should be considered when interpreting the findings. The included studies were highly heterogeneous with respect to study design, sample size, intervention characteristics, outcome measures, and follow-up duration, limiting direct comparisons across studies. Many studies were small-scale, feasibility, or pilot investigations with relatively short follow-up periods, reducing confidence in the sustainability of reported benefits. Methodological limitations, including moderate-to-high risk of bias in some studies and inconsistent reporting of theoretical frameworks and intervention fidelity, further restrict the strength of the evidence. In addition, many interventions experienced declining user engagement over time, highlighting challenges related to long-term implementation and retention. Finally, most studies were conducted in high-income countries, particularly the United States, United Kingdom, and Canada, limiting the generalizability of findings to low- and middle-income settings where healthcare infrastructure, digital access, and implementation challenges may differ substantially. Consequently, the findings should be interpreted as preliminary evidence supporting the potential of digital interventions rather than definitive evidence of their effectiveness.

Conclusions

Digital health interventions show encouraging potential to enhance medication adherence, self-management, and pain control in individuals with SCD. However, current evidence remains preliminary, as most studies were small or short-term and varied in design and quality.

Mobile apps, SMS reminders, and cognitive behavioral therapy–based tools appear especially promising, yet their long-term effectiveness and real-world applicability are uncertain.

Equitable access also requires attention. Most studies originated from high-income countries, whereas individuals in lower-resource settings may face barriers such as limited connectivity, affordability, and digital literacy. Adapting interventions to these contexts is essential for inclusive implementation and global impact.

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Conflict of Interest

None.

Data Accessibility

Joyce Joseph.

Ethical Issues

Ethical approval was not required because this study was a systematic review of published literature and did not involve human participants or identifiable data.

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Research Highlights

What is the current knowledge?

Digital health interventions are increasingly being used to support medication adherence and self-management in individuals with SCD.

What is new here?

This review found that mobile applications, SMS reminders, digital cognitive behavioral therapy, and web-based interventions were associated with improvements in medication adherence, disease knowledge, self-management, and pain-related outcomes, although evidence for long-term effectiveness remains limited.

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