Summary of the components of different eHealth interventions for all included studies.

First author, date, reference	Intervention Components
Jonassaint, 2015 [60]	**SMART app** • A native application for iOS (iPhone, iPod Touch, or an iPad) • Pain intensity was assessed using an electronic VAS with a slider scale (0-10) • Pain categories: ''less'', ''same'' or ''worse'' than typical pain, or ''unbearable'' • A ''pain delta score'' was automatically calculated with the pain difference from baseline • An automated warning message with a suggested intervention were triggered if patients reported pain as "Unbearable" or "pain delta score" of ≥1.5 of baseline score • Pain reported as one or more pain locations with or without other associated symptoms • Patients reported pharmacological and non-pharmacological treatment strategies
Hardy, 2016 [57]	**Cogmed app** • A home-based, computerized, interactive, audio-visual cognitive training program, installed via Internet download and compatible with Apple iOS and android-based tablet computers • Series of game-like exercises with repeated practice of different tasks for visuospatial and auditory span memory • Every exercise is adapted to the skill level of the individual user based on a trial-by-trial basis making tasks are always appropriately challenging **Coaching**: A clinical psychologist served as trained intervention or "coach" who was available to provide support all participants by phone throughout the study

Leonard, 2017 [61]	**Intensive Training Program "ITP"**
	
	• A provider-developed mobile app
	• Downloaded directly onto participants' iOS devices (iPhone, iPod, or iPad)
	• Patients were given a loaner device, if they didn't have a device
	• The ITP mobile app has the following functions:
	   o Time-stamped monitoring that enables "real-time" adherence tracking
	   o Daily self-recorded videos ("selfies") of medication administration
	   o Videos were uploaded to a secure encrypted HIPAA-compliant server

	o Remote access to provider-led disease education modules o Patient support through reminder alert messages o Behavioral reinforcement with provider messages and feedback about adherence every 7 to 10 days, based on the recorded "selfies"

Creary, 2014 [53]	**Mobile-DOT (**Multi-dimensional strategy)
	
	• Alert reminders:
	   o Automated daily alerts to remind patients to take hydroxyurea
	   o Alert sent at time preferred by patients
	   o Alerts stopped when a video is submitted
	   o Up to four text messages and e-mail were sent daily
	• Videos:
	   o Participants created daily videos of them taking hydroxyurea
	   o Videos submitted electronically to the secure study website
	   o Captured by smartphones or computers
	   o Included participants' study ID
	   o Self-recorded videos for children $\geq$12 yrs, younger ones had assistance from parents
	• Feedback:
	   o Submitted videos were reviewed by research team within 72 hours of receipt
	   o SMS and e-mail feedback was sent to participants if they missed 2 or more video submissions in a 30-day period
	   o Participants were called if they missed 3 or more video submissions in a 30-day period
	   o Positive reinforcement (at least two text messages or e-mails) was provided if they participants had adherence of 90% or more
	• Incentives:
	   o If participants achieved 90% or more of adherence to hydroxyurea for each 30-day period, they would receive $1/day

Estepp, 2014 [54]	**Text messaging "SIMON"** • Scheduled daily text message reminders for 12 months • Customizable for content, frequency, and duration • Participants created their own messages • Changes in text messages regimen checked every 3-4 clinic visits • Messages delivery was monitored (received and undelivered) • Participants could optionally reply

	• Messages sent through web-based application

Pernell, 2017 [63]	**Text messaging "REDCap"**
	
	• Two-way SMS medication reminders sent via Research Electronic Data Capture software
	• Utilized the automated invitations feature in REDCap
	• Daily and twice daily reminders based on prescribed medication regimens
	• Three arms of the study (asthma, hydroxyurea, both asthma and hydroxyurea)
	• The SMS reminders included the following text: "Did you take your [hydroxyurea] [asthma] medication [this morning] [this evening] [today]?"
	• SMS reminders were customized based on participants' time preference of the day
	• Separate reminders were sent if participants were on hydroxyurea and asthma medications
	• Text messaging algorithm:
	  o Participants were prompted to reply '(1) yes' or '(0) no' as to whether they took their medication
	  o Participants that responded '(0) no' received an additional SMS reminder two hours later reminding them to take their medication
	  o If the participant did not respond to the initial text message, one additional text reminder with the same message was sent one hour later

Inoue, 2016 [58]	**Electronic Pill Bottle "GlowCap™"** • A trained research nurse gave detailed one-on-one instructions on how to use the device • The device served as a medicine container as well as a signal transmitter • Every time the cap is opened, an electronic signal or a time stamp was sent to the central database with the recorded date and time • A separate reminder device that was plugged into a household electric outlet • The device transmitted a reminder—first by flashing lights, then by sounding chimes if the patient is late opening the cap • If 2 hours elapsed without the patient opening the cap of the device, the patient then received a telephone call reminder
McClellan, 2009 [62]; Schatz, 2015 [64]	**Internet-delivered Cognitive Behavioral Therapy "I-CBT"** Participants were given either a Motorola Q or a Samsung Saga smartphone A single-session training in CBT methods for pain management CBT coping skills session: o Psycho-education using participatory activities (Pain in sickle cell disease, Gate Control

	Theory, and active vs. passive coping)
	o Rationale and demonstration of distraction, deep breathing, progressive muscle relaxation, and guided imagery using participatory activities
	o Demonstration of deep breathing, progressive muscle relaxation, and guided imagery using the smartphone
	o Demonstration of how to use the daily diary using the smartphone
	o "Show What You Know Quiz"
	Smartphone application:
	o Daily diary application to complete ratings of pain and activity
	o Skill practice/use application to access audio files for deep breathing, progressive muscle relaxation, and guided imagery
	Written materials
	o Pain management flowchart (Child's usual medications and how to take them; reminders to use distraction, deep breathing, progressive muscle relaxation, and guided imagery; and information about when to call the doctor (developed by hematologist)
	o Coping skills handout (Brief rationale and instructions for skills; description of the child's favorite places for guided imagery; list of best activities the child generated for implementing distraction)
	o Information about the technical aspects of the smartphone
	Telephone calls
	o Weekly check-in calls with study staff (once per week)
	o Calls to address missing diaries (after 3 consecutive days of missing diaries)
	o Technical support for smartphone issues (as requested)
	Audio icons and files
	o The audio files were unique to the study and developed by one of the coauthors
	o Modeled after widely available scripts for these activities as found in numerous CBT manuals and commercial recordings for teaching these skills
	o For example, a picture of a balloon would initiate the audio file for deep breathing, and the balloon icon had been incorporated into demonstrations and written materials provided at the training session
Ezenwa, 2016 [55]	**Guided Relaxation (GR) Intervention** • A single 12-minute GR video clip administered at the baseline visit to determine its immediate effects on stress and pain • Six video clips ranging from 2-20 minutes in length for home use

	- Video clips had similar content, longer ones had more repetitions of the same content - Video clips were delivered on tablets that were programmed to prompt patients to track their stress and pain daily and allowed patients to select a video clip to watch - GR patients were instructed to watch any of the six video clips at stress onset and as often as they desired, but at least once daily to obtain a minimal intervention dose - Video clips were developed and validated in psycho-neuro-immunology studies - Some of the active ingredients in the GR video clips include colourful smoke-like images that slowly change shapes against a dark background (images, therefore, do not represent any concept with potential negative connotations), a soothing female voice and slow-paced guided relaxation instructions - Input from patient team members was used to modify these video clips to produce a patient-centered stress reduction GR intervention - Patients recommended variety in the video lengths so that they could be more easily used throughout the day as needed
Bakshi, 2017 [52]	**e-Diary Web-based Intervention** - A secure web-based application and database as a pain intensity diary - Participants reported pain intensity scores 0-10 point with a Numerical Rating Scale (NRS) - Participants were requested to report their pain scores 3 times a day at least 4 hours apart - Participants could submit additional reports as well - Participants also received automatic electronic reminders 3 times a day to log pain score - All reports were electronically time stamped and recorded on a secure database - e-diary allowed participants to see their previously reported pain scores - Text messaging was allowed to report pain if patients unable to use the web-based system - Hospital pain records were also collected from medical records - Research staff contacted participants when their pain intensity score was higher than their predetermined medical intervention level - Token monetary incentives were planned to encourage adherence to e-Diary
Jacob, 2013 [59]	**e-Diary or web-based intervention** - Patients accessed the platform twice daily - Participants reported: - Symptoms Checklist (total of 27 symptoms) - Visual Analog Scales (VAS) for pain - Adolescent Pediatric Pain Tool for marking the locations and the quality of pain (affective,

	evaluative, sensory, and temporal dimensions of pain)
	o Medications checklist (name, dose, and frequency of medications taken for pain), and the mount of relief received from medications
	o Non-pharmacological strategies that were used to relieve pain and the amount of relief received from these strategies
	o Sleep
	o Thoughts/Feelings checklist
	o Healthcare visits
	• Advanced provider nurse (APN) with expertise in SCD remotely monitored platform
	• The APN contacted participants (via text messages or phone calls) in the event that pain and other symptoms required attention, to maintain contact and monitor their progress
	• Smartphones with wireless service plans were provided at no cost

Gallo, 2014 [56];
 	
Wilkie, 2013 [65]
	CHOICES intervention
	
	• Wed-based, tailored, multimedia education program on reproductive options/consequences
	• For men and women with sickle cell disease (SCD) and sickle cell trait (SCT)
	• The goal is to develop and implement a parenting plan that supports their informed reproductive health decision and reproductive health behaviors
	• Highly interactive and experiential program
	• Required an average of 2 hours to complete
	• Simplified concept of teaching around the circle with four basic concepts:
	   o Concrete experience (video, audio or text-based case study, or clinical practice simulation) where participants were involved in a concrete experience related to reproductive issues relevant to people with SCD or SCT
	   o Reflective observation where participants reflected on the concrete experience from different perspectives (partner, family members, spiritual leader, etc.)
	   o Abstract conceptualization where participants were engage with content about SCD, SCT, and reproductive issues and behaviors
	   o Active experimentation where participant explored the content in video clips of the perspectives of other couples who made a variety of decisions and engaged in a variety of behaviors and discussed the consequences they faced

Hazzard, 2002 [67]	**STARBRIGHT World** • Curriculum: o Health-education information from reliable and accurate websites and programs developed by STARBRIGHT Foundation (e.g. Sickle Cell Slime-O-Rama Game)

	o Functionality of having children and teens being able to interact with other hospitalized children through computer systems, such as video conferencing, chat rooms, and e-mail o Distraction and entertainment during inpatient stay via different recreational activities, such as online games, arts and crafts projects • STARBRIGHT World is a private computer network developed for hospitalized children by the STARBRIGHT Foundation • Two versions of the curriculum for patients age 8-12 and 13-18 years old • 3 educational sessions (45 min for Session 1, and 15 min for Sessions 2 and 3) • Participants completed a worksheet for every day of the curriculum • Research staff received training on the curriculum and different related activities

Yoon, 2007 [66]	**CD-ROM educational game "Sickle Cell Slime-O-Rama Game ®"**
	
	• Part of the starlight Series (www.starlight.org)
	• Seven questions per round, 2-3 choices per question
	• Questions included 3 categories:
	   o Sickle cell disease facts
	   o Taking care of your health
	   o Pain management
	• With each answer, the program indicated whether the choice was correct or not
	The program provided the right answer with an explanation if it was not correct