Feasibility, Safety, and Effectiveness of a Mobile Application in Cardiac Rehabilitation

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ABSTRACT

Background: Cardiac rehabilitation (CR) is underutilized globally despite evidence of clinical benefit. Major obstacles for wider adoption include distance from the rehabilitation center, travel time, and interference with daily routine. Tele-cardiac rehabilitation (tele-CR) can potentially address some of these limitations, enabling patients to exercise in their home environment or community.

Objectives: To evaluate the clinical and physiological outcomes as well as adherence to tele-CR in patients with low cardiovascular risk and to assess exercise capacity, determined by an exercise stress test, using a treadmill before and following the 6-month intervention.

Methods: A total of 22 patients with established coronary artery disease participated in a 6-month tele-CR program. Datos Health (Ramat Gan, Israel), a digital health application and care-team dashboard, was used for remote monitoring, communication, and management of the patients.

Results: Following the 6-month tele-CR intervention, there was significant improvement in exercise capacity, assessed by estimated metabolic equivalents with an increase from 10.6 ± 0.5 to 12.3 ± 0.5 ($P = 0.002$). High-density lipoproteins levels significantly improved, whereas low-density lipoproteins, triglyceride, glycosylated hemoglobin, and systolic and diastolic blood pressure levels were not significantly changed. Exercise adherence was consistent among patients, with more than 63% of patients participating in a moderate intensity exercise program for 150 minutes per week.

Conclusions: Patients who participated in tele-CR adhered to the exercise program and attained clinically significant functional improvement. Tele-CR is a viable option for populations that cannot, or elect not to, participate in center-based CR programs.

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KEY WORDS: cardiac rehabilitation, cardiovascular disease, coronary artery disease, mobile application, tele-cardiac rehabilitation (tele-CR)

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Cardiac rehabilitation (CR) is highly recommended for patients presenting with cardiovascular disease [1]. Exercise therapy as a central element of CR [2]. Indeed, CR is a cost-effective method to significantly reduce all-cause and cardiac mortalities, as well as to decrease hospitalizations by 12–34%, while concurrently improving quality of life, well-being, and overall functional capacity [3,4]. Despite the clear indication and proven benefits, CR is underutilized for secondary prevention with only 14–31% of eligible patients participating [5]. The barriers to participation in traditional structured exercise programs in center-based CR settings include; low referral rates, difficulty attending (transportation, time constraints, inconveniences), and the associated direct and indirect costs [6,7].

Recent advances in technology and remote access to care are attempting to address these barriers and increase CR participation in eligible patients. Mobile technology has the potential to overcome these barriers to cardiac rehabilitation and become a useful tool for improving access to health promotion interventions. Studies have shown that when CR is implemented via smartphone as opposed to traditional center-based care, uptake, adherence, and completion of the program increases significantly [8]. Furthermore, using mobile technology in cardiac rehabilitation has the unique advantage of being able to influence health behaviors in real-time while the patient is not at the rehabilitation center [9]. Mobile technology combined with specialty designed applications has proven to increase motivation, physical activity, and weight loss in generally healthy populations [10].

In recent years, it has been increasingly shown that multifactorial individualized tele-health and community- or home-based rehabilitation are effective alternative models of rehabilitation as they have produced similar reductions in risk factors when compared with hospital-based programs [11]. In 2018 the American College of Cardiology and American Heart Association updated their guidelines to include alternative models of CR delivery (home-based, electronic/mobile technology based) as potential options rather than traditional center-based CR [12].

We designed a pilot study to assess the feasibility, safety, and effectiveness of an exercise rehabilitation program using a combination of mobile application and multidisciplinary caregiver control centers on safety and adherence to the exercise program as well as clinical and physiological outcomes in a population of low-risk patients.

PATIENTS AND METHODS

STUDY POPULATION

A single center, prospective single arm study was conducted to evaluate the effects of a cardiac rehabilitation exercise program, using a smart phone application and care team management system. The study protocol was reviewed and approved by the ethics review board at Sheba Medical Center. A total of 22 patients with established coronary artery disease referred to the outpatient Cardiac Prevention and Rehabilitation Institute at Sheba Heart Center agreed to participate and were enrolled in the study.

Principal inclusion criteria were: preserved left ventricular function (left ventricular ejection fraction ≥ 50%). Exclusion criteria included: severe orthopedic or neurological or cognitive impairment, clinical ischemia, non-invasive evidence of ischemia, diagnosis of heart failure, low functional capacity defined as < 4 METs at baseline stress test, or change in medication prescription during the program.

The primary endpoint was the safety, feasibility, and adherence to the cardiac rehabilitation program as assessed by smart watch recorded minutes of aerobic exercise > 70% max per week, number of resistance training session per week, and patient questionnaires. Safety was addressed by collecting data on hospital/doctor visits during the trial. The secondary endpoint was change in exercise capacity as assessed by stress test prior to and following the 6-month program.

The following variables were assessed longitudinally in each month of the exercise program: number of minutes of exercise at target heart rate (HR), below and above target HR, average HR, number of minutes of aerobic exercise (aerobic minutes), frequency of aerobic exercise per week, frequency of resistant exercise, the Borg Rating of Perceived Exertion scale, daily step count, and mobile application usage (amount of time of mobile application usage per week). Clinical and exercise stress testing outcomes were measured pre- and post-CR program using the same protocol, including all standard parameters and lab testing for high-density lipoproteins (HDL), low-density lipoproteins (LDL), triglyceride (TG) fasting glucose, and hemoglobin A1c (HbA1c). We calculated average heart rate reserve (HRR) for each aerobic exercise session using the following equation: (average HR of exercise / max HR attained at the baseline stress test) × 100.

TELE-CARDIAC REHABILITATION PROGRAM

The secondary prevention tele-cardiac rehabilitation (tele-CR) program duration was 6-months, consisting of an intake physician consultation, nurse assessment and education, as well as dietitian, psychologist and exercise physiologist evaluation. A physical education specialist served as the tele-CR expert following appropriate training. The tele-CR expert educated and assisted the patients with setup of the watch and applications and consultations were provided every 4 weeks. The tele-rehabilitation specialist monitored progression on a daily basis and provided consultation every week, using Datos Health (Ramat Gan, Israel) disease management and messaging system or by telephone call. In addition, patients had the opportunity to watch educational videos and read articles related to the program available through the Datos application. The physiologist updated the exercise program as needed every 5 weeks. This change was reflected in each of the patient application (the target heart rate display changed). The psychologist and dieticians provided telephone consultation based on patient needs.

Target HR was determined by exercise physiologists based on the exercise testing results and medical history, according to European Society of Cardiology (ESC) cardiac rehabilitation guidelines, and was updated based on the individual's progress [13]. According to ESC guidelines, the goals were as follows: at least 150 minutes of moderate intensity aerobic activity (~70% of HRR), and two sessions of resistance training per week. Our team pre-defined a goal to be that the patient would spend > 70% of the session duration at or above the target heart rate. Patients began the exercise at the rehabilitation center, and gradually over a period of 6 months, reduced the number of visits, while concomitantly increasing the number of home/community based exercise sessions (a reduction of 2 on-site sessions per month, ultimately reduced to no on-site sessions for the final 2 months). As such, 20 on-site sessions were completed over the course of the trial, as opposed to the normal practice of 8 sessions per month totaling 42. Patients were encouraged to be engaged in any form of home/community aerobic exercise (dancing, swimming, and walking). Videos, educational material, and telephone coaching were used to educate and support patients.

TELE-MONITORING AND CARE TEAM INTEGRATION

A digital health application and care-team dashboard by Datos Health was used for remote patient monitoring to provide continuity of care throughout the program and to integrate derived insights directly to the clinician and multidisciplinary team, which included a nurse, physiologist, nutritionist, sociologist, and kinesiologist. This system offered a remotely monitored cardiac rehabilitation program, incorporating structured exercise using a smartwatch, as well as monitoring of blood pressure, glucose, activity, and patient reported outcomes. The patients received an application with a personalized care plan and monitoring devices as well as automated personalized feedback following each training session in addition to reminders and summaries of their overall progress. The care team viewed the results periodically, provided additional feedback, and adjusted the program as necessary.

During all exercise sessions, patients wore a smartwatch with matching smartphone Polar application (Polar Inc, M430; Kempele, Finland) to collect and upload data to the Polar cloud, including activity type, HR during exercise, and step count. Data were extracted, processed, and presented to the patients via the Datos Health smartphone application. In addition, the relevant information regarding adherence and progress were graphically presented to the care team, using a dedicated care management portal developed for this program by Datos Health. The care team had full access to both a group overview with adherence data, and an individual patient view where details of personalized physical activity, HR zones, steps per week, and resistance training were presented. No personal health information was uploaded to these systems. Using the Datos Health smartphone application, it was possible to send secure text messages and automatic reminders to patients as well as educational and motivational messages based on a rule engine. The Datos Health smartphone application had the capacity to send questionnaires to the patients and modify the questionnaires as needed during different stages of the cardiac rehabilitation.

The following self-report questionnaires were sent to the patients: Patient Health Questionnaire (PHQ-9) and Patient Reported Outcomes Measurement Information System 10 (PROMISE 10).

Adherence was assessed as follows:

- Percent of target exercise minutes completed
- Percent of exercise time spent at designated target HR zones
- Average daily step count
- Number of exercise sessions (> 10 minutes per month)
- Mobile application usage (the amount of time that the patients used the mobile application).

Safety of the tele-CR program was assessed and any adverse events were recorded. Remote patient management time was recorded at months 1, 3, and 6. The following patient management variables were recorded: time of response, time of call, number of applies, number of messages, and number of calls.

STATISTICAL ANALYSIS

Baseline characteristics are presented as mean ± SD or percentages as appropriate. The paired sample *t*-test was used to assess the differences between baseline and following program completion values of the following variables; resting and maximal HR, HRR, resting and maximal diastolic and systolic blood pressure, exercise testing time, maximal METS, LDL, triglyceride, HDL, fasting glucose, and HbA1c levels. The differences of the means of HRR and step count for each month of the exercise program were compared using repeated measure analysis of variance (ANOVA) followed by Sidak adjustment for multiple comparison. A Pearson's correlation coefficient was performed to examine the relationship between HR reserve and METS value achieved.

A *P* value < 0.05 was considered statistically significant. Statistical analyses were performed using the statistical package SPSS version 14.0 (IBM Chicago, IL).

RESULTS

Baseline characteristics of study patients are presented in Table 1. One patient dropped out of the study prior to starting the program, reporting that he found the technology too complex.

Following the 6-month tele-CR intervention, there was a significant improvement in exercise capacity, assessed by estimated METS, using pre- and post-exercise stress tests, increasing from 10.6 ± 0.5 to 12.3 ± 0.5 (*P* = 0.002) [Figure 1]. In addition, HDL levels significantly improved from pre- to post-6-month tele-CR intervention, from 41 ± 2.4 to 44.5 ± 2.6, *P* = 0.016. Other clinical outcomes were not significantly different between pre- and post-exercise training, including HR, systolic blood pressure, diastolic blood pressure, LDL, TG, and HbA1c. No adverse events occurred during the study period

Table 1. Baseline characteristics of patients

Variables	Mean (SE) or percentage (n)
Mean age (years)	52.7 ± 0.81
Male % (n)	77.3% (n=17)
Metabolic co-morbidities	
Dyslipidemia % (n)	68.2% (n=15)
Hypertension % (n)	45.4% (n=10)
Diabetes mellitus % (n)	13.6% (n=3)
Non metabolic co-morbidities	
Myocardial infarction % (n)	68.2% (n=15)
Status post coronary artery bypass % (n)	13.6% (n=3)
Status post percutaneous coronary % (n)	81.2% (n=18)
Musculoskeletal disorders % (n)	9.1% (n=2)
Malignancy % (n)	4.5% (n=1)
Gastrointestinal disorders % (n)	13.6% (n=3)
Psychological depression/anxiety % (n)	13.6% (n=3)
Past smoking % (n)	13.6% (n=3)
Current smoking % (n)	13.6% (n=3)
Physical and functional status	
BMI (kg/m^2)	26.6 ± 0.6
Rest heart rate (bpm)	73 ± 2.3
Maximal heart rate (bpm)	153 ± 4.8
Systolic blood pressure (mmHg)	122 ± 2.6
Diastolic blood pressure (mmHg)	77 ± 1.3
Maximum METs (baseline stress test)	10.6 ± 0.6
Metabolic status	
Fasting glucose (mg/dl)	100.6 ± 3.2
Hemoglobin A1c (%)	6.2 ± 0.6
HDL (md/dl)	41 ± 2.5
LDL (mg/dl)	78 ± 6.8
Triglycerides (md/dl)	123.4 ± 14.9

bpm = beats per minute, HDL = high-density lipoproteins, LDL = low-density lipoproteins, MET = maximal metabolic equivalent, SE = standard error

Figure 1. Pre and post 6-month tele-cardiac rehabilitation intervention metabolic equivalents changes
MET = maximal metabolic equivalent

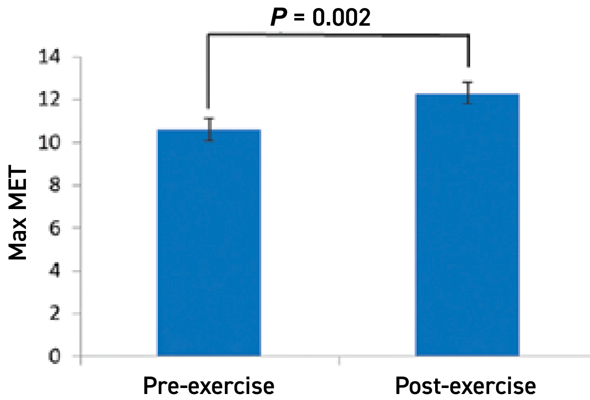
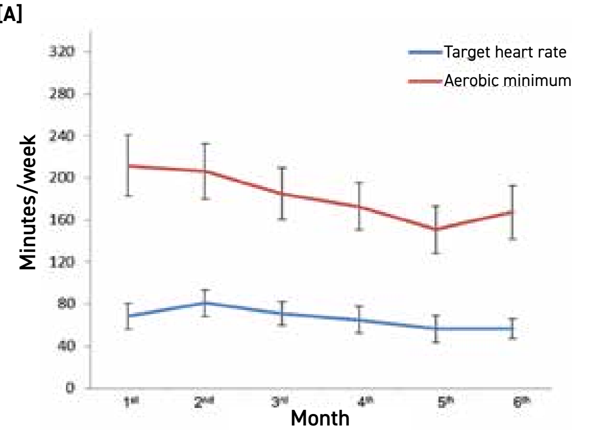
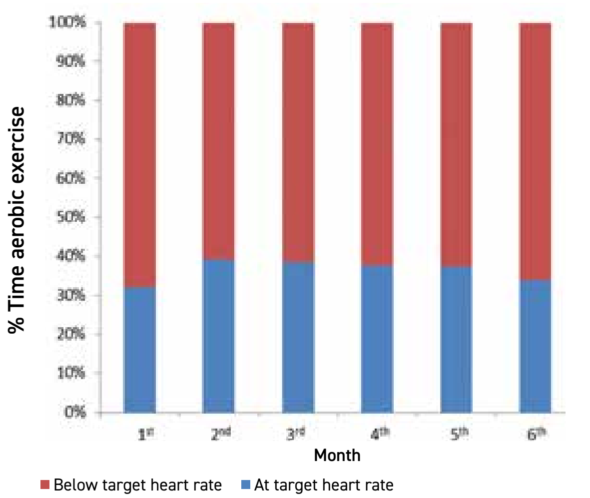


Figure 2. The average minutes per week that patients performed aerobic exercise **[A]** Exercise at the target heart rate across 6 months **[B]** Percentage of time of aerobic exercise below and at the target heart rate across 6 months

[A]



[B]



with the exception of two emergency department visits due to abdominal pain and chest pain, both of which were discharged following evaluation. Patient satisfaction with the program in its entirety was high (4.05 of 5) and the use of our application was high (weekly average of 4 days a week).

The average minutes per week that patients performed aerobic exercise was 182.5 ± 19.7, while the average minutes at target HR or 10% above target was 66.4 ± 9.7 [Figure 2A], representing 30–40% of the exercise session [Figure 2B]. The average HR during aerobic exercise was 108.5 ± 3.3 (beats per minutes) with no significant changes in the average HR across the 6 months. The average HRR was 73.2 ± 1.7% across the 6 months of exercise training, with significant improvement from the second month ($P = 0.001$) with no significant changes thereafter. The average HRR values from months 1 to 6 were 70.8 ± 1.4, 73.4 ± 1.4, 74.4 ± 1.7, 73.0 ± 2.1, 73.4 ± 2.1, and 74.2 ± 2.1. Activity type recorded was mainly treadmill and outdoor walking or light jogging. Resistance training was reported (via the Polar watch) at an average of one session per week. Exercise adherence was consistent among our patients as exercise training variables were not significantly different across months 1 through 6 of the CR program. More than 63% attained the goal of 150 minutes of aerobic exercise per week. Conversely, adherence to two resistance training sessions per week was poor (18% of patients). Session duration training at or above target HR was 36.4%, which was less than our predefined study goal of 70%. The average perceived exertion reported using the Borg scale was 11.9 ± 1.5. Unfortunately, patient response rate to the questionnaires were suboptimal, 57% for the PHQ9 and 69% for PROMISE 10.

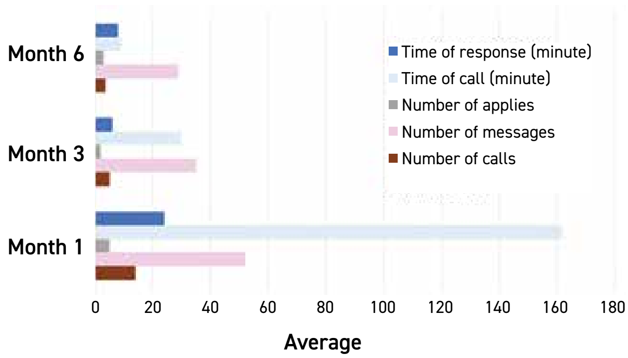
The average minutes below target HR was not significantly different across the 6 months, with an average of 122.9 ± 20.0. The average number of resistance training sessions per week was 0.9 ± 0.1, with no significant differences across the 6 months. The average daily steps was 11344.1 ± 1029.4, with no significant differences across the 6 months. The average mobile application usage was 3.7 ± 0.3, with a trend of higher usage at the third month compared to the other 5 months.

The average minutes per week for remote patient management were 186.5 on the first month, 37 on the third month, and 17.75 on the sixth month [Figure 3].

DISCUSSION

The principal findings of our study included: technology was well accepted and adherence to the program was good, attaining guideline recommended durations; over a period of 6 months levels of activity were maintained and satisfaction was high; significant improvement in exercise capacity was obtained (change in METs) comparable to changes reported in meta-analysis studies [14]; and exercise intensity and resistance training was below set goals and further planning and effort should be invested in this domain.

Figure 3. Remote patient management



Throughout the 6 months, we found a number of elements to be important for program success, including an individualized amount of human interaction with patients and motivational messages, encouragement to maintain lifestyle changes, and feedback and encouragement to continue the program [15]. These findings are consistent with behavioral change techniques proposed by Heron et al. [15] and Fogg [16]. The ability to send secure messages, permitting asynchronous secure compliment communication with patients led to significant time savings for the patient in the form of reduced travel and wait times, as did the ability to send surveys and questionnaires, that when completed, appeared in our care team dashboard as a time series event, allowing for trend analysis.

A major barrier to performing cardiac rehabilitation is difficulty attending the session due to transportation issues, time constraints, and other inconveniences. These barriers can be significantly elevated by the time-savings and convenience that a remote-rehabilitation program provides. By performing the CR at home, the patients avoid commute and wait times. This expediency also increases patient freedom to perform the rehabilitation at their own convenience thus avoiding scheduling conflicts or other inconveniences.

Another element for success was appropriate technology developed by tight collaboration with a technology company that was inspired by and followed the Agile principles. It was paramount that the patient side of the application be simple to setup and use and interfere minimally with everyday life. This condition was facilitated by a smartwatch that measured HR without the need of chest belt and relatively simple user interface. In addition, most patients wore the watch daily without the stigmatizing effects of a medical device. In addition, the Datos Health application and portal allowed monitoring and follow-up of patients by a multidisciplinary team using messages, educational materials, and other media. The system automatically sent notifications related to the activities of the patients. Patients were fully engaged in the program, with the ability to review graphs and receive information about their adherence and progress. On the care team side, summarized adherence data were reported and alerts automatically sent to both patients and the care team when deviations were noted. The ability to tailor alerts and messages using a user configurable rule engine permitted individualized monitoring schemes and avoided alert fatigue. This user configurability provided patients with further involvement in their care, allowing them to tailor it to their own needs, while still providing at least a minimal level of alerts and messages.

Improvement in exercise capacity has been recognized as the single most important predictor of both cardiac-related and all-cause deaths in patients with CVD [17], suggesting that the improvement achieved in this program has the potential to decrease mortality in these patients. Despite only about one-third of our patients achieving the desired exercise intensity, two-thirds of them completed the duration goal of 150 minutes per week, which may account for the increase in exercise capacity. Perhaps, this good adherence to increased exercise volume is able to offset the sub-optimal intensity. This finding increases the feasibility of mobile application usage for a combined remote and center based cardiac rehabilitation program; however, it may not be generalizable to a fully remote program.

Our results are consistent with results of research groups exploring the role of tele-CR, while we extend these finding with a longer program duration and the use of wearable devices used throughout the day such as accessible HR monitoring without the use of additional hardware. Improvement in exercise capacity noted in our study is comparable to the improvement reported by Kraal et al. in the FIT@HOME study [18]. The TELEREHAB III study by Frederix et al. [19] also reported significant changes in exercise capacity over a 24-week hybrid program, although this study used accelerometers and didn't use watches that incorporated both accelerometers and HR monitors. Furthermore, we aimed to maximize patient adherence through automation of the data acquisition and upload process. Data visualization, interaction with the care team, and education were based on the application, which was easily installed on the patient's own smartphone. Accordingly, studies have shown that the rates of adherence to home-based cardiac rehabilitation settings were similar or higher to that of the traditional on-site program (with reported adherence between 55%–76%) and produced similar gains in cardiovascular fitness and physiologic outcomes [20]. The reduced patient cost of rehabilitation is likely related to improved rates of exercise adherence.[20]

Currently, up to 89% of adults in the United States own a smartphone with the ability to personally review and interact with recorded data, receive automated feedback, and connect instantly with other users and healthcare providers [21]. This usage provides the possibility that incorporating smartphone technology may be an applicable tool in the majority of patients eligible for CR and increase patient participation.

Promotion of patient participation in their own care is an evolving area of interest, and placing patients at the center of care has been described to improve patient satisfaction and improve adherence to treatment by enhancing healthcare provider-patient communication [22] and patient empowerment [23]. Using mobile application technology has the potential to increase adherence to treatment by allowing different modes of communication between the healthcare provider-patient relationship and by allowing the patients to gain control of their rehabilitation.

Our patients exercised at or above target HR for 36% of the session duration and performed 50% of the target weekly frequency of resistance training. Also, the intensity level of exercise was low as the perceived exertion on the Borg scale was lower than our set target of 13–14 points. The rate of patient response to the questionnaires, distributed by the application, was very low and may be related to the technological barriers or to the delivery of the rehabilitation. This limitation needs to be addressed in future studies, in which patients can learn that questionnaire completion can help both them and the rehabilitation providers to understand whether or not the goals of rehabilitation are being achieved.

The major limitation of our study is the small sample size. An additional limitation is that our study did not employ a control group and the inclusion criteria invariably can lead to selection bias, enrolling patients who are comfortable with technology use compared to the general population. However, one of the major objectives of this pilot study was to assess safety as well as feasibility of using this new digital health application and care team dashboard for remote monitoring, communication and management of CR patients. Therefore, a small group of patients is preferred. In our ongoing study, we are including this technology in a larger sample size and a control group. Since this study was a pilot, we included low-risk patients. Indeed, exercise rehabilitation programs have been shown to improve clinical outcomes also in patients who have a low risk profile [24]. Our team's future objectives are to include patients at higher risk as well as older patients. In addition, although our patients exhibited a modest increase in exercise capacity, research has shown that even a modest increase in exercise capacity is associated with more favorable clinical outcomes [25].

Furthermore, the initial exercise was supervised similar to traditional CR, and it was only later in the program that community sessions become central. Nevertheless, we recorded no decline in activity once transition to community only CR occurred. It is important to highlight that although the selected patient cohort had co-morbidities, they were at low cardiovascular risk. According to the Israeli Ministry of Health, these patients are eligible for either centered-based or remote CR.

CONCLUSIONS

Tele-CR, and specifically a hybrid center/remote program, is a viable option for attaining good adherence and functional improvement. Healthcare providers should strive to integrate alternative models of rehabilitation, such as telehealth interventions tailored to individual risk factor profiles as well as community- or home-based programs to ensure there are choices available for patients that best fit their needs, risk factor profile, and preferences [11]. Further studies should focus on the effects of tele-CR programs in populations that cannot, or elect not to, participate in center-based CR programs due to barriers that can be overcome by tele-CR.

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Capsule

Bromodomain inhibitors revisited

Bromodomain and extraterminal domain (BET) proteins contribute to the pathogenesis of cancer and immune diseases through their effects on transcriptional regulation. BET proteins contain two nearly identical bromodomains, BD1 and BD2, structural modules that have attracted great interest as targets for drug development. First-generation drugs that inhibited both BD1 and BD2 showed promising therapeutic activity in preclinical models but proved to be less efficacious in clinical trials. **Gilan** and colleagues took a different approach and designed drugs that selectively inhibited BD1 or BD2. They found that BD1 and BD2 inhibitors altered gene expression in different ways and that BD2 inhibitors had greater therapeutic activity than BD1 inhibitors in preclinical models of inflammation and autoimmune disease.

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Eitan Israeli

Capsule

What happens next with the corona epidemic?

Four months into the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) outbreak, we still do not know enough about post-recovery immune protection and environmental and seasonal influences on transmission to predict transmission dynamics accurately. However, we do know that humans are seasonally afflicted by other, less severe coronaviruses. **Kissler** and colleagues used existing data to build a deterministic model of multiyear interactions between existing coronaviruses, with a focus on the United States, and used this to project the potential epidemic dynamics and pressures on critical care capacity over the next 5 years. The long-term dynamics of SARS-CoV-2 strongly depends on immune responses and immune cross-reactions between the coronaviruses, as well as the timing of introduction of the new virus into a population. One scenario is that a resurgence in SARS-CoV-2 could occur as far into the future as 2025.

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Eitan Israeli

Pleasure in the job puts perfection in the work

Aristotle (384–322 BCE), ancient Greek philosopher and scientist born in the city of Stagira, Chalkidice, on the northern periphery of Classical Greece