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Appropriate exercise prescription in primary and secondary prevention of cardiovascular disease: why this skill remains to be improved among clinicians and healthcare professionals.
A call for action from the EXPERT Network

EXPERT stands for 'EXercise Prescription in Everyday practice & Rehabilitative Training', this working group is endorsed by the European Association of Preventive Cardiology (EAPC)

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Abstract

In Europe alone, on a yearly basis millions of people need an appropriate exercise prescription to prevent the occurrence or progression of cardiovascular disease (CVD). A general exercise recommendation can be provided to these individuals (at least 150 min of moderate-intensity endurance exercise, spread over 3-5 days/week, complemented by dynamic moderate-intensity resistance exercise 2 days/week). However, recent evidence shows that this one size does not fit all and that individual adjustments should be made according to the patient's underlying disease(s), risk profile and individual needs, to maximise clinical benefits of exercise. In this paper, we 1. argue that this general exercise prescription simply provided to all patients with CVD, or elevated risk for CVD, is insufficient for optimal CVD prevention, and 2. show that clinicians and healthcare professionals perform heterogeneously when asked to adjust exercise characteristics (e.g. intensity, volume and type) according to the patient's condition, hereby leading to suboptimal CVD risk factor control. Since exercise training is a class 1A intervention in the primary and secondary prevention of CVD, the awareness of the need to improve exercise prescription has to be raised among clinicians and healthcare professionals, if optimized prevention of CVD is ambitioned.

Introduction

Cardiovascular diseases (CVD) remain the most important causes of premature death across the globe.[1] Data from the European Society of Cardiology (ESC) show that many individuals are at high risk of CVD or already suffer from a CVD.[2] The European prevalence rates for arterial hypertension, obesity, hyperlipidaemia, and diabetes in adults without established CVD are 25%, 22.5%, >50%, and 6.1% respectively.[2] Moreover, around 80% of the global population does not achieve a sufficient amount of physical activity (PA).[3] Hence, this leads to a huge prevalence and incidence of CVD: in 2019, Europe counted 113 million people with CVD, and another 12.6 million individuals experienced CVD for the first time.[2] Collectively, this accounts for an estimated 85 million Disability Adjusted Life Years (DALYs) in Europe. The rise of CVD is not only an issue in Western countries/regions, since increments in CVD prevalence and incidence have been noticed in the South and East, as well.[1]

Physical activity and exercise are key in the primary and secondary prevention of CVD.[4-6] PA is defined as any bodily movement produced by skeletal muscles that results in an increase of energy expenditure.[7] Physical exercise or exercise training is PA that is structured, repetitive, and purposeful to improve or maintain one or more components of physical fitness.[7] Exercise training or exercise-based rehabilitation programs lead to significant improvements in health-related physical fitness, CVD risk factor control, and quality of life, in patients with different chronic CVDs, further leading to reduced CV event rates, hospitalisations and/or mortality during follow-up.[4,8-11] Hence, exercise training is therefore classified as an intervention with the highest level of evidence for the treatment and prevention of CVD by numerous international position statements and guidelines.[4-7] Consequently, millions of individuals annually would benefit from an individualised exercise prescription that effectively prevents or attenuates the progression of CVD. How well clinicians (medical doctors) and healthcare professionals (e.g. physiotherapists, clinical exercise physiologists, (cardiac) nurses) are able to prescribe such tailored exercise programs has been a topic of investigation in the last decade.[12-14]

Definitions of primary and secondary prevention of CVD

Throughout this paper, the primary prevention of CVD is defined as the prevention of CVD (e.g. acute coronary syndrome, stroke, peripheral arterial disease, etc.) in persons with significantly elevated risk to develop CVD (e.g. persons with obesity, diabetes, hypertension, or dyslipidaemia). Hence, these are not individuals with a fully negative CVD risk profile ('healthy' persons). The secondary prevention of CVD is defined as the prevention of recurrent or additional CVD (e.g. acute coronary syndrome, restenosis, stroke, etc.) in persons with established CVD (e.g. persons with acute coronary syndrome, critical coronary stenosis, stroke, peripheral arterial disease, etc.).

How accurately do clinicians and healthcare professionals prescribe exercise in the primary and secondary prevention of CVD?

In general, in primary and secondary prevention of CVD at least 150 minutes of low-to-moderate-intensity endurance exercise training per week should be performed, ideally spread over 3-5 days per week, as part of a healthy lifestyle. An energy expenditure of 1000-2000 kcal per week should be achieved in this way, and endurance exercise training should be complemented by dynamic resistance exercise training two times per week on non-consecutive days at a moderate intensity.[5-7]

From such recommendations, it may seem that prescribing exercise to patients with CVD, or an elevated risk, is easy and straightforward, and always has the same content, so it can be done by any clinician or healthcare professional, regardless of prior (specific) training/education.

However, the reality is very different and, in line with pharmacological treatment, person-tailored exercise prescriptions are needed to target a specific risk factor or manage a specific CVD. For example, to optimise glycaemic control (in type 2 diabetes) or maximally reduce adipose tissue mass (in persons with obesity) would require different exercise prescriptions.[15] Data show that clinicians and healthcare professionals perform poorly, when it comes to tailoring the exercise prescription according to the goal of the exercise intervention (which can, at least in part, be affected by the patient's phenotype, underlying diseases and co-morbidities and individual goals (e.g. CVD risk factors)).[12-14]

For example, 53 clinicians and healthcare professionals from Belgium, the Netherlands, Germany, France, the United Kingdom, Italy, Spain, Austria and Portugal, including cardiologists (68%), physiotherapists (11%), cardiovascular rehabilitation scientists (7%), physiatrists (6%), and sports physicians, general practitioners, rehabilitation physicians and exercise physiologists (2% in each category), were requested to formulate exercise prescriptions for five standardised patient cases (see Table 1). These were cases in primary (e.g. case 2) and secondary (e.g. cases 1, 3, 4, and 5) prevention of CVD. The participants were quite experienced, based on their reported years of experience (median 10 (interquartile range (IQR) 15) years). However, none of the participants had any experience with the use of the EXPERT tool or did receive any training on exercise prescriptions as formulated in the EXPERT tool. They were requested to define the exercise intensity, session duration, weekly exercise frequency, minimal program duration and exercise type (e.g. additional resistance training), considering all CVD risk factors, including medication intake and exercise capacity (peak oxygen uptake (VO_{2peak})). Figure 1 shows that the totally prescribed exercise volume ranged from 300 up to 9000 peak-effort training minutes, which is a significant variance.[12] Similar patient cases were used in a study that involved 26 primary care physicians (from Italy)[13] and 47 physiotherapists (from Belgium),[14] with identical findings/outcomes (very large inter-clinician variances). This also highlights the low level of agreement (76.4±26.1, on a maximal score of 180) between physiotherapist's exercise prescriptions and European (ESC/EAPC) recommendations, even though >90% of the participants agreed on the

declaration that they 'fully understand how to prescribe exercise in accordance with the current CV guidelines'. Hence, a gap exists between the perceptions of clinicians and healthcare professionals on their exercise prescription skills and their actual prescription skills that are not fully in line with the contemporary recommendations.

This series of surveys indicates that state-of-the-art exercise prescription to patients with CVD, or an elevated CVD risk, is far from established and that clinicians and healthcare professionals need guidance that goes beyond existing guidelines and position statements (i.e. how to tailor exercise interventions based on the patient's CVD, risk profile, physical fitness, pharmacological treatment and individual needs).

It can, however, be argued that such tailoring is unnecessary because evidence shows that simply increasing the level of PA already elicits mortality-reducing effects.

Just getting people physically active helps to prevent premature death; is tailoring of exercise prescription for primary and secondary prevention of CVD then needed?

In 90,211 participants without prior or concurrent CVD in the UK Biobank cohort, the hazard ratios (HRs) for CVD were decreased in a dose-response manner by PA (most vs. least active individuals for moderate-intensity PA: 0.46; for vigorous-intensity PA: 0.41; and for total volume of PA: 0.47.[16] Similar dose-response relations have been found between the amount of PA and risk for premature death or incident CVD in many other large studies (see Figure 2).[17-23] Additionally, clinical trials also revealed that engagement in short bouts (15-30 min) of high-intensity exercise, could elicit significant mortality reductions.[20] Hence, getting people active would be a great success in terms of mortality reductions.

But plenty of evidence has been delivered in the last decade(s) showing that a one-size-fits-all approach in exercise prescription (every patient with CVD, or an elevated CVD risk, should execute at least 150 minutes of low-to-moderate-intensity endurance exercise training per week, ideally spread over 3-5 days per week, complemented by dynamic resistance exercise training two times per week at a moderate intensity) is not effective enough at the individual level.

For example, in healthy individuals, it already has been revealed that one in five adults following general PA guidelines do not demonstrate any improvement in cardiorespiratory fitness (CRF).[24] This non-response to exercise training was completely abolished by increasing the dose of exercise,[25] as an example of tailored exercise prescription to increase its efficacy.

Similar findings have been reported in CVD patients (secondary prevention): the volume of exercise is the key driver towards improvements in CRF and thus should be prescribed appropriately.[26-28] Moreover, in patients with CVD, or with elevated CVD (primary and secondary prevention), it is essential to optimise all CV risk factors to enhance long-term outcomes (hospitalisations and mortality),[4] next to improvements in CRF. In these patients the provision of PA trackers (which provide

general (one-size-fits-all) exercise advice) leads to significant increments in PA among people with CVD.[19] Yet, despite the significantly positive impact on PA, no effect was found on arterial blood pressure, high-density and low-density lipoprotein cholesterol level, and body weight.[29] Another meta-analysis confirmed that PA tracker interventions failed to affect most of the CVD risk factors, and the remaining factors to only a minor extent (waist circumference, LDL cholesterol and systolic blood pressure).[30] Moreover, exercise-based cardiac rehabilitation without proper tailoring of exercise characteristics is less effective to optimally improve CVD risk and CRF in patients with CVD (secondary prevention).[31,32] Indeed, in people with elevated CVD risk (primary prevention), moderate-intensity PA, equivalent to 40 minutes of walking per day, attenuates but does not completely offset CVD risk among 29,333 participants.[33]

What clinical benefits do we miss in primary and secondary prevention of CVD if we do not tailor the exercise prescription appropriately?

Table 2 presents the additional clinical benefits as a result of tailoring exercise prescription for various CVD risk factors, when compared with the one-size-fits-all approach (i.e. 150 minutes of low-to-moderate-intensity endurance exercise training per week, spread over 3-5 days per week, complemented by dynamic resistance exercise training two times per week at a moderate intensity). From these data, it can be observed that depending on which CVD risk factor is being targeted, very different exercise modalities may require significant adjustment. For example, if significant and clinically meaningful fat mass reduction is ambitioned in a person with obesity, the one-size-fits-all exercise prescription should be adapted towards a high-volume aerobic exercise prescription (250-420 min/week of aerobic exercise then becomes the target).[41] Such adaptation leads to a significantly greater weight loss, fat mass loss and waist circumference reduction.[42] Moreover, if blood pressure reduction is one of the aims of the exercise intervention, the one-size-fits-all exercise prescription may not be sufficiently effective, and patients with hypertension should then be exposed to an appropriate exercise session duration (>30 min/session)[45], an appropriate intensity of endurance exercise (at least moderate-intense)[45], and an appropriate number of sets of resistance exercise (≥8 sets).[46] These adaptations lead to significant greater reduction in systolic blood pressure.[45,46] How to adapt the one-size-fits-all exercise prescription in case of hyperglycaemia, dyslipidaemia, a lowered endurance capacity and muscle strength are explained as well in Table 2.

Hence, this requires thorough education of clinicians and healthcare professionals and also detailed examination of the patient's clinical status (e.g. CVD risk factors and components of physical fitness).

Proposal of a staged approach for optimized CVD risk factor control in primary and secondary prevention of CVD

Because an increment in PA leads to mortality reductions, getting people from a sedentary lifestyle to an active lifestyle is a major step forward and should always be ambitioned. However, when it comes to maximally improving CRF and the entire CVD risk profile, and in particular in people with elevated CVD risk or established CVD, the general 'one-size-fits-all' PA intervention is insufficiently effective. Therefore, a general PA intervention is well-suited to initiate a first engagement in PA (first stage), but to maximise the impact of exercise intervention on the entire CVD profile, tailoring the exercise prescription becomes highly relevant (second stage, see Figure 3).

How to overcome the clinician's and healthcare professional's struggle with tailoring an exercise prescription?

There have been previous attempts to improve exercise prescription skills by clinicians and healthcare professionals. For example, it has been tested whether a computerized decision support (CDS) system, based on guidelines, can improve the personalisation of exercise prescriptions in ten Dutch cardiac rehabilitation centres.[34] Despite the introduction of such a CDS system, it did not improve the overall concordance of actual cardiac rehabilitation prescription by healthcare professionals to the personalised training prescription (from 60% to 62%, P=0.82).

The EXPERT (EXercise Prescription in Everyday practice & Rehabilitative Training) tool (an online training and CDS system, see Figure 4) is a potent method to encourage standardisation of exercise prescription and enhance the implementation of exercise recommendations into practice, which is meant for all clinicians and healthcare professionals involved in primary and secondary prevention of CVD.[35,36] The EXPERT tool was developed by Hasselt university, Belgium, by input provided by the CVD EXPERT Network group (involving >30 CV rehabilitation experts out of >10 European countries), and is endorsed by the EAPC. In the EXPERT tool, European (ESC/EAPC) exercise training recommendations and safety precautions are available for ten CVDs (coronary artery disease (with or without percutaneous coronary intervention or coronary artery bypass graft surgery), heart failure, cardiomyopathy, intermittent claudication, implantable cardioverter defibrillator or pacemaker, ventricular assist devices, heart transplantation, valve disease or surgery, congenital heart disease, pulmonary arterial hypertension, and in-hospital phase rehabilitation), five CVD risk factors (obesity, diabetes (type 1 and 2), hypertension, dyslipidaemia), and three common chronic non-CV conditions (sarcopenia, chronic pulmonary disease, renal failure). In the decision support system, the user can activate these CVD's or risk factors, leading to the corresponding exercise prescriptions. In addition, from fill out of the patient's body height and weight, arterial blood pressure, blood lipid profile, fasting glycaemia, resting and peak heart rate during exercise testing, and peak oxygen uptake, these CVD risk

factors are automatically activated when certain thresholds are exceeded (leading to the corresponding exercise prescriptions). Clinicians or healthcare professionals can also activate certain medications with significant repercussions for exercise prescription and performance (i.e. beta-blockers, statins, exogenous insulin administration, meglitinide/sulfonylurea) and adverse events during exercise testing (i.e. myocardial ischemia, exercise-induced atrial fibrillation, exercise-induced ventricular tachycardia, implantable cardioverter-defibrillator firing threshold), for further refinement of exercise prescription. Next to exercise training recommendations, the EXPERT tool also mentions contraindications for certain types of exercise, as well as which safety precautions should be taken into account, based on the patient's profile. The safety advice include which symptoms during exercise training may be anticipated and how to monitor these, and how to adapt training modalities to prevent eliciting/worsening in these symptoms. The tool also incorporates a training centre (as a stand-alone called the EXPERT Training tool) where users can learn how to prescribe exercise to patients with CVD (risk) by solving patient cases (n>50 available). The clinician or healthcare professional consults the patient's characteristics. Only after filling out of his/her own exercise prescription, he/she gets immediate feedback in the tool by showing the recommendations from the EXPERT algorithm. Hence, the targets of the use of the EXPERT tool are a greater clinical effectiveness of CV rehabilitation, enhanced medical safety of CV rehabilitation, and improved adherence to, or getting to know better, the EAPC/ESC exercise prescription recommendations for CVD (risk).

The EXPERT Training tool is now available on https://www.escardio.org/Education/Practice-Tools/CVD-prevention-toolbox/expert-tool. Translations of the EXPERT Training Tool into other languages are being foreseen. In addition to the validation activities that were already done, both the EXPERT decision support system and the EXPERT Training Tool are being validated in different patient cohorts and in different healthcare professionals (e.g. physiotherapists, nurses). As a result, a wider distribution to these populations and to healthcare professionals can be ambitioned.

In a recent trial, 23 Belgian physiotherapists first prescribed exercise intensity, frequency, session duration, program duration and exercise type (endurance and resistance training) for the same three patient cases on secondary prevention of CVD; the agreement with ESC/EAPC recommendations (based on a maximal agreement score of 60/per case) was assessed.[37] Next, they completed a one-month digital training by using the EXPERT Training tool and completed 31±13 (out of 45 available) training cases. Thereafter, the same three patient cases as at entry of study were filled out again, with re-assessment of level of agreement with ESC/EAPC recommendations. It was found that after using the EXPERT Training tool the physiotherapists prescribed significantly greater exercise frequencies, program durations and total exercise volumes in all three patient cases (p<0.05). In case 1, 2 and 3, the agreement score (with ESC/EAPC recommendations) increased from 29±9 (out of 60) to 41±9, from 28±9 to 41±10, and from 34±7 to 45±8, respectively (p<0.001). Hence, the total agreement score

increased from 91±17 to 127±19 (out of 180; improvement by +44±32%, p<0.001) (see Figure 5). This study shows that exercise prescriptions to patients with CVD, generated by healthcare professionals, can be significantly improved by advanced education and specific training, which should already start in the respective university courses.[37] In fact, how to properly prescribe PA and exercise (also in the primary and secondary prevention of CVD) should be delivered significantly better in the teaching curricula of medicine, physiotherapy, nursing, clinical exercise physiology, etc. to be able to deliver appropriate PA and exercise prescription to patients with CVD, or elevated risk for CVD, in the near future.[38-40]

In final, recommended actions which will assist to achieve tailored exercise prescriptions in the primary and secondary prevention of CVD are provided in Table 3.

Conclusion

Many people need an individualised exercise prescription because of an increased CVD risk or established CVD. Even though exercise training has the highest level of evidence in the primary and secondary prevention of premature CVD morbidity and mortality, many clinicians and healthcare professionals did never acquire the skills needed to maximally tailor this potent therapeutic option. This likely leads to suboptimal prevention by exercise training. The EXPERT Training tool has been shown to aid in alleviating this deficit.

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Tables

Table 1 Survey patient cases

Case 1	Case 2	Case 3	Case 4	Case 5
Age: 65 years Body height: 171 cm Body weight: 65 kg Sex: male VO2max: 2500 ml/min, 38.5 ml/kg/min (116% of predicted normal value) Resting HR: 55 bts/min Peak exercise HR: 123 bts/min Total cholesterol: 180 mg/dl Fasting glycaemia: 92 mg/dl Blood pressure: 145/82 mmHg Medication intake: beta-blocker, nitrate, statin, antiplatelet. Referred to rehabilitation for: acute myocardial infarction with PCI. Comorbidities: None.	Age: 55 years Body height: 160 cm Body weight: 85 kg Sex: female VO2max: 1600 ml/min, 18.8 ml/kg/min (108% of predicted normal value) Resting HR: 102 bts/min Peak exercise HR: 151 bts/min Total cholesterol: 267 mg/dl Fasting glycaemia: 108 mg/dl Blood pressure: 115/72 mmHg Medication intake: statin, ACE-inhibitor, orlistat, antiplatelet, metformin, sulfonylurea. Referred to rehabilitation for: obesity. Comorbidities: type 2 diabetes. Additional information: gonarthrosis present.	Age: 70 years Body height: 182 cm Body weight: 80 kg Sex: male VO2max: 1500 ml/min, 18.7 ml/kg/min (73% of predicted normal value) Resting HR: 52 bts/min Peak exercise HR: 112 bts/min Total cholesterol: 189 mg/dl Fasting glycaemia: 102 mg/dl Blood pressure: 125/80 mmHg Medication intake: statin, antiplatelet, beta-blocker, digitalis, mucolytics, bronchodilators. Referred to rehabilitation for: AMI with CABG. Comorbidities: Heart failure with preserved ejection fraction, mild COPD.	Age: 65 years Body height: 165 cm Body weight: 90 kg Sex: female VO2max: 1450 ml/min, 16.1 ml/kg/min (90% of predicted normal value) Resting HR: 52 bts/min Peak exercise HR: 100 bts/min Total cholesterol: 234 mg/dl Fasting glycaemia: 115 mg/dl Blood pressure: 135/75 mmHg Medication intake: beta-blocker, statin, exogenous insulin, nitrate, erythropoietin. Referred to rehabilitation for: stable myocardial ischemia (threshold at 87 bts/min) Comorbidities: renal failure, type 1 diabetes. Additional information: chronic nonspecific low back pain present.	Age: 79 years Body height: 170 cm Body weight: 59 kg Sex: male VO2max: 1250 ml/min, 21.2 ml/kg/min (88% of predicted normal value) Resting HR: 56 bts/min Peak exercise HR: 111 bts/min Total cholesterol: 178 mg/dl Fasting glycaemia: 125 mg/dl Blood pressure: 135/87 mmHg Medication intake: beta-blocker, bronchodilator, antiplatelet. Referred to rehabilitation for: peripheral vascular disease. Comorbidities: cachexia and frailty, COPD.

Table 2 Additional clinical benefits of appropriate tailoring of exercise on CVD risk

CVD risk factor	Adjustment in exercise prescription	Additional clinical benefit (when compared with 150 min of moderate-intense exercise/week, and moderate-intense dynamic resistance training)
Obesity	Exposing to appropriate exercise volume (250-420 min/week)[41]	At five months: greater weight loss (-8.2+-4 vs. -3.7+-5 kg; P<0.001), fat mass loss (-5.9+-4 vs. -2.8+-3 kg; P<0.001) and waist circumference reduction (-7+-5 vs. -5+-5 cm; P=0.02)[42]
Hyperglycaemia (in type 2 diabetes)	Exposing to appropriate weekly exercise frequency (≥5 days/week)[43]	At 3-6 months: A greater frequency of exercise sessions associates with greater reductions in HbA1c (weighted r = -0.64)[43]
	Exposing to appropriate sets of resistance exercise (≥21 sets)[44]	At 3-6 months: a resistance program with 21 or more sets per session have a larger effect size on HbA1c (effect size by -0.65) than one with fewer than 21 sets per session (effect size by -0.16, P = 0.03)[44]
Arterial hypertension	Exposing to appropriate exercise session duration (>30 min/session)[45]	At 3-6 months: exercise sessions with a duration of 30-45 min have a greater impact on resting SBP (by -3.8 mmHg) vs. shorter sessions (by -0.43 mmHg)[45]
	Exposing to appropriate intensity of endurance exercise (at least moderate-intense)[45]	At 3-6 months: exercise sessions of greater intensity have a greater impact on resting SBP (by -4.8 mmHg) vs. low-intensity exercise sessions (by +0.07 mmHg)[45]
	Exposing to appropriate sets of resistance exercise (≥8 sets)[46]	A greater number of exercises per session (≥8 vs. <8) is significantly associated with greater SBP reduction[46]
Dyslipidaemia	Exposing to appropriate type of endurance exercise (e.g. aerobic interval training)[47]	At 3-6 months:

		For LDL-c, a greater decrease (effect size) is observed in response to aerobic interval training (by − 0.55) vs. aerobic continuous exercise (by − 0.38)[47] For HDL-c, a greater increase (effect size) is observed in response to aerobic interval training (by + 0.46) vs. aerobic continuous exercise (by + 0.36)[47]
Lowered endurance capacity	Exposing to appropriate exercise volume (close to 2000 kcal/week)[27,48]	At 3-6 months: In HF patients: every increment in weekly exercise energy expenditure by >460 kcal is associated with a greater mean increase in VO$_{2peak}$ by 2.6 ml/kg/min, P<0.05[48] In CAD patients: A greater total energy expenditure is significantly related to greater improvements in exercise capacity (effect size: 0.91 ml/min/kg per 100J/kg, P<0.01)[27]
Lowered muscle strength	Exposing to appropriate resistance exercise intensity (70-79% of the 1RM)[49]	At 3-6 months: The resistance training intensity (p < 0.01) has a significant effect on muscle strength, with the largest effect sizes for intensities of 70-79% of the 1RM (between-subject standardized mean differences of 1.89)[49]

Abbreviations: hbA1c, glycated haemoglobin; SBP, systolic blood pressure; LDL, low density lipoprotein; HDL, high density lipoprotein; VO$_{2peak}$, peak oxygen uptake; 1RM, one-repetition maximum;

Table 3 Recommended actions to achieve tailored exercise prescriptions in the primary and secondary prevention of CVD

Action	Responsible party
In clinical practice, exercise prescriptions should be adjusted according to the patient's phenotype, which thus necessitates the assessment of the entire CVD risk profile and physical fitness (e.g. endurance capacity, muscle strength), and analysis of pharmacological treatment and co-morbidities	Clinicians and healthcare professionals
How to adjust the exercise prescription according to the patient's phenotype could be described in greater detail in clinical guidelines (instead of disease-specific guidelines only), and disagreement between national and international guidelines should be remediated	(Inter)national scientific organisations
How to adjust the exercise prescriptions according to the patient's phenotype could be brought into clinical practice, or supported, by validated clinical decision support systems or training systems	Universities, international scientific organisations and IT companies
How to adjust the exercise prescription according to the patient's phenotype should be taught in detail in (para)medical curricula	Universities and university colleges

Figure legends

Figure 1 Inter-clinician variance in exercise prescription for five patient cases (on x-axis)

Reproduced from reference 12, with permission
One point in the figure may reflect multiple clinicians as similar exercise modality selections have occurred between clinicians.

Figure 2 Relationship between physical activity and mortality risk according to the presence of cardiovascular disease.

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Figure 3 Exercise prescription in CVD prevention: a stepwise approach

Figure 4 The EXPERT Tool

Figure 5 Participants' total agreement score (out of 180) at entry and after online training by the EXPERT Training tool (n=23)

From reference 14