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ORIGINAL RESEARCH

Cost-Minimization Analysis for Cardiac Revascularization in 12 Health Care Systems Based on the EuroCMR/SPINS Registries

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ABSTRACT

OBJECTIVES The aim of this study was to compare the costs of a noninvasive cardiac magnetic resonance (CMR)–guided strategy versus 2 invasive strategies with and without fractional flow reserve (FFR).

BACKGROUND Coronary artery disease (CAD) is a major contributor to the public health burden. Stress perfusion CMR has excellent accuracy to detect CAD. International guidelines recommend as a first step noninvasive testing of patients in stable condition with known or suspected CAD. However, nonadherence in routine clinical practice is high.

METHODS In the EuroCMR (European Cardiovascular Magnetic Resonance) registry (n = 3,647, 59 centers, 18 countries) and the U.S.-based SPINS (Stress-CMR Perfusion Imaging in the United States) registry (n = 2,349, 13 centers, 11 states), costs were calculated for 12 health care systems (8 in Europe, the United States, 2 in Latin America, and 1 in Asia). Costs included diagnostic examinations (CMR and x-ray coronary angiography [CXA] with and without FFR), revascularizations, and complications during 1-year follow-up. Seven subgroup analyses covered low- to high-risk cohorts. Patients with ischemia-positive CMR underwent CXA and revascularization at the treating physician's discretion (CMR+CXA strategy). In the hypothetical invasive CXA+FFR strategy, costs were calculated for initial CXA and FFR in vessels with ≥50% stenoses, assuming the same proportion of revascularizations and complications as with the CMR+CXA strategy and FFR-positive rates as given in the published research. In the CXA-only strategy, costs included CXA and revascularizations of ≥50% stenoses.

RESULTS Consistent cost savings were observed for the CMR+CXA strategy compared with the CXA+FFR strategy in all 12 health care systems, ranging from 42% ± 20% and 52% ± 15% in low-risk EuroCMR and SPINS patients with atypical chest pain, respectively, to 31% ± 16% in high-risk SPINS patients with known CAD ($P < 0.0001$ vs 0 in all groups). Cost savings were even higher compared with CXA only, at 63% ± 11%, 73% ± 6%, and 52% ± 9%, respectively ($P < 0.0001$ vs 0 in all groups).

CONCLUSIONS In 12 health care systems, a CMR+CXA strategy yielded consistent moderate to high cost savings compared with a hypothetical CXA+FFR strategy over the entire spectrum of risk. Cost savings were consistently high compared with CXA only for all risk groups. (J Am Coll Cardiol Img 2022;15:607–625) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

CAD = coronary artery disease

CMR = cardiac magnetic resonance

CT = computed tomography

CV = cardiovascular

CVD = cardiovascular disease

CXA = x-ray coronary angiography

FFR = fractional flow reserve

MACE = major adverse cardiac event(s)

MI = myocardial infarction

PCI = percutaneous coronary intervention

Cardiovascular disease (CVD) causes more patient mortality in the United States than all forms of cancer and chronic respiratory disease combined, with coronary artery disease (CAD) being the leading cause and accounting for 43% of CVD deaths.[1] In the United States, total costs for CVD amounted to $351 billion, 62% of which was spent on CAD alone.[1] Similarly, in the European Union, total costs for CVD in 2015 amounted to €210 billion, of which €59 billion was spent for CAD.[2] In selected high-income European countries, national CVD costs rose to 19% of total health care expenditure in 2016.[3] These numbers underline that CAD continues to be a major source of public health burden, and its relevance is expected to grow with the aging of the population. The first diagnostic step in CAD management is of particular importance, as it determines downstream therapeutic costs, which are often 5 to 10 times higher than diagnostic costs.[4]

Both the American Heart Association/American College of Cardiology guidelines update[5] and the European Society of Cardiology guidelines[6] indicate that noninvasive stress testing for diagnosis and risk stratification is the appropriate initial study in the majority of patients with suspected CAD. Among the noninvasive stress tests, cardiac magnetic resonance (CMR) is now well recognized as a reliable and safe technique to evaluate ischemia in patients with known or suspected CAD, as shown in single- and multicenter studies.[7-11] Importantly, the randomized, controlled MR-INFORM (MR Perfusion Imaging to Guide Management of Patients With Stable Coronary Artery Disease) study demonstrated that outcomes were not different for patients with suspected CAD managed using initial CMR stress testing compared with a strategy combining invasive x-ray coronary angiography (CXA) and fractional flow reserve (FFR).[12] Accordingly, noninvasive stress testing with CMR is recommended in the European guidelines as a Class 1 indication[6] and as a Class 2a indication in the United States, with consideration of physical capacity.[5,13]

In addition, on the basis of large randomized, controlled trials,[14,15] U.S.[5] and European[16] guidelines as well as appropriate use criteria[17] uniformly recommend the use of FFR as a Class 1 indication to assess the hemodynamic significance of coronary artery stenoses of intermediate degree in patients with stable CAD, unless significant ischemia is demonstrated on noninvasive testing. Nevertheless, data from large U.S. and European registries show substantial nonadherence in routine clinical settings. In a large U.S. registry with 766 hospitals including approximately 400,000 patients with stable CAD, only 31% of percutaneous coronary interventions (PCIs) of intermediate lesions were preceded by FFR testing.[18] In Europe, the corresponding numbers are even lower, ranging from 13% to 16% in the ERIS (Evolving Routine Standards in Intracoronary Physiology) study[19] and the EAPCI registry including 10 countries.[20] Interestingly, in the U.S.-based Veterans Affairs CART (Clinical Assessment Reporting and Tracking) program, analyzing approximately 18,000 patients, the presence or absence of prior ischemia testing had no influence of FFR use.[21] In line with this observation, 70% to 75% of patients in the United States and Europe who underwent revascularizations on the basis of CXA only (ie, without FFR testing) had no ischemia documented on a noninvasive stress test

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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TABLE 1 Costs for Diagnostic Procedures, Revascularizations, and Treatment of Complications

	Belgium	France	Germany	Greece	Italy	Norway	Switzerland	United Kingdom	United States	Brazil	Mexico	Beijing
Year	2019	2020	2020	2019	2020	2020	2019	2019	2019	2019	2019	2019
CMR (outpatient)	207	264	550	271	639	412	1,237	542	505	72	1,048	58
CXA (outpatient)	553	844	773	587	2,388	1,828	2,190	1,062	937	54	3,720	872
FFR (outpatient)	24	166	861	2,735	2,388	3,012	1,656	381	77	159	1,424	1,425
PCI (in-hospital)	11,123	2,322	3,293	1,151	5,575	7,030	10,616	2,206	12,735	175	4,197	582
CABG (in-hospital)	18,310	13,280	17,294	8,327	16,248	28,878	35,720	8,429	23,987	2,200	18,934	14,538
1-y medication	90	359	140	151	465	158	501	31	168	173	563	1,163
Cardiologist visit	42	57	118	14	25	254	634	101[a]	375	21	30	15
Aborted SCD	2,975	3,567	6,479	4,211	25,715	7,457	27,474	9,189	38,832	5,403	2,598	8,723
Stroke	5,619	3,337	7,073	2,832	4,364	24,001	7,802	4,815	13,531	2,280	2,246	9,740
Nonfatal MI (without rehabilitation)	4,463	4,508	4,515	1,858	7,085	5,697	15,647	5,309	19,858	783	5,852	10,177
Nonfatal MI (with rehabilitation)	5,433	5,829	7,319	NA	10,893	6,644	23,292	5,883	28,966	860	6,906	NA

All costs are given in U.S. dollars. Currencies are converted to U.S. dollars for January 1 of the year the health care costs were calculated (https://www1.oanda.com/lang/fr/currency/converter/). Countries per region are listed in alphabetical order. [a]Only after coronary artery bypass grafting.

CABG = coronary artery bypass grafting; CMR = cardiac magnetic resonance; CXA = invasive x-ray coronary angiography; FFR = fractional flow reserve; MI = myocardial infarction; NA = not available; PCI = percutaneous coronary intervention; SCD = sudden cardiac death.

preceding CXA.[19,21] Thus, adherence to current guidelines and appropriate use criteria for the use of FFR is low in the United States, Europe, and elsewhere,[22] but little information is available on the economic consequences of adherence and nonadherence to recommendations for the health care systems. Accordingly, in the present study we investigated the costs of a CMR-guided pathway (CMR+CXA strategy) compared with an invasive strategy using CXA combined with FFR (CXA+FFR strategy) and a CXA-only strategy, which is no longer recommended.

METHODS

PATIENT POPULATION. To perform this cost-minimization analysis, the EuroCMR (European Cardiovascular Magnetic Resonance) and SPINS (Stress-CMR Perfusion Imaging in the United States) registries were used to evaluate potential cost savings on the basis of CMR performance and prognostic data representative of the general CMR use in a broad range of hospitals and health care systems. Specifically, the EuroCMR registry prospectively collected data from 3,647 patients with suspected CAD studied using CMR at 59 centers in 18 countries. Patients with known histories of myocardial infarction (MI) or coronary revascularization were excluded.[23,24] The SPINS registry collected data from 2,349 patients at 13 centers across 11 U.S. states[25,26] and also included patients with histories of PCI, MI, or heart failure.[26] Therefore, the 2 registries together represent a typical population, which is often referred for CAD assessment in daily routine practice. Collected data included demographics as well as subsequent treatment and major adverse cardiac events (MACE) during follow-up of 1 year after the CMR examination. In both registries, endpoints of MACE included all-cause death, cardiovascular (CV) death, sudden cardiac death, aborted sudden cardiac death, nonfatal MI, and stroke. PCI and coronary artery bypass grafting were also recorded. For ischemia testing, a first-pass perfusion approach was used with pharmacological vasodilation.[9-11] Patients were classified as ischemia positive if ≥1 segment was ischemic by visual reading (using a 16-segment model) performed by local CMR experts.[23,26] For participation in the EuroCMR registry, local Institutional Review Board approval was obtained, and patients provided written informed consent before study participation. For the SPINS registry, local Institutional Review Board approval was obtained to conduct the clinical follow-up, with a waiver of the requirement to obtain written informed consent.

DEFINITIONS OF STRATEGIES. For this cost-minimization analysis in 12 health care systems, we adopted a modeling approach as described previously.[27] Patients positive for ischemia on CMR were referred for CXA with revascularizations performed at the discretion of the treating physician (CMR+CXA strategy) (Supplemental Figure 1). For this strategy, costs included those for the initial CMR, for the CXA in the ischemia-positive patients, for revascularizations, and for treatment of complications. For the 2 invasive strategies, first, a hypothetical CXA+FFR strategy was designed, which is initiated with an x-ray coronary angiographic examination, and in case of ≥50% coronary stenosis, FFR is added (Supplemental Figure 2). In the CXA-only strategy, all patients with ≥50% diameter coronary stenoses are assumed to be revascularized without hemodynamic

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TABLE 2 Demographics of the EuroCMR and SPINS Populations

	Atypical CP, EuroCMR	Atypical CP, SPINS	All Euro CMR (Suspected CAD)	Suspected CAD, SPINS	Typical AP, EuroCMR	Typical AP, SPINS	SPINS With Known CAD	*P* Value (Chi-Square)
Demographics	1,786 (49.0)	446 (19.0)	3,647 (100.0)	1,530 (65.1)	582 (16.0)	419 (17.8)	819 (34.9)	–
Male	46	41	59	47	43	44	63	<0.0001
Age (y)	61.1 ± 13.1	59.9 ± 11.7	61.6 ± 12.7	62.0 ± 11.3	62.6 ± 12.4	60.5 ± 11.4	63.5 ± 11.3	<0.0001[a]
History of PCI	0.0	0.0	0.0	0.0	0.0	0.0	65.7	NC
History of MI	0.0	0.0	0.0	0.0	0.0	0.0	43.7	NC
History of heart failure	0.0	0.0	0.0	0.0	0.0	0.0	29.9	NC
Risk profile								
Hypertension	39	77	62	76	35	78	83	<0.0001
Dyslipidemia	40	67	42	65	46	67	80	<0.0001
Diabetes mellitus	11	27	13	26	15	28	33	<0.0001
Smoker	26	32	26	30	26	33	37	<0.0001
Family history of CAD	28	33	27	33	29	35	32	<0.0001
Ischemia on CMR								
Ischemia	322 (18.0)	42 (9.4)	761 (20.9)	200 (13.1)	203 (34.9)	83 (19.8)	205 (25.0)	<0.0001
Need for FFR (>50% stenosis)	590 (33.1)	147 (32.9)	1,225 (33.6)	508 (33.2)	208 (35.7)	144 (34.4)	294 (35.9)	0.73
Treatment								
Revascularizations	81 (4.5)	18 (4.0)	226 (6.2)	76 (5.0)	75 (12.9)	37 (8.8)	111 (13.6)	<0.0001
PCI only	70 (3.9)	13 (2.9)	179 (4.9)	44 (2.9)	53 (9.1)	19 (4.5)	73 (8.9)	<0.0001
CABG only	10 (0.6)	3 (0.7)	41 (1.1)	28 (1.8)	19 (3.3)	17 (4.1)	35 (4.3)	<0.0001
PCI and CABG	1 (0.1)	2 (0.4)	6 (0.2)	4 (0.3)	3 (0.5)	1 (0.2)	3 (0.4)	0.31
Outcome (complications)								
Primary endpoint: CV death + nonfatal MI	12 (0.7)	2 (0.4)	19 (0.5)	11 (0.7)	2 (0.3)	4 (1.0)	26 (3.2)	<0.0001
CV death	7 (0.4)	0 (0.0)	8 (0.3)	5 (0.3)	0 (0.0)	1 (0.2)	12 (1.5)	0.0007
All-cause death	15 (0.8)	0 (0.0)	34 (0.9)	22 (1.4)	7 (1.2)	5 (1.2)	27 (3.3)	<0.0001
Nonfatal MI	5 (0.2)	2 (0.4)	11 (0.3)	6 (0.4)	2 (0.3)	3 (0.7)	14 (1.7)	<0.0001
Aborted SCD[b]	4 (0.2)	0 (0.0)	8 (0.3)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	NC
SCD	2 (0.1)	0 (0.0)	3 (0.1)	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	NC
Stroke	10 (0.6)	0 (0.0)	18 (0.5)	8 (0.5)	1 (0.2)	1 (0.2)	7 (0.9)	0.38

Values are n (%), %, or mean ± SD. Differences for age were assessed using one-way ANOVA; the other parameters were tested using the chi-square test (overall *P* value). [a]ANOVA post hoc testing yielded higher age of the SPINS population with known CAD compared with all other groups expect SPINS with suspected CAD and EuroCMR with typical angina ($P < 0.02$, Scheffé post hoc testing). [b]Aborted SCD corresponds to physical resuscitation and/or appropriate ICD shock in the EuroCMR registry and to appropriate ICD shock only in the SPINS registry.

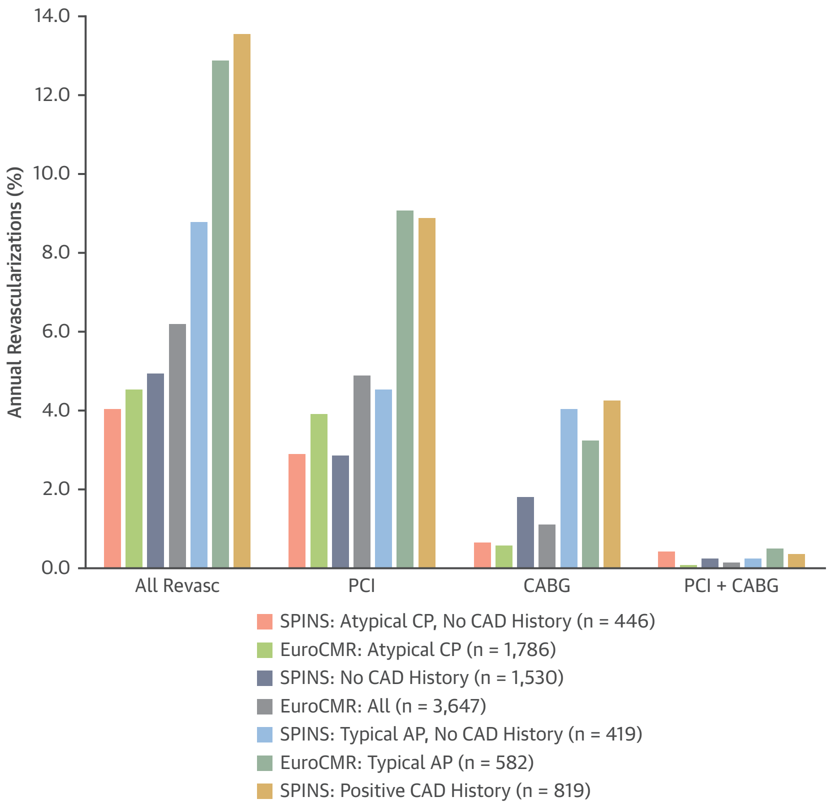
AP = angina pectoris; CAD = coronary artery disease; CP = chest pain; CV = cardiovascular; EuroCMR = European Cardiovascular Magnetic Resonance; NC = not computable; SPINS = Stress-CMR Perfusion Imaging in the United States; other abbreviations as in Table 1.

testing (Supplemental Figure 3), as described elsewhere.[28] This 50% stenosis threshold for revascularization was chosen as used in the large trials that assessed FFR performance vs CXA only.[14,19] Both studies showed that in the CXA-only group, the degree of stenosis was in the range of 50% to 60% in one-half of all revascularized patients[14] with intermediate stenosis.[19] For calculations to yield CXA+FFR and CXA only, see Supplemental Appendix A. These 3 strategies were calculated for the populations with suspected CAD (the entire EuroCMR and subgroup of SPINS) as well as for subgroups with atypical chest pain, with typical angina pectoris, and for patients with known CAD of the SPINS population.

Finally, the annual rates of revascularizations and complications were applied to the 3 strategies for all 7 risk groups: the entire EuroCMR (suspected CAD) and SPINS with suspected CAD, patients with atypical chest pain and patients with typical angina pectoris in EuroCMR and SPINS, and patients with known CAD in SPINS.

COSTS OF THE DIFFERENT PROCEDURES AND STRATEGIES. The analysis was performed from a health care payer perspective and included 11 countries and the Beijing area of China (with the latter representing approximately 20 million people). As economic conditions vary substantially across China, only the highly developed Beijing area was analyzed (see Supplemental Appendix B for a description of health care systems). We used reimbursement rates (tariffs) to assess the costs of procedures (Supplemental Appendix B).

FIGURE 1 **Revascularizations Rates in the EuroCMR and SPINS Populations**



In the entire SPINS (Stress-CMR Perfusion Imaging in the United States) cohort (n = 2,349), slightly more revascularizations were performed compared with the entire EuroCMR (European Cardiovascular Magnetic Resonance) population (n = 3,647) (8.0% vs 6.2%, respectively; $P <$ 0.01). Revascularization rates in the typical angina pectoris (AP) populations were higher than in the atypical chest pain (CP) populations for both the EuroCMR (12.9% vs 4.5%, respectively; $P < 0.001$) and SPINS (8.8% vs 4.0%, respectively; $P < 0.001$) populations.
CABG = coronary artery bypass grafting; CAD = coronary artery disease; PCI = percutaneous coronary intervention;
revasc = revascularizations.

The average costs per patient for the 3 strategies were calculated by multiplying the proportion of patients in the different branches of the diagram (Supplemental Figures 1 to 3) by the unit costs of the various tests, revascularizations, and/or treatments of complications (**Table 1**).

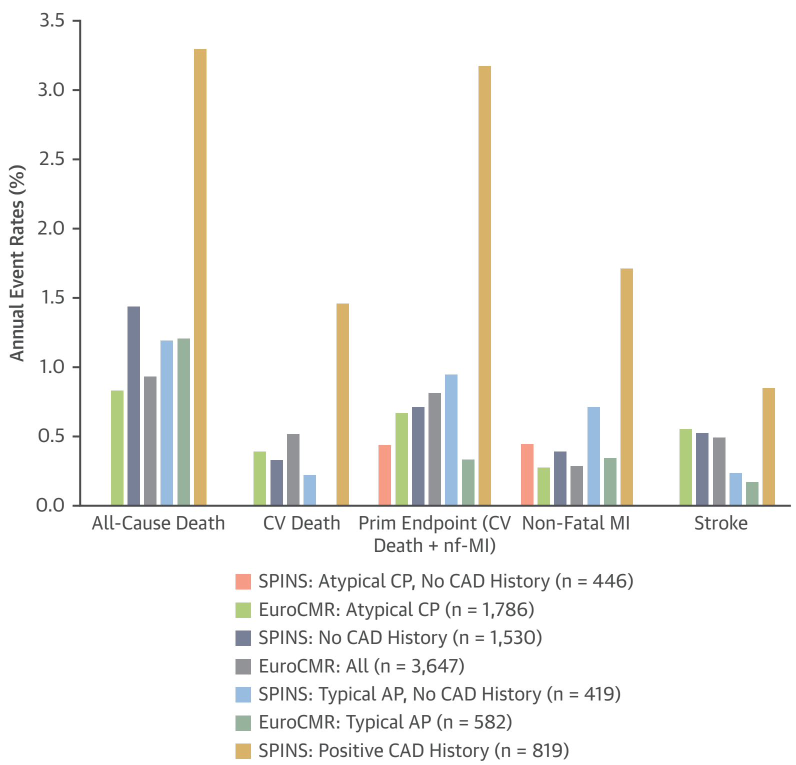
SENSITIVITY ANALYSIS. To assess the impact of various cost parameters on the results, 1-way deterministic sensitivity analyses were performed in which input parameters were varied 1 at a time, while the remaining values were kept constant at their baseline values. Accordingly, the models were rerun with changes in the costs of the diagnostic tests of CMR, FFR, and CXA and under the assumption that in the CXA-only strategy, only 50% of patients with >50% stenosis would be revascularized, as observed in the ERIS study.[19] As the CMR+CXA strategy and the CXA+FFR strategy were assumed to yield the same proportion of ischemia-positive patients, the revascularization procedures would not differ for the 2 strategies, and consequently, costs for treatment were not varied.

STATISTICAL ANALYSIS. Categorical data are reported as frequencies and continuous data as mean ± SD. Differences between patient groups were assessed using unpaired Student's *t*-test, 1-way analysis of variance, and Pearson chi-square statistics as appropriate. Values of $P < 0.05$ were considered to indicate statistical significance.

RESULTS

DEMOGRAPHICS. Key demographic data on the EuroCMR and SPINS populations are provided in

FIGURE 2 Outcomes in the EuroCMR and SPINS Populations



Overall, low event rates were recorded in both the EuroCMR and the SPINS registries. By far the highest complications rate was observed in patients with known histories of CAD (overall $P < 0.001$, Pearson chi-square test). CV = cardiovascular; MI = myocardial infarction; nf = nonfatal; Prim = primary; other abbreviations as in Figure 1.

Table 2. The revascularization rate increases with increasing risk profile, as illustrated in Figure 1 (and supported by Table 2, with $P < 0.0001$ for the global differences) from patients with atypical chest pain (low risk, CV death, and nonfatal MI: 0.4%-0.7% per year) to those with typical angina (intermediate risk, CV death, and nonfatal MI: 0.3%-1.0% per year). Finally, the highest revascularization rate was observed in patients with known histories of CAD (high risk, CV death, and nonfatal MI: 3.2% per year) (Figure 2, Table 2) (overall $P < 0.0001$). Slightly more revascularizations were performed in the entire SPINS cohort (8.0% [n = 2,349] vs 6.2% [n = 3,647] in the entire EuroCMR; $P < 0.01$). Not surprisingly, the rates of revascularizations in the typical angina populations were higher than in the atypical chest pain populations for both the EuroCMR (12.9% vs 4.5%, respectively; $P < 0.001$) and SPINS (8.8% vs 4.0%, respectively; $P < 0.001$) populations. Concerning complications, as shown in Figure 2, patients with known histories of CAD had the highest rate (overall $P < 0.001$, chi-square test).

COST ANALYSIS. **Suspected CAD in the EuroCMR and SPINS population.** The cost reductions by the CMR+CXA strategy compared with the invasive CXA+FFR strategy and CXA-only strategy in the 12 health care systems are shown in Table 3, Figures 3 and 4, and the Central Illustration, respectively. When considering the invasive CXA-only strategy (Figure 4), cost savings with CMR+CXA were higher in the SPINS population (70.3% ± 5.3% vs 61.7% ± 9.1% in EuroCMR; $P = 0.01$, unpaired Student's *t*-test). Inclusion or exclusion of rehabilitation costs after nonfatal MI or of costs for a cardiologist visit in the first year after revascularization did not significantly influence the differences between the CMR+CXA and CXA+FFR strategies (see summary in Table 3).

COST ANALYSES IN SUBGROUPS OF VARYING CV RISK. **Atypical chest pain in the EuroCMR and SPINS**

TABLE 3 Cost Calculations per Patient in the 3 Arms for the 12 Health Care Systems

	Costs, CMR+CXA	Costs, CXA+FFR	Costs, CXA Only	% Cost Reduction of CMR+CXA Versus CXA+FFR	% Cost Reduction of CMR+CXA Versus CXA Only	% Cost Reduction of CXA+FFR Versus CXA Only
Belgium (€)						
EuroCMR						
Main analysis (n = 3,647) (with cardiologist visit and rehabilitation)	1,021	1,213	4,342	15.8	76.5	72.1
Main analysis (n = 3,647) without rehabilitation and without cardiologist visit	1,017	1,210	4,339	16.0	76.6	72.1
• Atypical chest pain (n = 1,786)	795	1,003	4,053	20.7	80.4	75.3
• Atypical chest pain (n = 1,786) without rehabilitation and without cardiologist visit	790	1,000	4,050	21.0	80.5	75.3
• Typical angina pectoris (n = 582)	1,904	2,032	4,773	6.3	60.1	57.4
• Typical angina pectoris (n = 582) without rehabilitation and without cardiologist visit	1,898	2,029	4,770	6.5	60.2	57.5
SPINS						
Main analysis suspected CAD (n = 1,530) (with cardiologist visit and rehabilitation)	989	1,175	4,713	15.8	79.0	75.1
• Atypical chest pain (n = 446)	792	1,094	4,594	27.6	82.8	76.2
• Typical angina pectoris (n = 419)	1,408	1,729	4,992	18.6	71.8	65.4
• Known history of CAD (n = 819) (with cardiologist visit and rehabilitation)	2,051	2,249	4,873	8.8	57.9	53.8
France (€)						
EuroCMR						
Main analysis (n = 3,647) (with cardiologist visit and rehabilitation)	689	1,067	2,035	35.4	66.1	47.6
Main analysis (n = 3,647) without rehabilitation and without cardiologist visit	683	1,062	2,030	35.7	66.4	47.7
• Atypical chest pain (n = 1,786)	563	972	1,744	42.1	67.7	44.3
• Atypical chest pain (n = 1,786) without rehabilitation and without cardiologist visit	557	967	1,739	42.4	68.0	44.4
• Typical angina pectoris (n = 582)	1,169	1,424	2,427	17.9	51.8	41.3
• Typical angina pectoris (n = 582) without rehabilitation and without cardiologist visit	1,160	1,419	2,422	18.3	52.1	41.4
SPINS						
Main analysis suspected CAD (n = 1,530) (with cardiologist visit and rehabilitation)	707	1,145	2,713	38.3	73.9	57.8
• Atypical chest pain (n = 446)	580	1,114	2,333	48.0	75.1	52.2
• Typical angina pectoris (n = 419)	992	1,511	3,116	34.4	68.2	51.5
• Known history of CAD (n = 819) (with cardiologist visit and rehabilitation)	1,270	1,633	2,685	22.2	52.7	39.2
Germany (€)						
EuroCMR						
Main analysis (n = 3,647)	1,044	1,342	2,527	22.2	58.7	46.9
Main analysis (n = 3,647) without rehabilitation and without cardiologist visit	1,030	1,334	2,519	22.8	59.1	47.0
• Atypical chest pain (n = 1,786)	886	1,193	2,139	25.7	58.6	44.2
• Atypical chest pain (n = 1,786) without rehabilitation and without cardiologist visit	875	1,191	2,137	26.5	59.1	44.3
• Typical angina pectoris (n = 582)	1,624	1,825	3,015	11.0	46.1	39.5
• Typical angina pectoris (n = 582) without rehabilitation and without cardiologist visit	1,606	1,823	3,013	11.9	46.7	39.5
SPINS						
Main analysis suspected CAD (n = 1,530) (with cardiologist visit and rehabilitation)	1,094	1,416	3,417	22.7	68.0	58.6
• Atypical chest pain (n = 446)	911	1,415	2,940	35.6	69.0	51.9
• Typical angina pectoris (n = 419)	1,428	1,984	3,950	28.0	63.8	49.8
• Known history of CAD (n = 819) (with cardiologist visit and rehabilitation)	1,694	2,030	3,122	16.6	45.7	35.0

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TABLE 3 Continued

	Costs, CMR+CXA	Costs, CXA+FFR	Costs, CXA Only	% Cost Reduction of CMR+CXA Versus CXA+FFR	% Cost Reduction of CMR+CXA Versus CXA Only	% Cost Reduction of CXA+FFR Versus CXA Only
Greece (€)						
EuroCMR						
Main analysis (n = 3,647) without rehabilitation and with cardiologist visit	510	1,497	1,213	65.9	58.0	-23.4
• Atypical chest pain (n = 1,786) without rehabilitation and with cardiologist visit	435	1,426	1,029	69.5	57.7	-38.6
• Typical angina pectoris (n = 582) without rehabilitation and with cardiologist visit	791	1,739	1,458	54.5	45.8	-19.3
SPINS						
Main analysis suspected CAD (n = 1,530) without rehabilitation and with cardiologist visit	523	1,519	1,690	65.6	69.1	10.1
• Atypical chest pain (n = 446) without rehabilitation and with cardiologist visit	419	1,493	1,410	71.9	70.3	-5.9
• Typical angina pectoris (n = 419) without rehabilitation and with cardiologist visit	689	1,770	1,922	61.1	64.2	7.9
• Known history of CAD (n = 819) without rehabilitation and with cardiologist visit	828	1,847	1,619	55.2	48.9	-14.1
Italy (€)						
EuroCMR						
Main analysis (n = 3,647) (with cardiologist visit and rehabilitation)	1,537	3,327	4,120	53.8	62.7	19.2
Main analysis (n = 3,647) without rehabilitation and without cardiologist visit	1,524	3,316	4,109	54.0	62.9	19.3
• Atypical chest pain (n = 1,786)	1,310	3,183	3,780	58.8	65.3	15.8
• Atypical chest pain (n = 1,786) without rehabilitation and without cardiologist visit	1,300	3,172	3,769	59.0	65.5	15.8
• Typical angina pectoris (n = 582)	2,347	3,851	4,583	39.1	48.8	16.0
• Typical angina pectoris (n = 582) without rehabilitation and without cardiologist visit	2,333	3,840	4,572	39.2	49.0	16.0
SPINS						
Main analysis suspected CAD (n = 1,530) (with cardiologist visit and rehabilitation)	1,385	3,310	4,844	58.2	71.4	31.7
• Atypical chest pain (n = 446)	1,210	3,682	4,350	67.1	72.2	15.4
• Typical angina pectoris (n = 419)	1,809	4,230	5,689	57.2	68.2	25.6
• Known history of CAD (n = 819) (with cardiologist visit and rehabilitation)	2,351	4,288	5,063	45.2	53.6	15.3
Norway (NOK)						
EuroCMR						
Main analysis (n = 3,647)	16,334	36,331	55,098	55.0	70.4	34.1
Main analysis (n = 3,647) without rehabilitation and without cardiologist visit	16,177	36,293	55,098	55.4	70.6	34.1
• Atypical chest pain (n = 1,786)	13,264	33,639	48,357	60.6	72.6	30.4
• Atypical chest pain (n = 1,786) without rehabilitation and without cardiologist visit	13,138	33,600	48,318	60.9	72.8	30.5
• Typical angina pectoris (n = 582)	27,991	46,237	64,269	39.5	56.4	28.1
• Typical angina pectoris (n = 582) without rehabilitation and without cardiologist visit	27,718	46,198	64,230	40.0	56.8	28.1
SPINS						
Main analysis suspected CAD (n = 1,530) (with cardiologist visit and rehabilitation)	16,737	37,565	71,070	55.4	76.4	47.1
• Atypical chest pain (n = 446)	12,015	35,111	60,547	65.8	80.2	42.0
• Typical angina pectoris (n = 419)	22,739	45,312	77,662	49.8	70.7	41.7
• Known history of CAD (n = 819) (with cardiologist visit and rehabilitation)	16,737	37,565	71,070	55.4	76.4	47.1

Continued on the next page

TABLE 3 Continued

	Costs, CMR+CXA	Costs, CXA+FFR	Costs, CXA Only	% Cost Reduction of CMR+CXA Versus CXA+FFR	% Cost Reduction of CMR+CXA Versus CXA Only	% Cost Reduction of CXA+FFR Versus CXA Only
Switzerland (CHF)						
EuroCMR						
Main analysis (n = 3,647) (with cardiologist visit and rehabilitation)	2,841	3,796	7,287	25.2	61.0	47.9
Main analysis (n = 3,647) without rehabilitation and without cardiologist visit	2,785	3,771	7,262	26.1	61.6	48.1
• Atypical chest pain (n = 1,786)	2,401	3,456	6,483	30.5	63.0	46.7
• Atypical chest pain (n = 1,786) without rehabilitation and without cardiologist visit	2,355	3,431	6,458	31.4	63.5	46.9
• Typical angina pectoris (n = 582)	4,434	5,075	8,367	12.6	47.0	39.3
• Typical angina pectoris (n = 582) without rehabilitation and without cardiologist visit	4,348	5,050	8,392	13.9	48.2	39.8
SPINS						
Main analysis suspected CAD (n = 1,530) (with cardiologist visit and rehabilitation)	2,802	3,879	9,031	27.8	69.0	57.0
• Atypical chest pain (n = 446)	2,480	4,224	8,505	41.3	70.8	50.3
• Typical angina pectoris (n = 419)	3,674	5,484	10,448	33.0	64.8	47.5
• Known history of CAD (n = 819) (with cardiologist visit and rehabilitation)	4,792	5,915	9,279	19.0	48.4	36.3
United Kingdom (£)						
EuroCMR						
Main analysis (n = 3,647) (without cardiologist visit and with rehabilitation after MI)	807	1,125	1,629	28.3	50.5	30.9
Main analysis (n = 3,647) (cardiologist visit after CABG only and rehabilitation after MI)	808	not calculated				
Main analysis (n = 3,647) without rehabilitation and without cardiologist visit	806	1,124	1,627	28.3	50.5	30.9
• Atypical chest pain (n = 1,786) (without cardiologist visit and with rehabilitation after MI)	718	1,069	1,468	32.8	51.1	27.2
• Atypical chest pain (n = 1,786) without rehabilitation and without cardiologist visit	717	1,067	1,466	32.8	51.1	27.2
• Typical angina pectoris (n = 582) (without cardiologist visit and with rehabilitation after MI)	1,126	1,336	1,846	15.7	39.0	27.6
• Typical angina pectoris (n = 582) without rehabilitation and without cardiologist visit	1,125	1,334	1,844	15.7	39.0	27.7
SPINS						
Main analysis suspected CAD (n = 1,530) (without cardiologist visit and with rehabilitation after MI)	771	1,149	2,006	32.9	61.6	42.7
• Atypical chest pain (n = 446) (without cardiologist visit and with rehabilitation after MI)	685	1,244	1,893	44.9	63.8	34.3
• Typical angina pectoris (n = 419) (without cardiologist visit and with rehabilitation after MI)	940	1,473	2,318	36.2	59.5	36.4
• Known history of CAD (n = 819) (without cardiologist visit and with rehabilitation after MI)	1,196	1,553	2,135	23.0	44.0	27.3
United States ($)						
EuroCMR						
Main analysis (n = 3,647) with cardiologist and rehabilitation + drugs	1,794	2,009	5,534	10.7	67.6	63.7
Main analysis (n = 3,647) without rehabilitation and without cardiologist visit	1,744	1,979	5,503	11.9	68.3	64.0
• Atypical chest pain (n = 1,786)	1,450	1,748	5,032	17.0	71.2	65.3
• Atypical chest pain (n = 1,786) without rehabilitation and without cardiologist visit	1,414	1,717	5,001	17.6	71.7	65.7
• Typical angina pectoris (n = 582)	2,883	3,015	6,244	4.4	53.8	51.7
• Typical angina pectoris (n = 582) without rehabilitation and without cardiologist visit	2,816	2,984	6,213	5.6	54.7	52.0
SPINS						
Main analysis suspected CAD (n = 1,530) with cardiologist and rehabilitation + drugs	1,711	1,991	6,428	14.1	73.4	69.0
• Atypical chest pain (n = 446)	1,590	2,708	6,766	41.3	76.5	60.0
• Typical angina pectoris (n = 419)	2,883	3,604	7,806	20.0	63.1	53.8
• Known history of CAD (n = 819) with cardiologist and rehabilitation + drugs	3,378	3,960	7,133	14.7	52.6	44.5

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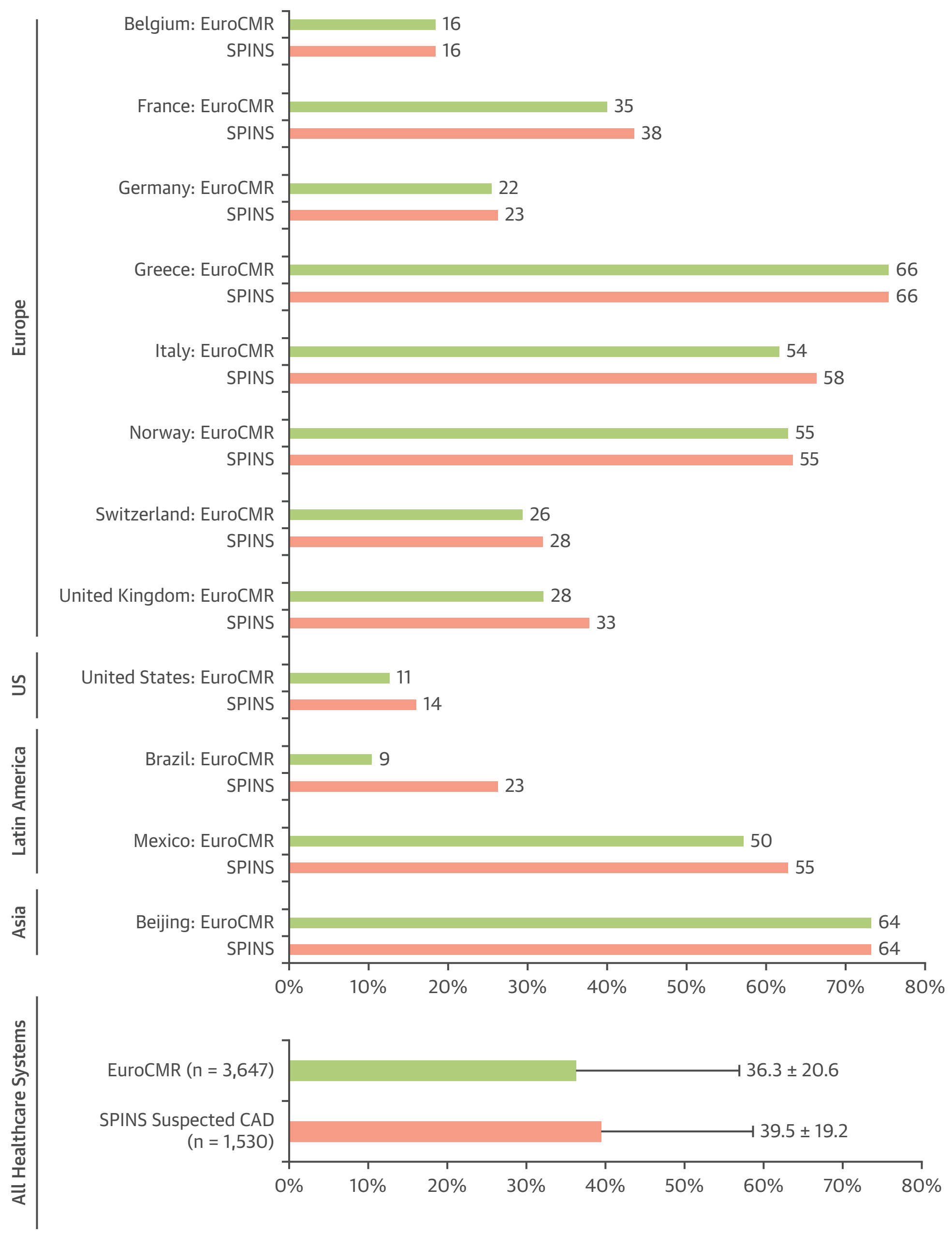
TABLE 3 Continued

	Costs, CMR+CXA	Costs, CXA+FFR	Costs, CXA Only	% Cost Reduction of CMR+CXA Versus CXA+FFR	% Cost Reduction of CMR+CXA Versus CXA Only	% Cost Reduction of CXA+FFR Versus CXA Only
Brazil (US $)						
EuroCMR						
Main analysis (n = 3,647) (with cardiologist visit and rehabilitation)	619	680	1,086	9.0	43.0	37.4
Main analysis (n = 3,647) without rehabilitation and without cardiologist visit	614	679	1,085	9.6	43.4	37.4
• Atypical chest pain (n = 1,786)	529	634	869	16.6	39.1	27.0
• Atypical chest pain (n = 1,786) without rehabilitation and without cardiologist visit	525	633	868	17.1	39.5	27.1
• Typical angina pectoris (n = 582)	866	924	1,375	6.3	37.0	32.8
• Typical angina pectoris (n = 582) without rehabilitation and without cardiologist visit	857	923	1,374	7.2	37.6	32.8
SPINS						
Main analysis suspected CAD (n = 1,530) (with cardiologist visit and rehabilitation)	612	798	1,707	23.3	64.1	53.3
• Atypical chest pain (n = 446)	491	997	1,593	50.8	69.2	37.4
• Typical angina pectoris (n = 419)	755	1,309	2,225	42.3	66.1	41.2
• Known history of CAD (n = 819) (with cardiologist visit and rehabilitation)	983	1,243	1,744	20.9	43.6	28.7
Mexico (pesos)						
EuroCMR						
Main analysis (n = 3,647) (with cardiologist visit and rehabilitation)	44,225	89,053	103,762	50.3	57.4	14.2
Main analysis (n = 3,647) without rehabilitation and without cardiologist visit	44,128	88,985	103,694	50.4	57.4	14.2
• Atypical chest pain (n = 1,786)	38,923	86,249	94,142	54.9	58.7	8.4
• Atypical chest pain (n = 1,786) without rehabilitation and without cardiologist visit	38,842	86,179	94,072	54.9	58.7	8.4
• Typical angina pectoris (n = 582)	65,970	99,200	116,508	33.5	43.4	14.9
• Typical angina pectoris (n = 582) without rehabilitation and without cardiologist visit	65,844	99,130	116,438	33.6	43.5	14.9
SPINS						
Main analysis suspected CAD (n = 1,530) (with cardiologist visit and rehabilitation)	41,335	91,828	129,132	55.0	68.0	28.9
• Atypical chest pain (n = 446)	35,418	89,764	112,676	60.5	68.6	20.3
• Typical angina pectoris (n = 419)	52,988	102,008	140,017	48.1	62.2	27.1
• Known history of CAD (n = 819) (with cardiologist visit and rehabilitation)	63,322	104,763	124,551	39.6	49.2	15.9
Beijing, China (¥)						
EuroCMR						
Main analysis (n = 3,647) without rehabilitation and with cardiologist visit	4,130	11,385	13,474	63.7	69.3	15.5
• Atypical chest pain (n = 1,786) without rehabilitation and with cardiologist visit	3,150	10,665	10,825	70.5	70.9	1.5
• Typical angina pectoris (n = 582) without rehabilitation and with cardiologist visit	7,576	13,941	16,957	45.7	55.3	17.8
SPINS						
Main analysis suspected CAD (n = 1,530) without rehabilitation and with cardiologist visit	4,437	12,354	20,831	64.1	78.7	40.7
• Atypical chest pain (n = 446) without rehabilitation and with cardiologist visit	3,381	12,497	16,815	72.9	79.9	25.7
• Typical angina pectoris (n = 419) without rehabilitation and with cardiologist visit	6,419	15,780	24,583	59.3	73.9	35.8
• Known history of CAD (n = 819) without rehabilitation and with cardiologist visit	9,082	16,498	20,306	45.0	55.3	18.8

Countries per region are listed in alphabetical order. Summary: inclusion or exclusion of costs for rehabilitation after a nonfatal MI or of costs for a cardiologist visit in the first year after revascularization: A) Population with suspected CAD: CMR+CXA vs CXA+FFR strategy: differences <1 percentage point in 7 countries and between 1 and 1.5 percentage points in 2 countries; costs for rehabilitation were not calculated for Greece and the Beijing area, and cardiologist visits after revascularizations were not calculated for the Beijing area; CMR+CXA vs CXA-only strategy: differences <1 percentage point in 8 countries and between 1 and 1.5 percentage points in 1 country. B) Atypical chest pain population: CMR+CXA vs CXA+FFR strategy: differences <1 percentage point in 9 countries and 1.1 percentage points in 1 country; CMR+CXA vs CXA-only strategy: differences ≤0.5 percentage point in 9 countries and 1.2 percentage points in 1 country. C) Typical angina population: CMR+CXA vs CXA+FFR strategy: differences <1 percentage point in 7 countries and between 1 and 1.4 percentage points in 3 countries; CMR+CXA vs CXA-only strategy: differences <1 percentage point in 8 countries and between 1 and 1.4 percentage points in 2 countries.

Abbreviations as in Tables 1 and 2.

FIGURE 3 **Cost Savings of CMR+CXA Compared With Invasive CXA+FFR in the Main EuroCMR and SPINS Populations**

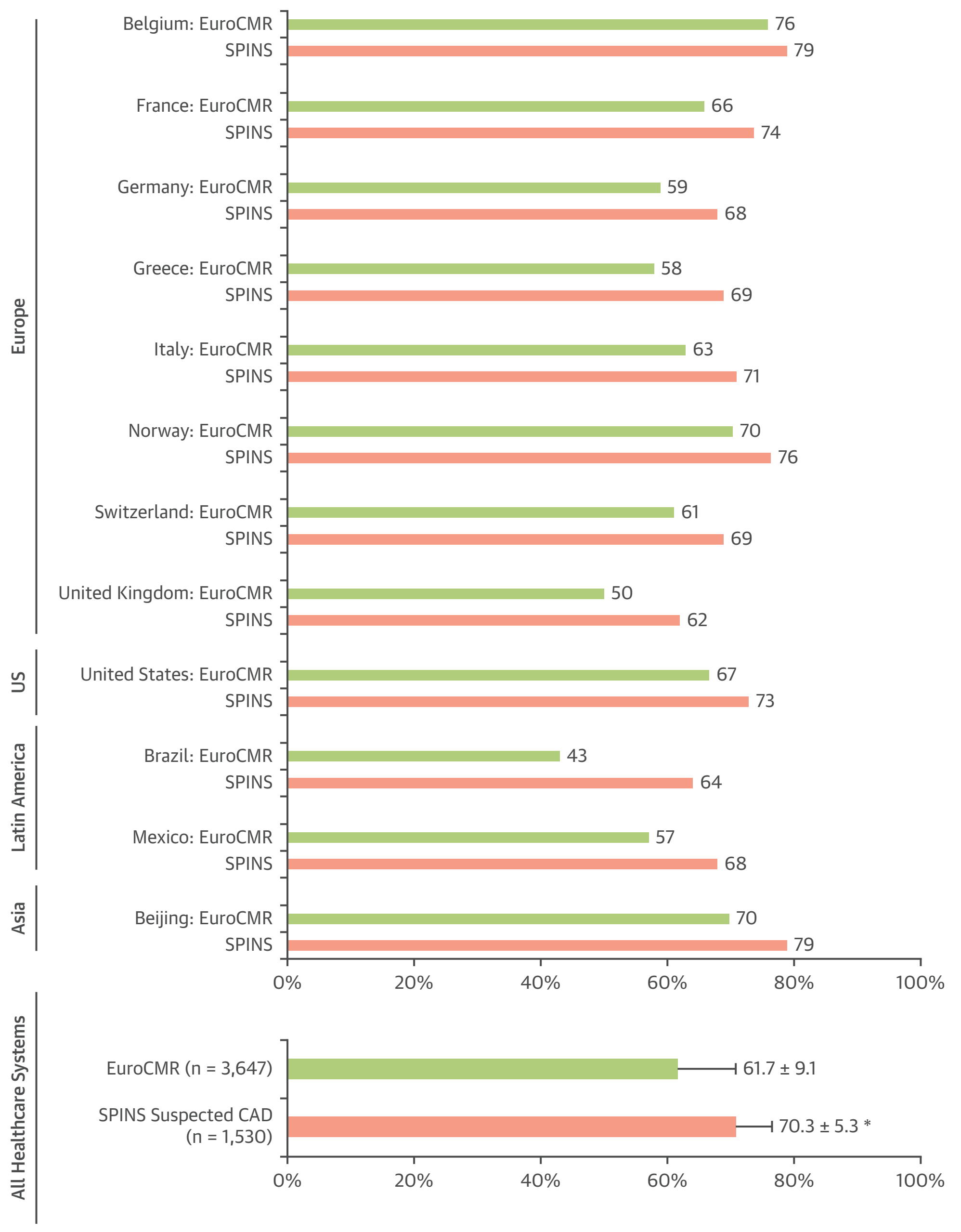


SPINS refers to the subgroup of patients with suspected coronary artery disease (CAD) (n = 1,530), EuroCMR refers to all patients (suspected CAD; n = 3,647). Mean of all countries: P = NS, EuroCMR vs SPINS (unpaired Student's t-test). In Figures 3 to 6, countries per region are listed in alphabetical order. CMR = cardiac magnetic resonance; CXA = x-ray coronary angiography; FFR = fractional flow reserve.

populations with suspected CAD. In these populations, cost savings of the CMR+CXA strategy compared with CXA+FFR were substantial, at 41.9% ± 20.1% (range 17.1%-70.5%) in EuroCMR and 52.3% ± 15.0% (range 27.6%-72.9%) in SPINS (P < 0.0001 vs 0 for both) (Figure 5, Central Illustration).

Compared with the CXA-only strategy, CMR+CXA yielded even higher cost savings in both the EuroCMR

FIGURE 4 **Cost Savings of CMR+CXA Compared With Invasive CXA Only in the Main EuroCMR and SPINS Populations**

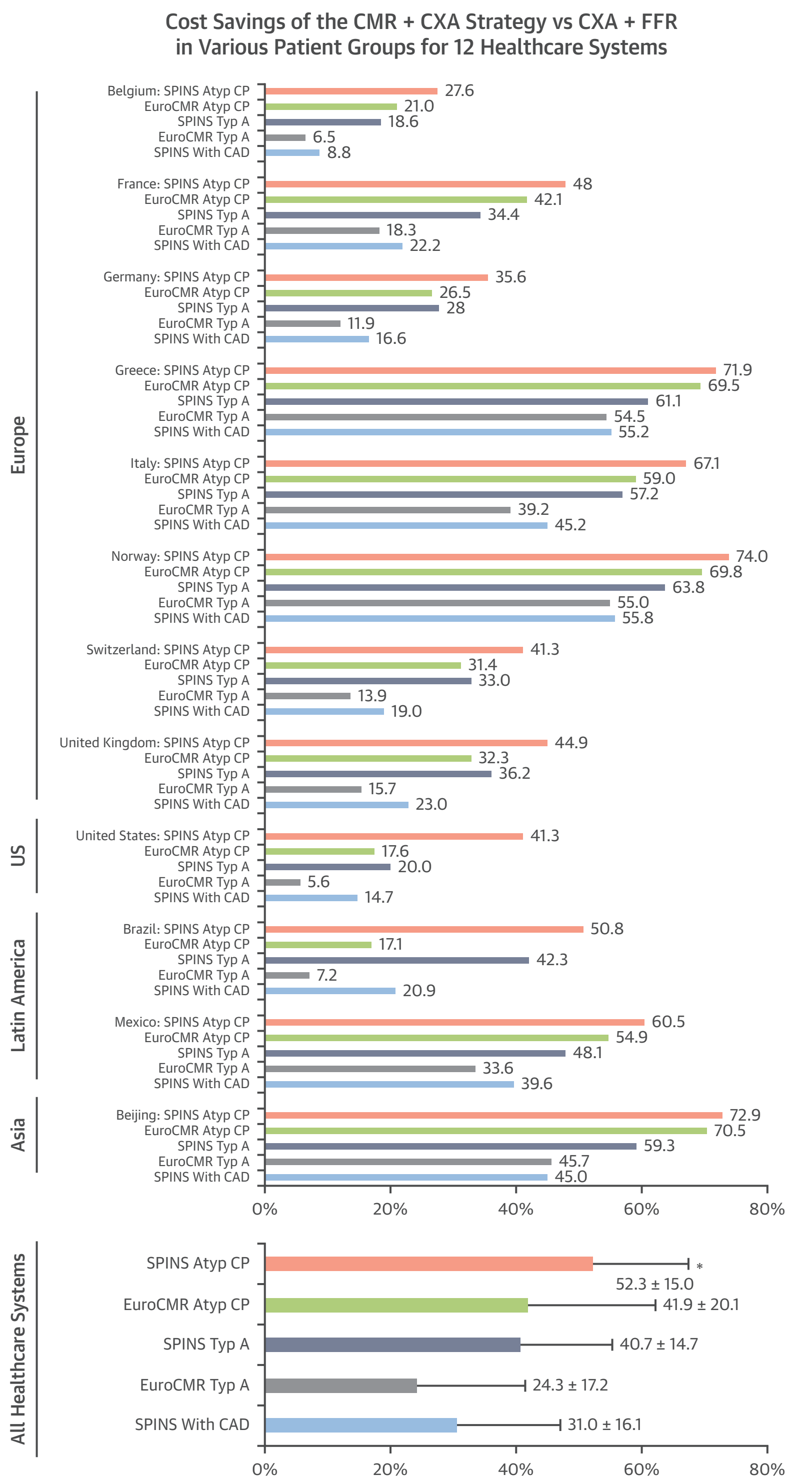


SPINS refers to the subgroup of patients with suspected CAD (n = 1,530), EuroCMR refers to all patients (suspected CAD; n = 3,647). *Mean of all countries: $P = 0.01$, EuroCMR vs SPINS (unpaired Student's *t*-test). Abbreviations as in Figures 1 and 3.

and SPINS populations (63.2% ± 11.0% and 73.2% ± 5.7%, respectively; $P < 0.0001$ vs 0 for both) (Figure 6).

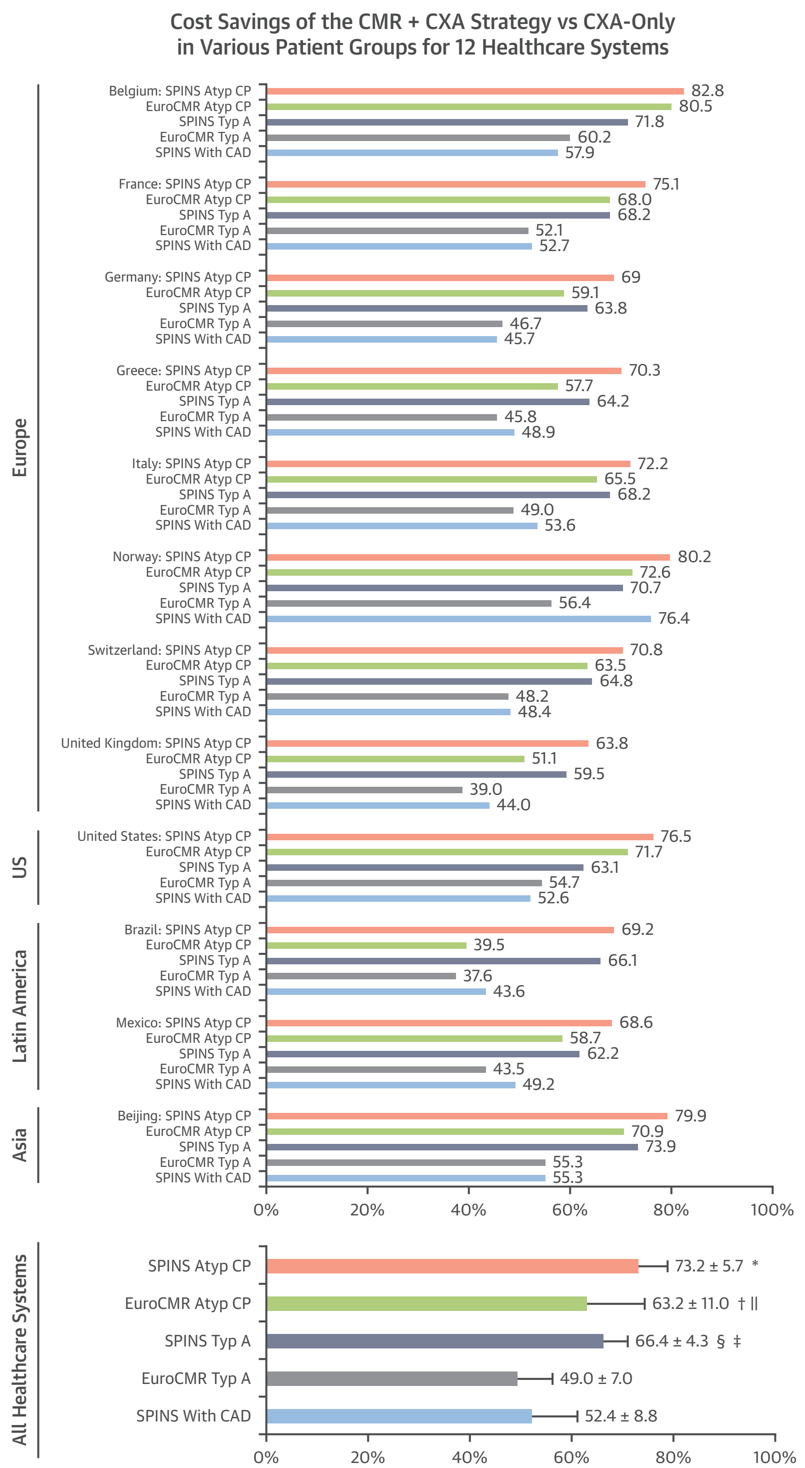
Typical angina in the EuroCMR and SPINS population with suspected CAD. Also in these populations, costs savings by the CMR+CXA strategy compared with CXA+FFR were consistently found, at 24.3% ± 17.2% (range 5.6%-54.5%; $P < 0.001$ vs 0) (Figure 5) for EuroCMR and 40.7% ± 14.7% (range 18.6%-61.1%) for SPINS ($P < 0.0001$ vs 0) (Figure 5). In the EuroCMR

FIGURE 5 Cost Savings of CMR+CXA Compared With Invasive CXA+FFR in Subgroups of the EuroCMR and SPINS Populations



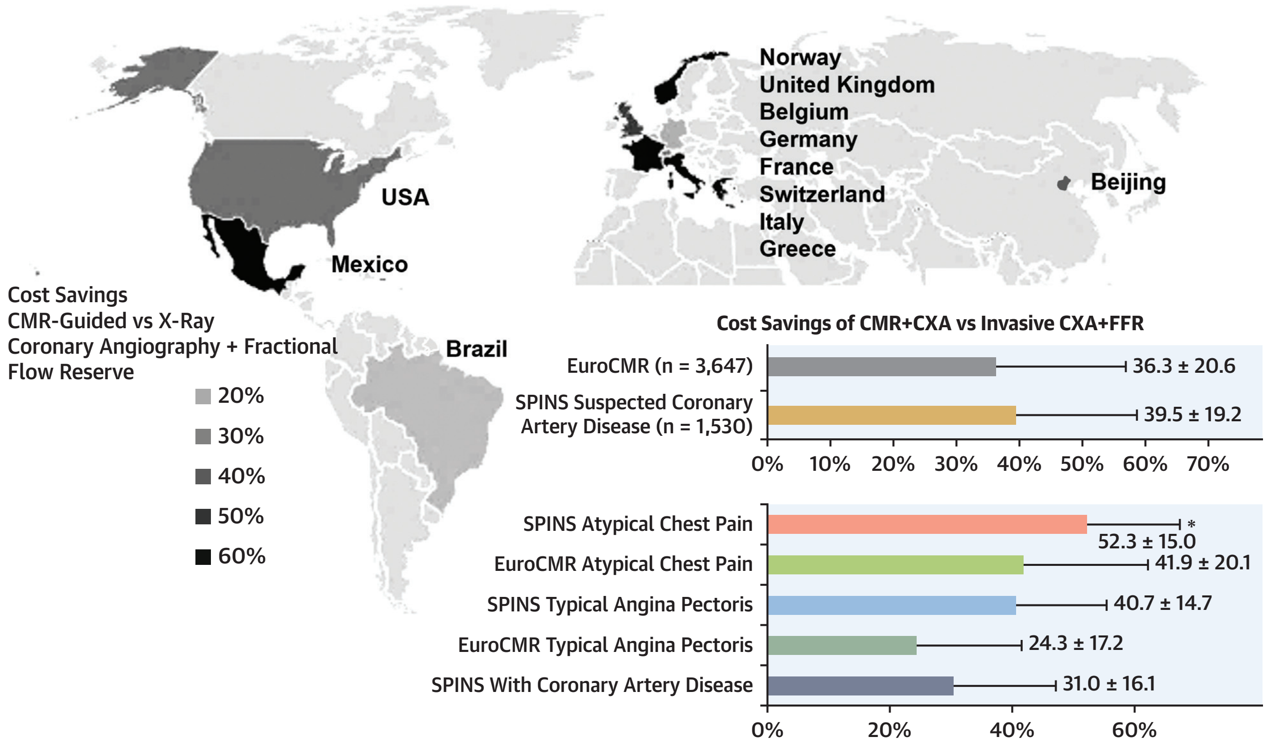
Mean of all health care systems: overall $P = 0.0017$ (analysis of variance with Scheffé post hoc testing). *$P < 0.005$ vs typical angina pectoris (Typ A) in EuroCMR. Atyp CP = atypical chest pain; other abbreviations as in **Figures 1 and 3**.

FIGURE 6 Cost Savings of CMR+CXA Compared With Invasive CXA Only in Subgroups of the EuroCMR and SPINS Populations



Mean of all health care systems: overall $P < 0.0001$ (analysis of variance). *$P < 0.0001$ vs SPINS with CAD and Typ A in EuroCMR. †$P < 0.03$ vs SPINS with CAD. ‡$P < 0.0001$ vs Typ A in EuroCMR. §$P < 0.002$ vs SPINS with CAD. ||$P < 0.002$ vs EuroCMR Typ A (Scheffé post hoc testing). Abbreviations as in Figures 1 and 3.

CENTRAL ILLUSTRATION **Cost Savings by Cardiac Magnetic Resonance-Guided Strategy Versus X-Ray Coronary Angiography Plus Fractional Flow Reserve**



Moschetti K, et al. J Am Coll Cardiol Img. 2022;15(4):607-625.

Consistent cost savings of the cardiac magnetic resonance plus x-ray coronary angiography (CXA) strategy compared with invasive CXA plus fractional flow reserve were found in all 12 health care systems and in all patient subgroups of the EuroCMR (European Cardiovascular Magnetic Resonance) and SPINS (Stress-CMR Perfusion Imaging in the United States) populations. *$P < 0.005$ compared with typical angina pectoris in EuroCMR. Created with Datawrapper.

population with typical angina, cost savings were lower compared with the atypical chest pain population of SPINS ($P < 0.005$, analysis of variance with Scheffé post hoc testing).

In comparison with the CXA-only strategy (Figure 6), CMR+CXA yielded even higher cost savings in both the EuroCMR and SPINS populations (49.0% ± 7.0% and 66.4% ± 4.3%, respectively; $P <$ 0.0001 vs 0 for both). When comparing cost savings of CMR+CXA vs CXA-only in the various subgroups (Figure 6), the lowest savings were observed for patients with typical angina in EuroCMR and patients with known CAD in SPINS (Figure 6).

Patients with known CAD in the SPINS population. The highest event rates were observed in the SPINS subgroup with known CAD (Figure 2) (overall $P < 0.0001$). Even in this population with known CAD, cost savings obtained by the CMR+CXA strategy compared with CXA+FFR were 31.0% ± 16.2% and were as high as 52.4% ± 8.8% compared with the CXA-only strategy ($P < 0.0001$ vs 0 for both).

SENSITIVITY ANALYSIS. A 10% change in the costs of CMR, FFR, or CXA (changes introduced into the model one by one) led to small variations in cost savings of the CMR+CXA strategy compared with the CXA+FFR or CXA-only strategy, ranging from 0.1 to 4.1 percentage points (Supplemental Table 1). Specifically, cost savings by CMR+CXA vs CXA+FFR decreased by 2.3, 1.0, and 2.3 percentage points on average if CMR costs increased by 10% or FFR or CXA costs decreased by 10%, respectively. Cost savings by CMR+CXA vs CXA only decreased by 1.5 and 0.4 percentage points on average if CMR costs increased by 10% or CXA costs decreased by 10%, respectively.

When reducing the number of patients in the CXA-only group who undergo revascularizations to 50%, as observed in the ERIS study,[19] the mean difference was 18.4 percentage points, while cost savings compared with CMR+CXA remained high at 45% ± 13%.

DISCUSSION

The main findings of this study can be summarized as follows: 1) on the basis of 2 large "real-world" international registries (EuroCMR and SPINS), cost savings were consistently found in all 12 health care systems studied in favor of the noninvasive CMR+CXA strategy compared with an invasive CXA+FFR strategy; 2) these cost savings produced by the noninvasive CMR+CXA strategy were even higher compared with the invasive CXA-only strategy; and 3) cost savings for the noninvasive CMR+CXA strategy were consistently found over the entire spectrum of CV risks ranging from low-risk to high-risk patient groups.

COST MINIMIZATION BY THE CMR-GUIDED STRATEGY TO MANAGE PATIENTS WITH SUSPECTED AND KNOWN CAD: COMPARISON WITH INVASIVE CXA+FFR. In patients with suspected CAD (ie, in the EuroCMR population and the corresponding subgroup of the SPINS population), the CMR+CXA strategy yielded cost savings compared with the invasive CXA+FFR strategy in every health care system studied (Figure 3, Central Illustration), averaging 36% ± 21% and 40% ± 19%, respectively. Importantly, the clinical presentation affected the calculated cost savings. Cost savings in patients with atypical chest pain of 42% ± 20% and 52% ± 15% for EuroCMR and SPINS, respectively, decreased to 24% ± 17% and tended to decrease to 41% ± 15%, respectively, in populations with typical angina (Figure 5, Central Illustration). This fact illustrates the importance of the pretest probability of CAD in the tested cohort with respect to the achievable cost reductions. Simulations by Moschetti et al[28] predicted the cost-effectiveness of CMR+CXA vs CXA+FFR in populations with an ischemia prevalence <62% to 83% for the German, U.K., Swiss, and U.S. health care systems, which was confirmed in a follow-up study[27] as well as in the present study. Similarly, cost savings of 52% ± 15% in the low-risk SPINS subgroup with suspected CAD and atypical chest pain decreased to 31% ± 16% in the high-risk SPINS subgroup with known CAD.

To our knowledge, economic evaluations of the CMR technique in the setting of CAD management are not available for most countries we studied. However, for the U.S. health care system, Ge et al[29] used a sophisticated state-transition model to calculate cost-effectiveness ratios for various diagnostic techniques. In their analyses, the CMR strategy strongly dominated the immediate CXA strategy (ie, the CXA+FFR strategy of the present study), and this finding was consistent in all their sensitivity analyses.[29]

CMR+CXA: COMPARISON WITH INVASIVE CXA-ONLY STRATEGY. FFR testing is gaining increasing acceptance and is recommended in most guidelines to be added to invasive CXA in patients with stable CAD.[5,6,16] Nevertheless, 70% to 75% of patients in the United States and Europe who underwent revascularizations on the basis of CXA-only results had no ischemia documented on noninvasive stress testing preceding CXA.[19,21] These numbers suggest a substantial underuse of physiological testing in many catheter laboratories and justify a cost-minimization analysis compared with an invasive CXA-only approach. Of note, 17% (~18,000 patients) of the U.S.-based Veterans Affairs CART program had intermediate coronary stenoses resulting in 4.2% of revascularizations, which is close to the 4.0% and 4.5% of revascularizations observed in the low-risk atypical chest pain groups of the present EuroCMR and SPINS registries, respectively.[21] This underlines that patients at low risk are indeed referred for invasive CXA-only work-up in routine cardiology. In our analysis, estimated cost savings of CMR+CXA vs CXA only were high and ranged from 62% ± 9% to 70% ± 5% in the total EuroCMR population and the SPINS population with suspected CAD, respectively (Figure 4). Even with a conservative CXA-only approach with revascularizations in only one-half of the patients,[19] cost savings reached 45% ± 13% to 56% ± 8%, respectively, in the present analysis. These substantial cost savings are most likely caused by the fact that the need for revascularizations is reduced by ischemia testing by FFR[15] or by stress CMR.[12] Two economic studies compared 8 different diagnostic noninvasive and invasive pathways in the U.K. and Swiss health care systems, and in agreement with the present study results, CMR-based strategies were more cost effective than an invasive CXA-only strategy in both health care systems.[4,30] Also, for the German[31] and Brazilian[32] health care systems, a CMR-based strategy was more cost effective than an invasive CXA-only strategy at CAD prevalence lower than 60% and 65%, respectively.

Studies have demonstrated that the major reason for not applying FFR is operators' confidence that clinical and angiographic data are sufficient.[19,33] The results of the present study demonstrating cost savings for guideline-based noninvasive strategies may help motivate operators and referring physicians to adhere to guidelines and may support decision makers in health care systems to increase the availability of noninvasive techniques to reduce costs.

In summary, the present results show that the recommendations of current guidelines[5,6] to use noninvasive testing as a first diagnostic step in patients with suspected or known stable CAD are also economically justified. The results also show that FFR testing as recommended in guidelines[5,6] can reduce costs, while CXA only is no longer recommended by any major guideline and incurs the highest costs.

STUDY LIMITATIONS. Concerning the 12 health care systems studied, assigning costs to the various procedures and hospital stays is a demanding task, as some tariff systems are heterogeneous (Supplemental Appendix B). Furthermore, substantial differences between geographic regions within a system exist, and this fact must be considered when interpreting the study results. The sensitivity analysis (Supplemental Table 1) was performed to address this point. Costs for FFR were not coded in all tariff systems. Therefore, for these systems, the FFR costs were calculated as the difference between 2 tariff positions or by estimating costs for material and physician payment (see Supplemental Appendix B). A sensitivity analysis with changing costs for CMR, FFR, and CXA yielded small differences in the cost savings of CMR+CXA compared with the invasive strategies (with a reduction in cost savings of CMR+CXA vs CXA+FFR of 1.0 to 2.3 percentage points on average if CMR costs increase by 10% or FFR or CXA costs decreased by 10%).

The costs in the 2 invasive arms were calculated on the basis of the relationship between the stenosis degree and FFR-positive findings reported in published research.[28,33] This modeling of the invasive strategies is certainly a limitation. In addition, the CMR+CXA strategy was not compared with other noninvasive imaging stress tests, an aspect that also warrants future testing. Also, a comparison against a cardiac computed tomography (CT)-based arm was not performed, as this was beyond the scope of this study.

For cost calculations in the CXA-only strategy, revascularizations for stenoses >50% were considered, as guidelines recommend FFR testing of intermediate stenoses, while calculations for >70% stenoses were not performed. Our calculations are based on 4.0% and 4.5% of revascularizations in the EuroCMR and SPINS populations with atypical chest pain, respectively, which match the 4.2% revascularizations observed in the large U.S. registry for patients with intermediate stenoses (40%-69% stenoses) undergoing first-line CXA only.[21] Finally, revascularizations of >70% stenoses only would leave approximately 90% of patients with FFR-positive ischemia untreated, as the sensitivity of anatomical CXA to detect ischemia is as low as 12% at this threshold of anatomical stenosis.[33]

In both registries, hard endpoints were assessed as outcomes, but not symptom relief, typically achieved by revascularizations. For calculating the hypothetical CXA+FFR strategy, the same number of revascularizations was assumed for the CMR+CXA strategy. If revascularizations are correlated with symptoms relief, one might expect similar symptoms relief for these 2 arms. In the CXA-only arm, <50% stenoses are not revascularized. A small portion of these stenoses might be FFR positive (ie, ischemic), and thus symptom relief might be smaller in this arm.

Finally, we did not compare the costs of a conservative vs invasive treatment, although this is a central question in the era of the ISCHEMIA (International Study of Comparative Health Effectiveness With Medical and Invasive Approaches) trial.[34] One may even ask whether ischemia testing is required at all in patients with chest pain. Abundant studies exist that demonstrate the prognostic impact of myocardial ischemia,[8,12,14,15,21,26] and growing evidence is also emerging demonstrating the prognostic power of CT-based anatomical or plaque coronary artery imaging.[35] Of note, the ISCHEMIA trial did not address this diagnostic challenge but tested a conservative versus an interventional treatment in a preselected cohort with proven moderate to severe ischemia.[34] Thus, ischemia detection was a prerequisite for participation in ISCHEMIA, and ischemia testing remains a backbone of CAD detection, while ISCHEMIA demonstrated that further studies on treatment options are needed. Interestingly, according to the investigators of the SCOT-HEART (Scottish Computed Tomography of the Heart Trial) study, a high certainty of a correct CAD diagnosis led to more intense drug treatment and, consequently, improved patient outcomes in the cardiac CT arm with a reduction in CV death and nonfatal MI of 41%.[35] Also, in the 10-year follow-up of the SYNTAX (Synergy Between PCI With Taxus and Cardiac Surgery) study, rigorous drug treatment following revascularization reduced MACE by 53% compared with patients with <3 drug types.[36] Thus, guideline-recommended optimal pharmacotherapy can substantially modify outcomes but is demanding and costly, accounting for >50% of total CAD management costs.[4] Hence, it appears reasonably applicable only in a targeted CAD population, and the correct diagnosis of CAD remains key to start adequate drug treatment with or without revascularizations. Of note, in the ISCHEMIA trial, the performance of CMR was not evaluable, as only 5.0% of recruited patients underwent this test.[34]

CONCLUSIONS

In the 12 health care systems studied, the CMR+CXA strategy was consistently less costly than a hypothetical invasive CXA+FFR strategy for CAD management, when costs for diagnostic work-up, treatment, and complications were taken into account. These cost savings were most prominent in the subgroups at low risk (with atypical chest pain), ranging from 42% to 52%, but were still present in the higher risk populations, such as those with typical angina or known CAD, ranging from 24% to 41%. Cost reductions with the CMR+CXA strategy were even more pronounced compared with a hypothetical CXA-only strategy, ranging from 49% to 73%. These findings warrant further confirmation in prospective trials.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: This study shows that stress CMR is a robust tool in routine clinical practice to reduce costs in patients with suspected or known CAD compared with invasive diagnostic strategies. This holds true for 12 health care systems in the United States, Europe, Latin America, and Asia, and potential cost savings were similar when calculations were based on the European or US registries including a total of 5,996 patients from 72 centers in 22 countries.

TRANSLATIONAL OUTLOOK: The findings of substantial cost reductions with the use of stress CMR warrant confirmation in large prospective trials. Despite the documented cost-effectiveness of stress CMR over other diagnostic tests in patients with suspected or known CAD, broad underuse of stress CMR is observed, and reasons for this pattern should be investigated.

REFERENCES

1. Benjamin EJ, Muntner P, Alonso A, et al. Heart disease and stroke statistics—2019 update: a report from the American Heart Association. *Circulation*. 2019;139:e56–e528.

2. Timmis A, Townsend N, Gale CP, et al. European Society of Cardiology: cardiovascular disease statistics 2019. *Eur Heart J*. 2020;41:12–85.

3. Wilkins E, Wilson L, Wickramasinghe K, et al. *European cardiovascular Disease Statistics 2017*. Brussels, Belgium: European Heart Network; 2017.

4. Pletscher M, Walker S, Moschetti K, et al. Cost-effectiveness of functional cardiac imaging in the diagnostic work-up of coronary heart disease. *Eur Heart J Qual Care Clin Outcomes*. 2016;2:201–207.

5. Fihn SD, Blankenship JC, Alexander KP, et al. 2014 ACC/AHA/AATS/PCNA/SCAI/STS focused update of the guideline for the diagnosis and management of patients with stable ischemic heart disease. *J Am Coll Cardiol*. 2014;64:1929–1949.

6. Knuuti J, Wijns W, Saraste A, et al. 2019 ESC guidelines for the diagnosis and management of chronic coronary syndromes. *Eur Heart J*. 2019;41:407–477.

7. Bruder O, Schneider S, Pilz G, et al. 2015 update on acute adverse reactions to gadolinium based contrast agents in cardiovascular MR. Large multinational and multi-ethnical population experience with 37788 patients from the EuroCMR registry. *J Cardiovasc Magn Reson*. 2015;17:58.

8. Vincenti G, Masci PG, Monney P, et al. Stress perfusion CMR in patients with known and suspected CAD: prognostic value and optimal ischemic threshold for revascularization. *J Am Coll Cardiol Img*. 2017;10:526–537.

9. Greenwood J, Maredia N, Younger J, et al. Cardiovascular magnetic resonance and single-photon emission computed tomography for diagnosis of coronary heart disease (CE-MARC): a prospective trial. *Lancet*. 2012;379:453–460.

10. Schwitter J, Wacker CM, van Rossum AC, et al. MR-IMPACT: magnetic resonance imaging for myocardial perfusion assessment in coronary artery disease trial: comparison of perfusion CMR with single photon emission computed tomography for the detection of coronary artery disease in a multicenter, multivendor, randomized trial. *Eur Heart J*. 2008;29:480–489.

11. Schwitter J, Wacker CM, Wilke N, et al. Superior diagnostic performance of perfusion-CMR versus

SPECT to detect coronary artery disease: the secondary endpoints of the multicenter multivendor MR-IMPACT II. *J Cardiovasc Magn Reson*. 2012;14:61–71.

12. Nagel E, Greenwood JP, McCann GP, et al. Magnetic resonance perfusion or fractional flow reserve in coronary disease. *N Engl J Med*. 2019;380:2418–2428.

13. Wolk MJ, Bailey SR, Doherty JU, et al. 2013 multimodality appropriate use criteria for the detection and risk assessment of stable ischemic heart Disease. *J Card Fail*. 2014;20:65–90.

14. Tonino PAL, De Bruyne B, Pijls NHJ, et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. *N Engl J Med*. 2009;360:213–224.

15. De Bruyne B, Pijls NH, Kalesan B, et al. Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. *N Engl J Med*. 2012;367:991–1001.

16. Neumann F-J, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS guidelines on myocardial revascularization. *Eur Heart J*. 2018;40:87–165.

17. Patel MR, Calhoon JH, Dehmer GJ, et al. 2017 Appropriate use criteria for coronary revascularization in patients with stable ischemic heart disease. *J Am Coll Cardiol*. 2017;69:2212–2241.

18. Desai NR, Bradley SM, Parzynski CS, et al. Appropriate use criteria for coronary revascularization and trends in utilization, patient selection, and appropriateness of percutaneous coronary intervention. *JAMA*. 2015;314:2045–2053.

19. Tebaldi M, Biscaglia S, Fineschi M, et al. Evolving routine standards in invasive hemodynamic assessment of coronary stenosis: the nationwide Italian SICI-GISE cross-sectional ERIS study. *J Am Coll Cardiol Intv*. 2018;11:1482–1491.

20. Barbato E, Dudek D, Baumbach A, Windecker S, Haude M. Current trends in coronary interventions: an overview from the EAPCI registries. *EuroIntervention*. 2017;13:Z8–Z10.

21. Parikh RV, Liu G, Plomondon ME, et al. Utilization and outcomes of measuring fractional flow reserve in patients with stable ischemic heart disease. *J Am Coll Cardiol*. 2020;75:409–419.

22. May AN, Kull A, Gulingam B, Francis JL, Lau GT. The uptake of coronary fractional flow reserve in Australia in the past decade. *Med J Aust*. 2016;205:127.

23. Wagner A, Bruder O, Schneider S, et al. Current variables, definitions and endpoints of the European CMR registry. *J Cardiovasc Magn Reson*. 2009;11:43.

24. Bruder O, Wagner A, Lombardi M, et al. EuroCMR registry—multinational results from 57 centers in 15 countries. *J Cardiovasc Magn Reson*. 2013;15:9.

25. Kwong RY, Petersen SE, Schulz-Menger J, et al. The global cardiovascular magnetic resonance registry (GCMR) of the SCMR: its goals, rationale, data infrastructure, and current developments. *J Cardiovasc Magn Reson*. 2017;19:23.

26. Kwong R, Ge Y, Steel K, et al. Clinical impact of Stress CMR Perfusion Imaging in the United States (SPINS) study of the SCMR registry. *J Am Coll Cardiol*. 2019;74:1741–1755.

27. Moschetti K, Petersen S, Pilz G, et al. Cost-minimization analysis of three decision strategies for cardiac revascularization: results of the "suspected CAD" cohort of the European CMR registry. *J Cardiovasc Magn Reson*. 2016;18:3.

28. Moschetti K, Favre D, Pinget C, et al. Comparative cost-effectiveness analyses of cardiovascular magnetic resonance and coronary angiography combined with fractional flow reserve for the diagnosis of coronary artery disease. *J Cardiovasc Magn Reson*. 2014;16:13.

29. Ge Y, Pandya A, Steel K, et al. Cost-effectiveness analysis of stress cardiovascular magnetic resonance imaging for stable chest pain syndromes. *J Am Coll Cardiol Img*. 2020;13:1505–1517.

30. Walker S, Girardin F, McKenna C, et al. Cost-effectiveness of cardiovascular magnetic resonance in the diagnosis of coronary heart disease: an economic evaluation using data from the CE-MARC study. *Heart*. 2013;99:873–881.

31. Boldt J, Leber AW, Bonaventura K, et al. Cost-effectiveness of cardiovascular magnetic resonance and single-photon emission computed tomography for diagnosis of coronary artery disease in Germany. *J Cardiovasc Magn Reson*. 2013;15:30.

32. Bertoldi EG, Stella SF, Rohde LE, Polanczyk CA. Long-term cost-effectiveness of diagnostic tests for assessing stable chest pain: modeled analysis of anatomical and functional strategies. *Clin Cardiol*. 2016;39:249–256.

33. Toth G, Hamilos M, Pyxaras S, et al. Evolving concepts of angiogram: fractional flow reserve discordances in 4000 coronary stenoses. *Eur Heart J*. 2014;35:2831–2838.

34. Maron DJ, Hochman JS, Reynolds HR, et al. Initial invasive or conservative strategy for stable coronary disease. *N Engl J Med*. 2020;382:1395–1407.

35. Newby DE, Adamson PD, Berry C, et al. Coronary CT angiography and 5-year risk of myocardial infarction. *N Engl J Med*. 2018;379:924–933.

36. Kawashima H, Serruys PW, Ono M, et al. Impact of optimal medical therapy on 10-year mortality after coronary revascularization. *J Am Coll Cardiol*. 2021;78:27–38.

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APPENDIX For supplemental figures, a table, FFR calculations, and a description of health care systems, please see the online version of this paper.