

Real-World Impact of Comparative Effectiveness Research Findings on Clinical Practice

Teresa B. Gibson, PhD; Emily D. Ehrlich, MPH; Jennifer Graff, PharmD; Robert Dubois, MD; Amanda M. Farr, MPH; Michael Chernew, PhD; and A. Mark Fendrick, MD

With the Affordable Care Act, public funding for comparative effectiveness research (CER) expands beyond the Agency for Healthcare Research and Quality (AHRQ) and the National Institutes of Health to include the Patient-Centered Outcomes Research Institute (PCORI).¹ According to the Institute of Medicine of the National Academies, “The purpose of CER is to assist consumers, clinicians, purchasers, and policy makers to make informed decisions that will improve healthcare at both the individual and population levels.”² The return on this investment in CER will be measured by if, and how quickly, results from the research are used in decision making and translated into clinical practice.

One of the most notable examples of the relationship between findings and practice is the Estrogen Plus Progestin trial, a component of the Women’s Health Initiative.³ The trial was stopped in May 2002 after investigators found that the associated health risks of combination hormone therapy among postmenopausal women outweighed the benefits. Almost immediately following publication, rates of hormone therapy in postmenopausal women were shown to drop precipitously, from 90 million prescriptions to 57 million—a 36.7% decrease.⁴

The Estrogen Plus Progestin trial is an example of a study where the evidence resulted in near-term changes in clinical practice. However, beyond a few notable studies,^{4,6} researchers have found that it can take several years for study findings to translate to practice.^{7,8} Additionally, fewer than 1 study in 1000 is reported by the mainstream media.⁹ Historically, one way that research findings have impacted medical practice has been through the development, dissemination, and use of clinical practice guidelines (CPGs).¹⁰

In this study, we used a large national administrative database to examine real-world utilization trends before and after publication of CER findings (and release of relevant CPGs) from 4 high-profile CER studies published within the last decade. We analyzed changes in utilization rates of procedures and treatments associated with widely communicated CER

ABSTRACT

Objectives

Unprecedented funding for comparative effectiveness research (CER) to help provide better evidence for decision making as a way to lower costs and improve quality is under way. Yet how research findings are adopted and applied will impact the nation’s return on this investment. We examine the relationship between the publication of findings from 4 seminal CER trials, the release of subsequent clinical practice guidelines (CPGs), and utilization trends for associated surgical interventions, diagnostic interventions, or medications.

Study Design

Retrospective, observational study.

Methods

Using a large national administrative claims database, we examined time series utilization trends before and after publication of findings from 4 CER trials published within the last decade.

Results

We found no clear pattern of utilization in the first 4 quarters after publication. However, we found that results for 2 of the studies were in concert with the release of CPGs and publication of study results. The trend in intensive statin therapy rose rapidly starting at the end of 2007, while the trend in standard therapy remained relatively constant (PROVE-IT). And, 9 months after trial publication, breast magnetic resonance imaging (MRI) utilization rates rose 43.2%, from 0.033 to 0.048 per 100 enrollees (Mammography With MRI).

Conclusions

Our analysis of 4 case studies supports the call others have made to translate and disseminate CER findings to improve application of research findings to clinical practice and the need for continued development and dissemination of CPGs that serve to synthesize research findings and guide practitioners in clinical decision making. Further research is needed to determine whether these findings apply to different medical topics.

Am J Manag Care. 2014;20(6):e208-e220

evidence and CPGs for up to 6 years following the evidence of the publication. Our approach was not normative or prescriptive, but was intended to examine historical trends and resulting changes in practice patterns within a large sample of enrollees with employer-sponsored health insurance and to discuss the implications of our findings for those seeking to increase the translation of research findings into practice.

Take-Away Points

Time series utilization trends before and after publication of findings from 4 CER trials published within the last decade revealed no clear pattern of utilization in the first 4 quarters after publication. Results for 2 of the studies (PROVE-IT, Mammography With MRI) were in concert with the release of clinical practice guidelines (CPGs) and publication of study results.

- Our findings support a continued effort to translate and disseminate CER results to improve application of research findings to clinical practice.
- Continued development and dissemination of CPGs to synthesize research findings and guide practitioners in clinical decision making is necessary.

METHODS

To distinguish case studies and conditions for our areas of focus, we performed an environmental scan via a literature review. We queried MEDLINE/PubMed,¹¹ Congressional Budget Office publications,¹² and AHRQ CER¹³ studies to find CER evidence reported between January 1, 2000, and December 31, 2009.

Studies (including randomized controlled trials, meta-analyses, or observational studies) which were highly cited in high-impact medical journals (**Table**) that compared 2 or more treatment options or reviewed the safety of a drug were selected. Based on these criteria, 23 studies were selected, characteristics of each study were abstracted (eg, type of comparators, primary aim as safety vs efficacy, study design), and then each was reviewed by the study team to determine which should be included in the quantitative analysis (**eAppendix A**, available at www.ajmc.com). The main criteria for the selected case studies were (1) high-profile study of a medication, surgical, or diagnostic intervention (published in a high-impact journal as ranked by ISI Web of Knowledge)¹⁴; and (2) widely cited results (ISI Web of Knowledge¹⁴ and Google Scholar citations). We also focused on quality criteria that included, as reviewed by the study team: (1) study design (adequate sample size with an experimental design); (2) clear findings (lack of ambiguity in the implications); and (3) findings that were not reversed or contradicted by subsequent evidence. Cost-effectiveness studies were excluded.

Of these, the study team selected 4 case studies that represented varying types of trials: 1 study compared medical therapies (PROVE-IT TIMI 22), 2 compared surgical versus nonsurgical treatments (COURAGE and SPORT) and 1 compared diagnostic screening procedures (called Mammography With MRI here for simplicity; see reference 20 for actual title).

We also examined the first release of related CPGs, following the publication of trial results. To determine when

guidelines might have started to influence uptake or discontinuation of a specific practice related to the clinical trial, we conducted an environmental scan via a literature review. The criteria for the scan limited results to articles that focused on clinical guidelines and that specifically cited 1 of the 4 seminal studies in relationship to guideline development. We queried Google Scholar for publications following the release of the trial(s) through the end of our study period in 2010. We then eliminated nonguidelines. We also conducted a keyword search of guidelines published by the AHRQ National Guidelines Clearinghouse for the same time period. From the combined list we retrieved the first clinical guideline (from search results), corresponding to each trial (**eAppendix B**).

Data Source and Analysis

This analysis was based on data contained in the Truven Health MarketScan Commercial Claims and Encounters Database and the MarketScan Medicare Supplemental and Coordination of Benefits Database for the period of January 1, 2003, to June 30, 2010. The MarketScan Database includes the enrollment, inpatient, outpatient, and outpatient pharmacy claims experience of tens of millions of individuals across the nation with employer-sponsored insurance or employer-sponsored Medicare Supplemental insurance. Health insurance was offered through a variety of capitated and fee-for-service health plan types, and prescription drug coverage was offered in conjunction with the medical benefit. Its sample size is large enough to allow creation of a nationally representative data sample of Americans with employer-provided health insurance. The enrollment characteristics in MarketScan are largely similar to nationally representative data for employer-sponsored insurance in the Medical Expenditure Panel Survey (MEPS), although a higher percentage of MarketScan enrollees reside in the South census region. The data cover all 50 states and the District of Columbia. Used primarily for research, these databases are fully Health Insurance Portability and Accountability Act compliant.¹⁵

■ **Table.** Selected Case Studies and Utilization Rate Measure Definitions

Case Study	Citation	Number of Citations	Journal Impact Factor (ISI) ^a	Numerator of Utilization Rate (treatment or procedure counts within the study cohort)	Denominator of Utilization Rate—Enrollees Meeting Patient Selection Criteria ^b
PROVE IT-TIMI	Cannon CP, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. <i>N Engl J Med.</i> 2004;350(15):1495-1504.	ISI: 1914 Google Scholar: 2488	44.016 (2005)	Number of days supplied per calendar quarter of: 1. Standard statin therapies ^c 2. Intensive statin therapies ^d	Number of MarketScan enrollees enrolled per calendar quarter <i>Subjects (18 years and older) who had evidence of:</i> Hospitalization with acute coronary syndrome <i>and no evidence of:</i> 1. Pregnancy 2. Use of CYP450 inhibitors 3. Prolonged QT interval 4. Hepatobiliary disease 5. Increased creatinine
Mammography With MRI	Warner E, et al. Surveillance of BRCA1 and BRCA2 mutation carriers with magnetic resonance imaging, ultrasound, mammography, and clinical breast examination. <i>JAMA.</i> 2004;292(11):1317-1325.	ISI: 408 Google Scholar: 627	23.494 (2005)	Number of procedures in a quarter for: 1. Mammography 2. Breast MRI 3. Breast ultrasound	Number of MarketScan enrollees enrolled per calendar quarter <i>Subjects (females, aged 25 years to 65 years) who had no evidence of:</i> 1. Pregnancy or lactation 2. Chemotherapy treatment 3. Metastatic disease 4. Double mastectomy
SPORT	Weinstein JN, et al. Surgical vs nonoperative treatment for lumbar disk herniation: the Spine Patient Outcomes Research Trial (SPORT): a randomized trial. <i>JAMA.</i> 2006;296(20):2441-2450.	ISI: 236 Google Scholar: 495	31.718 (2007)	Number of procedures (counted as a maximum of 1 procedure per patient per day) —Discectomy	Number of MarketScan enrollees enrolled per calendar quarter <i>Subjects (18 years and older) who had evidence of:</i> 1. Disk herniation 2. Radicular pain <i>and no evidence of:</i> 1. Cauda equina 2. Vertebral fractures 3. Spine infection or tumor 4. Pregnancy
COURAGE	Boden WE, et al. Optimal medical therapy with or without PCI for stable coronary disease. <i>N Engl J Med.</i> 2007;356(15):1503-1516.	ISI: 900 Google Scholar: 1342	50.017 (2008)	Number of procedures per calendar quarter —PCI	Number of MarketScan enrollees enrolled per calendar quarter <i>Subjects (18 years and older) who had evidence of:</i> 1. Chronic stable angina, Canadian Cardiovascular Society (CCS) class I-III 2. Coronary artery disease <i>and no evidence of:</i> 1. Unstable angina and symptoms refractory to maximal oral and intravenous medical therapy (persistent CCS class IV) 2. Cardiogenic shock 3. Pulmonary edema or heart failure unresponsive to standard medical therapy 4. Prior PCI or CABG 5. Valvular heart disease 6. Congenital or primary cardiac muscle disease 7. Ventricular tachycardia 8. Heart problem as indicated by positive stress test 9. Pregnancy

CABG indicates coronary artery bypass grafting; CYP450, cytochrome P450; ISI, Institute for Scientific Information; MRI, magnetic resonance imaging; PCI, percutaneous coronary intervention.

^aThomson Reuters, *Journal Citation Reports*, May 2012. The impact factor for the journal is presented for the year following the study publication, reporting on journal impact in the year of publication.

^bSee **eAppendix C** for a detailed description of the inclusion and exclusion criteria. If a patient had evidence of prescription fills for both standard and intensive statins, the patient was categorized based on the final statin prescription fill of the calendar quarter.

^cStandard therapy was defined as atorvastatin (10 mg); simvastatin (5-20 mg); pravastatin (10-80 mg); fluvastatin (20-80 mg); lovastatin (10-40 mg); or cerivastatin (0.2-0.4 mg).

^dIntensive therapy was defined as atorvastatin (20-80 mg); simvastatin (40-80 mg); lovastatin (60 mg); cerivastatin (0.8 mg); or rosuvastatin (5-40 mg).

Once having met study requirements, patients were followed until the end of their continuous enrollment, or until evidence appeared that they met the exclusion criteria, or until completion of 2 years of follow-up (except in the Mammography with MRI study, where patients were followed through the end of their continuous enrollment).

To study trends in the utilization rates for each case study, we calculated the quarterly utilization rates of each procedure (by calendar quarter). First, we selected the continuous cohort of firms contributing data to MarketScan each year from 2003 through 2010 Q1, representing approximately 4 million enrollees annually (eAppendix C), so trends would not be impacted by firms entering and leaving the sample. Within these firms, each enrollee selected for inclusion in the study had medical and pharmacy claims data available, was 18 years or older, was continuously enrolled in the 4 calendar quarters prior to the quarter of interest, and was not pregnant (no diagnosis of pregnancy).

Second, within this cohort of enrollees, we replicated (as was possible using claims data) the inclusion and exclusion criteria used in each clinical trial (based upon publication or online trial-specific materials) for patient selection (See the Table for summarized criteria and eAppendix D for detailed criteria and codes). To determine these sets of criteria, a nosologist (certified clinical coding expert) provided clinical codes (*International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM]* diagnosis codes, *ICD-9-Clinical Modification [ICD-9-CM]* procedure codes, and *Current Procedural Terminology, 4th Edition [CPT-4]* procedure codes) for each of the inclusion and exclusion criteria and the procedures listed in the clinical trial. As part of an iterative process, these codes were reviewed by a clinician expert in clinical coding and the resulting list was reviewed a second time by the nosologist. Through a consensus-driven process, any differences between the clinician and the nosologist were resolved in consultation with the project manager, and by 2 other clinicians. A similar process was employed for creating a list of pharmaceutical codes, incorporating a review of National Drug Codes by a licensed pharmacist.

The study clinicians relaxed some of the criteria (see eAppendix D for a description of how these criteria were relaxed) designated in the trial to focus on patients who were similar to those targeted by very specific study criteria for 2 reasons. First, clinical coding in administrative data sets can lack precision.¹⁶ Second, we hypothesized that these results would have spillover effects on clinical practice beyond patients meeting the restrictive clinical inclusion criteria used in the respective clinical trial. Therefore, we focused on patients highly similar to those included in the trial. For example, for the Mammography With MRI study, we did not require women to have a diagnosis on a claim indicating that they carried the BRCA1 or BRCA2 mutation, because test results are infrequently available in claims analyses.¹⁷ For the SPORT case study, we did not

exclude enrollees if they had a previous lumbar surgery. The relaxed criteria were then applied to the data set to find the set of enrollees in each calendar quarter meeting the patient selection criteria (the denominator). For the pre-period for each study, we required patients to be continuously enrolled at least 1 year prior to the quarter, to check for a number of inclusion and exclusion criteria. Claims incurred during this year were used to evaluate inclusion and exclusion criteria (eAppendix D). Once meeting study requirements, patients were followed until the end of their continuous enrollment, or until evidence appeared that they met the exclusion criteria, or until completion of 2 years of follow-up (except in the Mammography With MRI study, where patients were followed through the end of their continuous enrollment).

Finally, a list of the treatments or procedures of interest (eg, breast magnetic resonance imaging [MRI]) was created (numerator of each measure). Within the enrollees meeting the selection criteria, enrollees receiving each treatment or procedure were flagged in the database and the number of occurrences of the treatment or procedure of interest (the numerator) was recorded (note: eAppendix D contains the clinical criteria used in each case study). Using this information, we calculated aggregate quarterly trends in utilization rates for each treatment or procedure.

We present the descriptive findings in 2 formats. First, we display graphical trends before and after the publication of the CER evidence and guideline release. We show the timing of the first national CPG that referenced the study.

Second, we display utilization rates in tabular form at 3- and 6-month intervals and calculate the percent change from the prior value at each time interval.

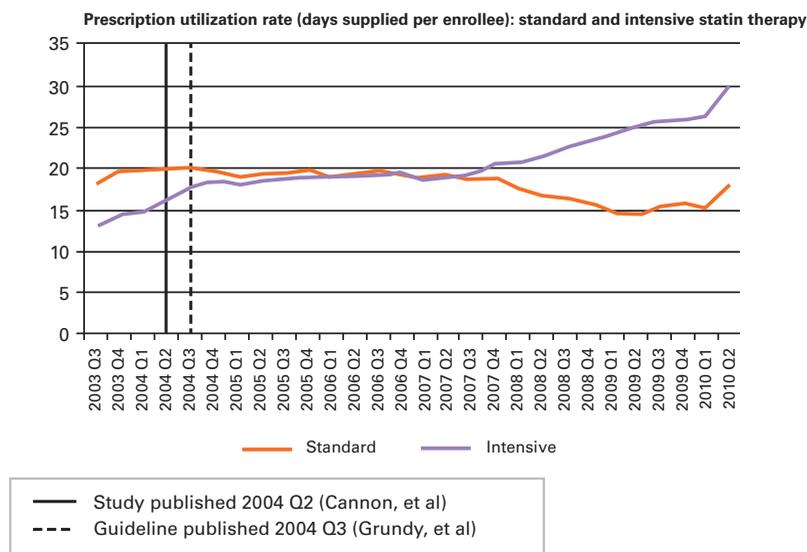
As a separate analysis, we replicated the study results using a stricter set of criteria using claims data, described in the clinical trial (without relaxation). These results represent a smaller group of enrollees (eAppendix E).

RESULTS

A consistent cohort of 66 data contributors (large firms and insurers) contributing data throughout the entire study period was selected for analysis, representing approximately 7 million enrollees each year. Between 2003 and 2010, the number of patients meeting the clinical trial inclusion criteria ranged from 86,080 for PROVE-IT to 5,159,253 for Mammography With MRI. Patient characteristics of these subjects are detailed in eAppendix C. All reported results reflect the relaxed version of the original study criteria.

The rest of this paper summarizes the main findings from each case study and the temporal trends in each study,

■ **Figure 1. PROVE-IT Trial**



Utilization rates before and after release of CER evidence

Quarter	2003 Q4	2004 Q2	2004 Q4	2005 Q2	2005 Q4	2006 Q2	2006 Q4	2007 Q2	2007 Q4	2008 Q2	2008 Q4	2009 Q2	2009 Q4	2010 Q2
Months since publication	-6	0	6	12	18	24	30	36	42	48	54	60	66	72
Months since guideline	-9	-3	3	9	15	21	27	33	39	45	51	57	63	69
Intensive rate	14.4	16.3	18.6	18.5	19.2	19.2	19.5	19.0	20.4	21.3	23.2	25	25.8	29.9
Standard rate	19.7	20.0	19.6	19.6	19.6	19.3	19.4	19.3	18.8	16.8	15.9	14.8	15.9	18.0
% Change Intensive		13.6	13.8	-0.3	3.5	0.4	1.3	-2.8	7.8	4.0	9.3	7.8	3.0	15.7
% Change Standard		1.6	-2.1	-0.3	0.2	-1.5	0.4	-0.7	-2.4	-10.4	-5.6	-7.1	7.7	13.1

CER indicates comparative effectiveness research. Utilization rate is days supplied per enrollee. Percent change calculated from prior period.

in chronological order of publication. **Figures 1** through **4** show the quarterly utilization trends for each case study.

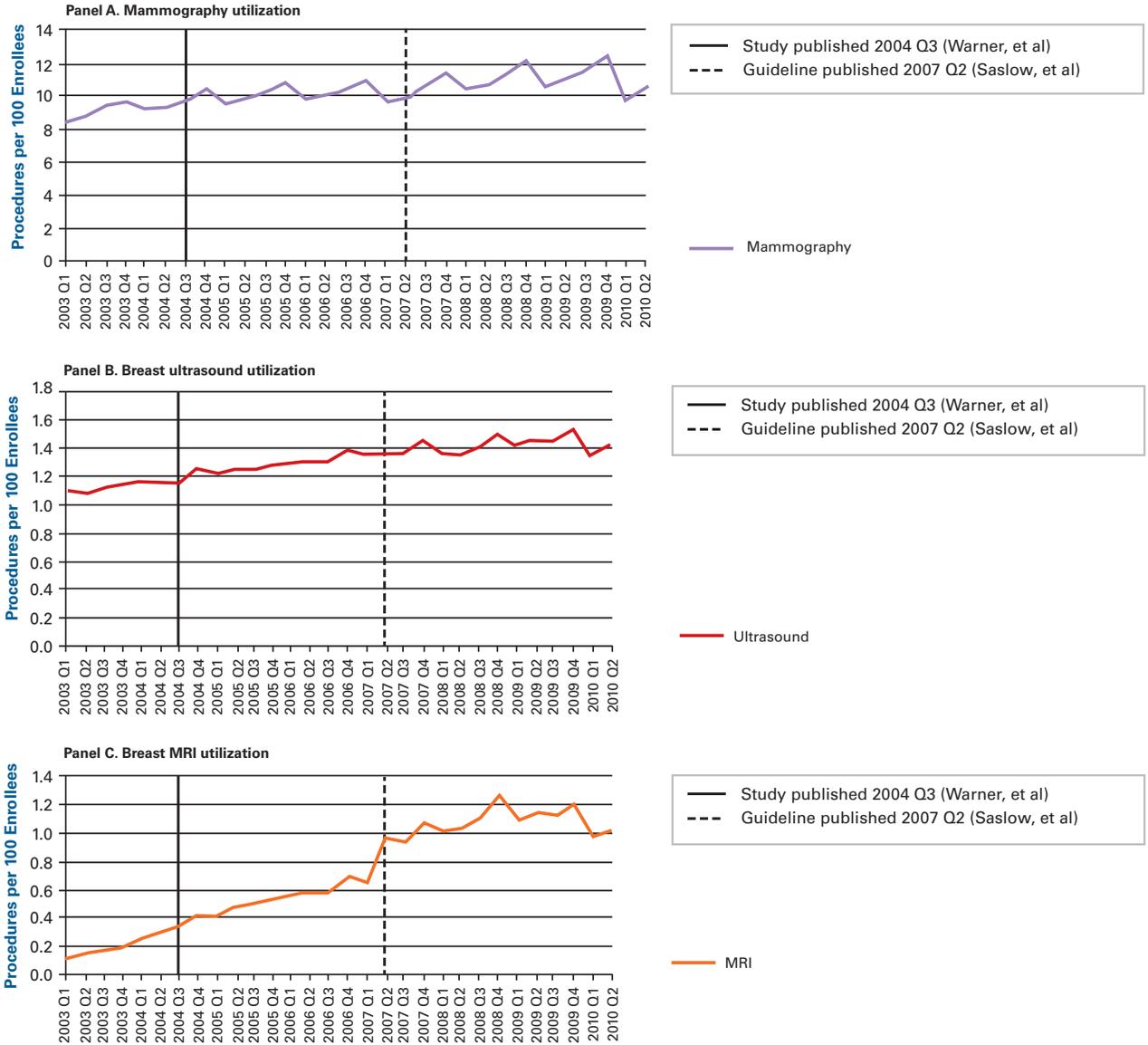
PROVE-IT (2004)

The PROVE-IT trial¹⁸ investigated whether standard therapy with 40 mg of pravastatin daily or intensive therapy with 80 mg of atorvastatin daily decreased a composite outcome, including all-cause mortality, myocardial infarction (MI), unstable angina, revascularization, and stroke among patients who had been recently hospitalized for acute coronary syndrome. Patients who obtained intensive lipid-lowering statin therapy had a lower risk of death or cardiovascular events than those on a standard statin regimen. The literature search yield-

ed 24 CPGs published during the review period (conclusion of the study through 2010). The first guideline was published in 2004 by the National Cholesterol Education Program.¹⁹ The CPG called for more aggressive lowering of low-density lipoprotein-cholesterol, and was published in response to 5 new statin trials, including PROVE-IT. Based upon these results, we hypothesized that after the release of the PROVE-IT trial results and publication of the CPG, prescription utilization rates (days supplied per person per quarter) would increase for patients on intensive statin therapy and decrease with standard statin therapy.

We found the use of intensive statin therapy increased; however, the increase in utilization started prior to the publication of PROVE-IT in 2004. After

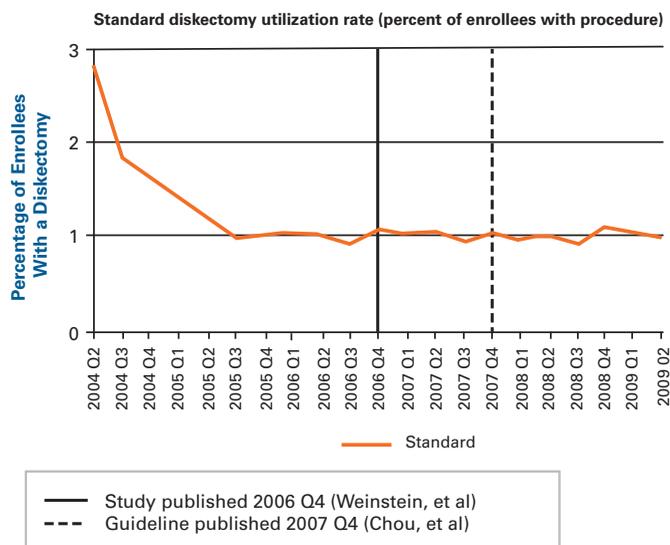
Figure 2. Mammography with MRI Utilization Rate (procedures per 100 enrollees)



Utilization rates before and after release of CER evidence

Quarter	2003 Q1	2003 Q4	2004 Q3	2005 Q2	2006 Q1	2006 Q4	2007 Q3	2008 Q2	2009 Q1	2009 Q4
Months since publication	-18	-9	0	9	18	27	36	45	54	63
Months since guideline	-51	-42	-33	-24	-15	-6	3	12	21	30
MRI rate	0.010	0.019	0.033	0.048	0.056	0.069	0.093	0.103	0.108	0.119
Mammography rate	8.44	9.79	9.79	9.91	9.87	11.07	10.68	10.71	10.6	12.5
Ultrasound rate	1.10	1.14	1.16	1.26	1.29	1.39	1.36	1.36	1.43	1.54
% change MRI		80.8	78.7	43.2	16.8	23.3	35.4	10.8	5.2	9.8
% change Mammography		16.0	0.0	1.2	-0.3	12.2	-3.6	0.2	-1.1	17.9
% change ultrasound		3.3	1.9	8.5	2.3	8.4	-2.5	0.3	4.9	7.3

■ **Figure 3. SPORTrial**



Utilization rates before and after release of CER evidence

Quarter	2004 Q2	2004 Q4	2005 Q2	2005 Q4	2006 Q2	2006 Q4	2007 Q2	2007 Q4	2008 Q2	2008 Q4	2009 Q2	2009 Q4
Months since publication	-30	-24	-18	-12	-6	0	6	12	18	24	30	36
Months since guideline	-36	-30	-24	-18	-12	-6	0	6	12	18	24	30
Standard diskectomy rate	2.83	1.62	1.21	0.99	0.99	1.08	1.04	1.02	0.99	1.10	0.98	1.08
% change		-42.8	-25.2	-18.3	-0.1	8.9	-3.1	-2.4	-3.1	11.6	-11	10.1

Utilization rate is percent of enrollees with procedure. Percent change calculated from prior period.

the initial rise, the trend in intensive therapy flattened for the next 3 years (after publication of results and release of the subsequent CPG) and rose rapidly starting at the end of 2007. In contrast, the trend in standard therapy remained relatively constant prior to publication and through the 3 years after publication of results and release of the CPG. Utilization of standard therapy declined starting at the end of 2007 and then leveled off after early 2009 (Figure 1).

MAMMOGRAPHY WITH MRI (2004)

The Mammography With MRI study²⁰ evaluated the sensitivity and specificity of 4 breast cancer surveillance methods: mammography, ultrasound, magnetic resonance imaging (MRI), and a clinical breast exam among carriers of BRCA1 or BRCA2 mutations. The sensitivity of MRI to detect breast cancer was highest, with 77% of all cancers detected found by MRI compared with 36% by

mammography, 33% by ultrasound, and 9.1% by clinical breast exam.

The literature search yielded 15 CPGs published during the review period. The first CPG was published in 2007 by the American Cancer Society.²¹ This updated CPG added annual MRI screening to mammography for women with greater than or equal to a 20% to 25% lifetime risk. Based on the results of this trial, we hypothesized that MRI utilization rates among women would increase.

We found that mammography rates (number of procedures per 100 enrollees) remained relatively consistent (with seasonal variation) and breast ultrasound utilization rates rose steadily over time. Compared with the other imaging technologies of mammography and ultrasound, there was a steady increase in MRI utilization prior to and following publication in 2004 through the end of 2006, and then a sharper increase after the CPG was released in 2007 Q2. In mid-2005, 9 months after publication, breast MRI utilization rates rose 43.2% from 0.033

to 0.048 per 100 enrollees. Despite the increase in utilization, the absolute rate of MRI utilization was far less than the utilization of ultrasound or mammography (0.048 vs 1.26 and 9.91 per 100 enrollees at 9 months after publication of the results and 9 months after release of the CPG) (Figure 2).

SPORT (2006)

The Spine Patient Outcomes Research Trial (SPORT)²² was designed to assess whether a standard open discectomy was more effective than non-operative treatment at decreasing pain and improving physical function among patients with intervertebral disk herniation. Additional outcome measures were patient self-reported improvement, work status, symptom satisfaction, and care satisfaction. Intent-to-treat analysis did not find statistically significant differences in pain reduction or physical function, but found differences in measures of sciatica severity and self-reported improvement. However, nonadherence to the assigned treatment was high. After 2 years of follow-up, 60% of the patients randomized to the surgical intervention and 45% of the patients randomized to usual care had surgery. Larger beneficial effects from surgery were seen for the as-treated analysis.

The literature search yielded 4 guidelines citing trial evidence. In 2007, the College of Physicians and the American Pain Society published the first CPG.²³ The SPORT trial was one of many back pain studies cited in this guideline release.

Based on the findings of this trial, we hypothesized that standard discectomy utilization rates (percent of eligible enrollees with the procedure) would increase after publication of the results in 2006 Q4 and release of the CPG in 2007 Q2. However, we found that standard discectomy rates remained relatively consistent (remaining around 1 discectomy per 100 enrollees) after release of the SPORT trial results (Figure 3).

COURAGE (2007)

The COURAGE trial,²⁴ implemented among patients with stable coronary artery disease, was designed to determine whether percutaneous coronary intervention (PCI) with optimal medical therapy (OMT) decreased the risk of death, nonfatal MI, or other major cardiovascular events compared with patients solely treated with OMT. COURAGE found that PCI with OMT did not reduce the risk of these study outcomes compared with OMT alone.

The literature search yielded 13 CPGs citing the trial evidence. In 2007, the American College of Cardiology/

American Heart Association published the first CPG that referenced the trial. The guideline update recommendations explicitly reflected “consensus of expert opinion following a thorough review primarily of late-breaking clinical trials...”²⁵ Based upon the trial results, we hypothesized that PCI utilization rates would not change or would decrease after the release of results in 2007 Q2. We do not present results on trends in OMT because not all of the therapies required are observable in claims (ie, aspirin). However, trends in OMT, that are observable in claims reflect no change in use after publication of results. We found the rates of PCI oscillated over time in the 2 years after publication. (Figure 4).

As a separate analysis for each of the 4 case studies, we used strict inclusion criteria as close as possible to the criteria defined in the trial (no relaxation of criteria). The trends are not directly comparable because of the limitations of the codes available in claims for some of these criteria, and the smaller sample sizes (eAppendix E).

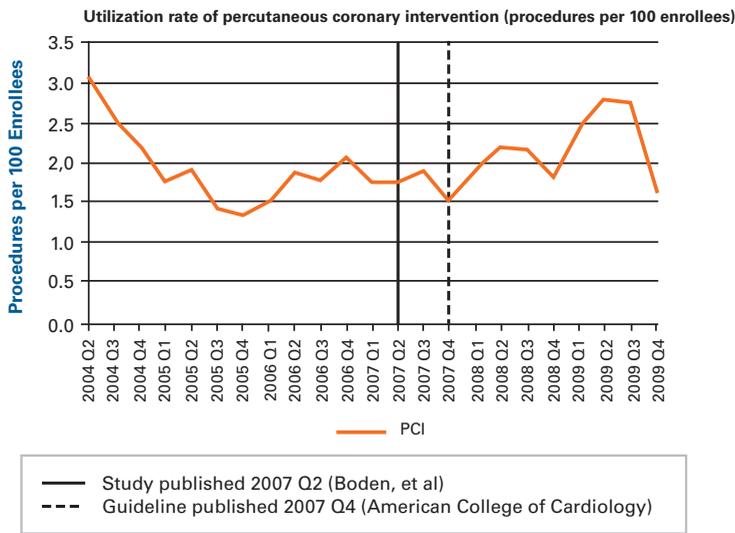
DISCUSSION

To examine the relationship between CER evidence and practice we analyzed pre- and post publication utilization trends related to treatments or diagnostic procedures compared in 4 high-quality, high-profile, published CER studies. In all cases, we found no clear pattern in utilization in the first 4 quarters after publication of these case studies. However, in 2 cases, PROVE-IT and Mammography With MRI, there appeared to be an association between evidence and practice: changes in lipid-lowering therapy and MRI trends began prior to publication of study results and persisted after publication of results and release of CPGs. In SPORT, discectomy utilization rates did not change; in COURAGE, PCI utilization rates varied.

While we studied trends among a very large cohort of enrollees with commercial insurance provided by large- and medium-sized firms, a few studies analyzed similar trends in different patient groups. Howard and colleagues used claims data from the US community, the Veterans Administration, and from England to study the impact of the impact of the COURAGE trial on the volume of PCI procedures. Using data from 2001 to 2008, they found a decline in PCI, but the lower rates were not sustained over time based upon inpatient discharge data 21 months after publication of COURAGE.⁶

In addition, Austin and colleagues analyzed claims data for statin prescribing patterns among adults 65 years and older in Ontario from 1997 to 6 months following

■ **Figure 4. COURAGE Trial**



OMT is administered on an outpatient basis; therefore cannot be fully observed in claims data.

Quarter	2004 Q2	2004 Q4	2005 Q2	2005 Q4	2006 Q2	2006 Q4	2007 Q2	2007 Q4	2008 Q2	2008 Q4	2009 Q2	2009 Q4
Months since publication	-36	-30	-24	-18	-12	-6	0	6	12	18	24	30
Months since guideline	-44	-38	-32	-26	-20	-14	-8	-2	4	10	16	22
PCI rate	3.12	2.20	1.94	1.33	1.87	2.08	1.76	1.51	2.19	1.81	2.79	1.63
% change		-29.5	-11.9	-31.5	40.7	11.2	-15.2	-13.9	44.5	-17.5	54.6	-41.7

OMT indicates optimal medical therapy.
Utilization rate is procedures per 100 enrollees.
Percent change calculated from prior period.

publication of PROVE-IT in 2004. The authors found a significant, sustained increase in the use of high-dose atorvastatin compared with moderate statin therapies.²⁶ We found a similar increase in the use of intensive therapy in our patient sample in the 6 months following publication, which was a continuation of the pre-publication trend. Use of standard therapy was relatively unchanged. We found no studies assessing trends in breast MRI or SPORT.

Some of the findings in our analysis may be explained by the design or context surrounding the 4 trials. First, all 4 studies that we examined reviewed treatments or procedures that were in widespread use at the time of the trial. For example, COURAGE and SPORT addressed the comparative effectiveness of surgery versus non-operative care using clinical and economic outcomes. Secondly, the trial findings concluded with clinical evidence in

support of one therapy over another. While informative, these types of studies may be less influential than studies that report results from an investigation of a new treatment or drug, or studies that show that treatments may be harmful, such as the Women’s Health Initiative, which in 2002 warned against overuse of hormone therapy after menopause.²⁷

The Role of Clinical Guidelines

The results from each of the 4 clinical trials in our study added to the body of knowledge from previously published clinical practice guidelines (eg, cholesterol management); and, in all cases, there were specific CPG revisions associated with each study. We investigated the association between the timing of relevant clinical guideline releases (citing evidence from these trials) and the observed utilization trends to determine whether

there appeared to be an impact of guideline release on trends.

For PROVE-IT, the 2004 update to the National Cholesterol Education Program's²⁸ clinical practice guidelines on cholesterol management advised physicians to consider new, more intensive treatment options for people at high risk (treatment goal shifted from less than 100 mg/dL to less than 70 mg/dL for very high risk patients).¹⁹ This guideline was published shortly following the release of PROVE-IT and built upon prior studies such as MIRACL²⁹ and the Heart Protection Study.³⁰ This preceded the large uptick we observed in intensive statin therapy starting in 2007.

More than 2 years following the publication of the Mammography With MRI study, the American Cancer Society updated guidelines for breast cancer screening to include MRI as an adjunct to mammography for specific risk groups.²¹ This guideline update occurred after the observed increase in MRI in 2007. With respect to low back pain, between the seminal guideline in 1994³¹ and the next major update in 2007,²³ the SPORT trial was one of many back pain studies cited in this guideline release.²³ Finally, in the case of the COURAGE trial, results confirmed a premise that PCI does not reduce the risk of death, MI, or other major cardiovascular events when added to "optimal medical therapy" compared with optimal medical therapy alone.³² The first guideline citing this trial was released in 2007; however, the update to the guidelines on stable angina, incorporating specific results from COURAGE, did not occur until 2011,²⁵ more than 3 years after the publication of the trial.

While experts generally acknowledge that some lag is necessary to ensure the safety and efficacy of new interventions, there is also a desire to optimize lags. Additional research is needed to understand the relationship between research outcomes and the dissemination of clinical findings.

IMPLICATIONS

Our study provides a descriptive, historical review of utilization rates over time and of translation into practice for cohorts of patients that were most likely to be affected by the evidence. We did not test statistical significance and we do not attempt to trace a causal path between the releases of evidence and realized clinical practice. In this section, we examine factors that are salient in a rapidly learning healthcare system where evidence and practice have close ties, including: stakeholder engagement, evidence clarity and maturity, timing, dissemination, knowledge translation, and incentives.

Stakeholder Engagement From Research Question to Development

In evaluating whether the evidence is adopted, we make the assumption that the right questions are posed and assessed. In many cases, the evidence may be based upon outcomes that (1) are not meaningful to the decision makers and other stakeholders, (2) evaluate irrelevant comparators, or (3) lack typical care settings or patients to inform clinical practice.³³ Stakeholder engagement from the early phases of research through conduct and interpretation may aid study design and recruitment.³⁴ For example, new projects have sought to include stakeholders to prioritize research on genomic tests in cancer to improve the relevance of future studies.³⁵

Evidence Clarity and Maturity

Few single studies have resulted in a wholesale change in clinical practice. To effect such a change, evidence generally must be cumulative, requiring multiple confirming studies, particularly when the evidence is conflicting with current practice.³⁶ Clarity and strength of research findings may be a function of the evidence maturity: the cumulative strength and concordance of the evidence. For example, even in the case of COURAGE, where the results were widely disseminated, the analysis continues to evolve. In 2011, four years after the publication of COURAGE, the National Heart, Lung and Blood Institute (NHLBI) released an \$84 million grant (ISCHEMIA) to study initial management strategies for patients with coronary artery disease. While the COURAGE trial emphasized the importance of OMT, the progression to new trials such as ISCHEMIA indicates a desire within the medical community for corroborating studies regarding treatment for this patient population.³⁷

Timing

The conduct of research may lead clinical practice, or may actually lag the current clinical practice, as a confirmatory approach. Much has been written about whether research itself influences practice in a linear fashion, or if research confirms expert opinion, the current practices, and the experience of routine practice.³⁸ As an example, intensive statin therapy was already increasing prior to the publication of PROVE-IT, and prior studies had investigated the effects of intensive statin therapy in acute coronary syndrome (MIRACL).²⁹

Dissemination and Policy

The process of disseminating research findings to patients and clinicians is complex.³⁹ Practitioners often look

to specialty societies, researchers, or other guideline writing groups for help interpreting evidence that is vast and sometimes confusing.⁴⁰ CPGs are a necessary first step to synthesize the evidence and serve as a catalyst for uptake. In the case of COURAGE, the amount of publicity in the medical and popular press was such that it seemed reasonable to expect a more significant timely increase in the application of study findings to clinical practice.²⁷ Perhaps, however, the lag in development of a CPG that included recommendations based on COURAGE played a role. Specific mechanisms for dissemination, including written reports, professional presentations, training programs, consumer guides, and marketing campaigns, have all been identified as important components of disseminating CER results.⁴¹

Further funding and research is needed to promote innovative approaches for disseminating CER results, and partnering may be needed to enable adoption of evidence.⁴¹

Knowledge Translation

The need to understand what causes the lag in adoption or abandonment of treatment options, as well as which approaches to translation work best, has sparked an area of research referred to as knowledge translation.

In recent years, several knowledge translation studies have identified some explicit factors of translation.^{42,43} For example, Lang and colleagues present a model for closing the evidence-to-practice gap moving from research to practice: (1) organization of the evidence, synthesis of research, and guidelines; (2) bedside evidence-based medicine (EBM), including access to decision rules and locally agreed-on clinical practice guidelines (eg, via handheld computers); (3) continuous quality improvement initiatives designed to support adherence to EBM and guidelines; and (4) the use of decision aids, patient education, and compliance aids.⁴⁴

Incentives

Misalignment of financial incentives with CER evidence has been suggested as one of the primary root causes of incomplete translation of results,⁴⁵ and this misalignment affects many stakeholder groups, including providers, patients, insurers, professional societies, and medical manufacturers. For example, the predominant fee-for-service payment structure rewards the performance more procedures and services, even sometimes when there is not sufficient evidence of clinical value.⁴⁶ By aligning incentives to reimburse providers based on what is known as best practice, we create a more favorable environment for the adoption of CER in the health system.⁴⁷ A variety of strategies should be considered to encourage

high-value care, including value-based insurance benefit design,⁴⁸ shared savings models; and bundled, severity-adjusted payments.⁴⁶

LIMITATIONS

This study is not without limitations. It is possible that factors other than the CER evidence will change the trend in utilization and spending for patients in the sample. Or, if more contemporary data had been included, different trends may have emerged. For example, over time, practice might have been informed by the singular study. In other cases, a study may be part of a growing body of evidence that translates to slower changes, and others still require synthesis of the evidence (through CPGs or others) to ultimately result in knowledge translation. And, although we selected seminal trials for review, we only reviewed 4 studies.

As with any data source, claims data have limitations in coding and the amount of clinical information available. In addition, the MarketScan sample population is based on a large convenience sample from large employers. In addition, since the study was not conducted on the patient level, factors that may be associated with the various outcomes cannot be adjusted for in analysis.

Using administrative claims, it is difficult to exactly replicate the study-specific inclusion and exclusion criteria as defined in the original trials. For example, we found that in the case of COURAGE, some criteria are not available on claims (eg, vessel inclusion classified as too severe vs less severe). In other cases, the criteria may overlap (eg, PCI is in the inclusion criteria and the exclusion criteria for COURAGE—exclude patients if a PCI within 6 months). Other studies have attempted to replicate the study-specific criteria as defined in the COURAGE trial, and we have used the codes in those analyses as a starting point for coding criteria.⁴⁹ The goal of our study was to use administrative claims to perform an observational analysis of utilization rates in clinically relevant patient populations. Details for the modifications to the inclusion and exclusion criteria for each of the 4 studies in our analysis are included in eAppendix D.

Finally, these findings may not be generalizable to the general US population, as persons who are uninsured, employed by small firms, or on Medicaid are not included in our sample.

CONCLUSION

CER evidence can increase the understanding and utilization of the most effective healthcare treatments, inter-

ventions, and procedures likely to result in improvements in outcomes and quality of care. Differences exist between evidence-based findings and the timing and adoption of the 4 studies examined. With increasing funding there is great potential in CER to address these differences, with an opportunity to fund areas that have gaps in scientific evidence. Specifically, future research could explore the potential heterogeneity in the adoption of CER findings. For example, if there are differences in trends in urban areas versus rural areas, Southeast versus Northwest regions of the United States, integrated health systems versus vertical care systems, or other stratifications, these could be used as a proxy for practice patterns and for lessons on knowledge translation. This study demonstrates that evaluating the impact on clinical practice, based on results of published CER trials and CPGs, is complex. Given the ill-defined nature of clinical practice and decision making, other nonevidence factors that influence clinician and patient uptake of effective medical services (eg, generic availability, payment patterns, public awareness campaigns) are worth exploring. As new mechanisms and policies are developed to increase stakeholder engagement, prioritize research, and proactively plan for dissemination, change may occur.

The greatest value of CER is the development of evidence that is translated and implemented in practice.⁵⁰ In the future, more of this type of analysis will occur, since by legislative statute, a review will occur examining the “extent to which research findings are used by healthcare decision-makers, the effect of the dissemination of such findings on reducing practice variation and disparities in healthcare...”⁵¹ Similar evaluations should continue to be conducted to assess the impact of CER on utilization and practice.

Acknowledgments

George Goldberg, MD, for clinical and coding consultation; Brian J. Moore, PhD, and Emily Vogtmann, PhD, for research assistance; nosologists Debra Ellis, RHIT, and Cary Rizor, RHIT. Dr Gibson also serves as lecturer, Healthcare Policy, Harvard Medical School, Boston, MA.

Author Affiliations: Truven Health Analytics, Ann Arbor, MI (TBG, EDE, AMF); National Pharmaceutical Council, Washington, DC (JG); Harvard Medical School, Boston, MA (MEC); The University of Michigan (AMF).

Source of Funding: This study was funded by the National Pharmaceutical Council.

Author Disclosures: Dr Gibson, Ms Ehrlich, and Ms Farr report employment with Truven Health Analytics, which has received consulting fees from the National Pharmaceutical Council. Dr Dubois reports employment with the National Pharmaceutical Council. The other authors report no relationship or financial interest with any entity that would pose a conflict of interest with the subject matter of this article.

Authorship Information: Concept and design (TBG, RD, AMF, MEC, AMF); acquisition of data (TBG, AMF); analysis and interpretation of data (TBG, EDE, RD, AMF, AMF); drafting of the manuscript (TBG, EDE, RD, AMF); critical revision of the manuscript for important intellectual content (TBG, RD, AMF, MEC, AMF); statistical analysis (TBG,

MEC); provision of study materials or patients (TBG); obtaining funding (TBG, RD); administrative, technical, or logistic support (TBG, EDE); supervision (TBG, RD).

Address correspondence to: Teresa B. Gibson, PhD, Truven Health Analytics, 777 E Eisenhower Parkway, Ann Arbor, MI 48108. E-mail: teresa.gibson@truvenhealth.com.

REFERENCES

1. Subtitle D - Patient-Centered Outcomes Research. Pub L No. 111-148, 124 Stat 727. http://www.gao.gov/about/hcacr/pcor_sec_6301.pdf. Accessed July 25, 2012.
2. Institute of Medicine. Initial National Priorities for Comparative Effectiveness Research. 2009.
3. Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA*. 2002;288(3):321-333.
4. Hersh AL, Stefanick ML, Stafford RS. National use of postmenopausal hormone therapy. *JAMA*. 2004;291(1):47-53.
5. Stafford RS, Bartholomew LK, Cushman WC, et al. Impact of the ALLHAT/JNC7 Dissemination Project on thiazide-type diuretic use. *Arch Intern Med*. 2010;170(10):851-858.
6. Howard DH, Shen YC. Comparative effectiveness research, COURAGE, and technological abandonment. *NBER Work Pap Ser*. August 2011.
7. Green LW, Ottoson JM, Garcia C, Hiatt RA. Diffusion theory and knowledge dissemination, utilization, and integration in public health. *Annu Rev Public Health*. 2009;30:151-174.
8. Lenfant C. Clinical research to clinical practice—lost in translation? *N Engl J Med*. 2003;349(9):868-874.
9. Suleski J, Ibaraki M. Scientists are talking, but mostly to each other: a quantitative analysis of research represented in mass media. *Public Underst Sci*. 2010;19(1):115-125.
10. Davis DA, Taylor-Vaisey A. Translating guidelines into practice: a systematic review of theoretic concepts, practical experience and research evidence in the adoption of clinical practice guidelines. *CMAJ*. 1997;157:408-416.
11. PubMed Research Center. United States National Library of Medicine. www.ncbi.nlm.nih.gov/pubmed/. Published January 1996. Accessed May 21, 2012.
12. Congress of the United States - Congressional Budget Office. Research on the Comparative Effectiveness of Medical Treatments. Congressional Budget Office website. <http://www.cbo.gov/sites/default/files/cbofiles/ftpdocs/88xx/doc8891/12-18-comparativeeffectiveness.pdf>. December, 2007.
13. Agency for Healthcare Research & Quality website. <http://www.effectivehealthcare.ahrq.gov/>. Accessed January 2, 2014.
14. ISI Web of Knowledge Database. <http://apps.webofknowledge.com>. Accessed May 21, 2012.
15. Hansen LG, Chang S. Health research data for the real world: the MarketScan databases. Truven Health Analytics. Published July 2012.
16. Jollis JG, Ancukiewicz M, DeLong ER, Pryor DB, Muhlbaiier LH, Mark DB. Discordance of databases designed for claims payment versus clinical information systems: implications for outcomes research. *Ann Intern Med*. 1993;119(8):844-850.
17. Schneeweiss S, Avorn J. Using healthcare utilization databases for epidemiologic research on therapeutics. *J Clin Epidemiol*. 2005;58(4):323-337.
18. Cannon CP, Braunwald E, McCabe CH, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. *N Engl J Med*. 2004;350(15):1495-1504.
19. Grundy SM, Cleeman JI, Merz CNB, et al. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III Guidelines. *J Am Coll Cardiol*. 2004;44(3):720-732.
20. Warner E, Plewes DB, Hill KA, et al. Surveillance of BRCA1 and BRCA2 mutation carriers with magnetic resonance imaging, ultrasound, mammography, and clinical breast examination. *JAMA*. 2004;292(11):1317-1325.
21. Saslow D, Boetes C, Burke W, et al. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA Cancer J Clin*. 2007;57(2):75-89.

22. Weinstein JN, Lurie JD, Tosteson TD, et al. Surgical vs. nonoperative treatment for lumbar disk herniation: the Spine Patient Outcomes Research Trial (SPORT): a randomized trial. *JAMA*. 2006;296(20):2441-2450.
23. Chou R, Qaseem A, Snow V, et al; Clinical Efficacy Assessment Subcommittee of the American College of Physicians; American College of Physicians; American Pain Society Low Back Pain Guidelines Panel. Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society. *Ann Intern Med*. 2007;147(7):478-91.
24. Boden WE, O'Rourke RA, Teo KK, et al. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med*. 2007;356(15):1503-1516.
25. King, S. B., Smith, S. C., Hirshfeld, J. W., et al. 2007 Focused Update of the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention A Report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines: 2007 Writing Group to Review New Evidence and Update the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention, Writing on Behalf of the 2005 Writing Committee. *Circulation*, 2008;117(2):261-295.
26. Austin PC, Mamdani MM. Impact of the pravastatin or atorvastatin evaluation and infection therapy-thrombolysis in myocardial infarction 22/reversal of atherosclerosis with aggressive lipid lowering trials on trends in intensive versus moderate statin therapy in Ontario, Canada. *Circulation*. 2005;112(9):1296-1300.
27. Winstein KJ. A simple health-care fix fizzles out. *The Wall Street Journal*. February 11, 2010. <http://online.wsj.com/article/SB100010424052748703652104574652401818092212.html>.
28. ATP III Update 2004: implications of recent clinical trials for the ATP III guidelines. <http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3upd04.htm>. Accessed July 25, 2012.
29. Schwartz GG, Olsson AG, Ezekowitz MD, et al. Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes: the MIRACL study: a randomized controlled trial. *JAMA*. 2001;285(13):1711-1718.
30. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20 536 high-risk individuals: a randomised placebo-controlled trial. *Lancet*. 2002;360:7-22.
31. Agency for Healthcare Policy and Research (AHCPR). Acute Low Back Problems in Adults - Clinical Practice Guideline. In: US Department of Health and Human Services. 1994:160.
32. Gibbons RJ, Abrams J, Chatterjee K, et al. ACC/AHA 2002 Guideline Update for the Management of Patients with Chronic Stable Angina - Summary Article: A Report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients with Chronic Stable Angina). *J Am Coll Cardiol*. 2003;41(1):159-168.
33. Green LW. Making research relevant: if it is an evidence-based practice, where's the practice-based evidence? *Fam Pract*. 2008;25(suppl 1):i20-i24.
34. Lomas J, Fulop N, Gagnon D, Allen P. On being a good listener: setting priorities for applied health services research. *Milbank Q*. 2003;81:363-388.
35. Thariani R, Wong W, Carlson JJ, et al. Prioritization in comparative effectiveness research: the CANCERGEN experience. *Med Care*. 2012;50(5):388-393.
36. Haas JS, Kaplan CP, Gerstenberger EP, Kerlikowske K. Changes in the use of postmenopausal hormone therapy after the publication of clinical trial results. *Ann Intern Med*. 2004 3;140(3):184-188.
37. Ischemia. Ischemia Trial website. <https://www.ischemiatrial.org/>. Accessed February 2013.
38. Heidenreich P, McClellan M. Biomedical research and then some: the causes of technological change in heart attack treatment. In: Murphy K, Topel R, eds. *Measuring the Gains from Medical Research: An Economic Approach*. Chicago, IL: University of Chicago Press; 2003:163-205.
39. Glasgow RE, Vinson C, Chambers D, Khoury MJ, Kaplan RM, Hunter C. National Institutes of Health approaches to dissemination and implementation science: current and future directions. *Am J Public Health*. 2012;102:1274-1281.
40. Hubbard T, Daimyo S, Desai K. From evidence to practice: a national strategy for CER dissemination; NEHI 2011: February.
41. Government Accounting Office (GAO). Comparative effectiveness. Agency for Healthcare Research and Quality's Process for Awarding Recovery Act Funds and Disseminating Results. GAO-12-332. February 2012.
42. Davis D, Evans M, Jadad A, et al. The case for knowledge translation: shortening the journey from evidence to effect. *BMJ*. 2003;327:33-35.
43. Jacobson N, Butterill D, Goering P. Development of a framework for knowledge translation: understanding user context. *J Health Serv Res Policy*. 2003;8(2):94-99.
44. Lang ES, Wyer PC, Haynes RB. Knowledge translation: closing the evidence-to-practice gap. *Ann Emerg Med*. 2007;49(3):355-363.
45. Timbie J, Schneider E. Dissemination and Adoption of CER Findings that Challenge Current Practices Academy Health Annual Research Meeting. June 24, 2012.
46. O'Kane M, Corrigan J, Foote S, et al. Crossroads in quality. *Health Aff (Millwood)*. 2008;27(3):749-758.
47. Garber AM. Evidence-based coverage policy. *Health Aff (Millwood)*. 2001;20:62-82.
48. Chernew ME, Fendrick AM. The business case for comparative effectiveness research: learning what works best: the nation's need for evidence on comparative effectiveness in healthcare. Institute of Medicine. March 2007. Appendix 7:1-13.
49. Weintraub WS, Spertus JA, Kolm P, et al. Effect of PCI on quality of life in patients with stable coronary disease. *N Engl J Med*. 2008;359(7):677-687.
50. Sox HC, Greenfield S. Comparative effectiveness research: a report from the Institute of Medicine. *Ann Intern Med*. 2009;151:203-205. ■

eAppendix A

	Citation
1	Allen KB, Dowling RD, Fudge TL, et al. Comparison of transmyocardial revascularization with medical therapy in patients with refractory angina. <i>N Engl J Med.</i> 1999;341:1029–36.
2	ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). <i>JAMA.</i> 2002 Dec 18;288(23):2981-97.
3	Boden WE, O'Rourke RA, Teo KK, Hartigan PM, Maron DJ, Kostuk WJ, Knudtson M, Dada M, Casperson P, Harris CL, Chaitman BR, Shaw L, Gosselin G, Nawaz S, Title LM, Gau G, Blaustein AS, Booth DC, Bates ER, Spertus JA, Berman DS, Mancini GB, Weintraub WS; COURAGE Trial Research Group. Optimal Medical Therapy With or Without PCI for Stable Coronary Disease. <i>N Engl J Med.</i> 2007 Apr 12;356(15):1503-16.
4	Bombardier C, Laine L, Reicin A, Shapiro D, Burgos-Vargas R, Davis B, Day R, Ferraz MB, Hawkey CJ, Hochberg MC, Kvien TK, Schnitzer TJ; VIGOR Study Group. Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. VIGOR Study Group. <i>N Engl J Med.</i> 2000 Nov 23;343(21):1520-8, 2 p following 1528.
5	Cannon CP, Braunwald E, McCabe CH, Rader DJ, Rouleau JL, Belder R, Joyal SV, Hill KA, Pfeffer MA, Skene AM; Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction 22 Investigators. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. <i>N Engl J Med.</i> 2004 Apr 8;350(15):1495-504.
6	Eckstein HH, Ringleb P, Allenberg JR, Berger J, Fraedrich G, Hacke W, Hennerici M, Stingele R, Fiehler J, Zeumer H, Jansen O. Results of the Stent-Protected Angioplasty versus Carotid Endarterectomy (SPACE) study to treat symptomatic stenoses at 2 years: a multinational, prospective, randomised trial. <i>Lancet Neurol.</i> 2008 Oct;7(10):893-902. Epub 2008 Sep 5.
7	Fishman A, Martinez F, Naunheim K, Piantadosi S, Wise R, Ries A, Weinmann G, Wood DE; National Emphysema Treatment Trial Research Group. A randomized trial comparing lung-volume-reduction surgery with medical therapy for severe emphysema. <i>N Engl J Med.</i> 2003 May 22;348(21):2059-73.
8	Gerson LB, Robbins AS, Garber A, Hornberger J, Triadafilopoulos G. A cost-effectiveness analysis of prescribing strategies in the management of gastroesophageal reflux disease. <i>Am J Gastroenterol.</i> 2000 Feb;95(2):395-407.
9	Ip S, Terasawa T, Balk EM, et al: Comparative Effectiveness of Radiofrequency Catheter Ablation for Atrial Fibrillation. Comparative Effectiveness Review No. 15. (Prepared by Tufts Medical Center Evidence-based Practice Center under Contract No. 290-02-0022.) Agency for Healthcare Research and Quality, 2009.
10	Kastelein JJ, Akdim F, Stroes ES, Zwinderman AH, Bots ML, Stalenhoef AF, Visseren FL, Sijbrands EJ, Trip MD, Stein EA, Gaudet D, Duivenvoorden R, Veltri EP, Marais AD, de Groot E; ENHANCE Investigators. Simvastatin with or without ezetimibe in familial

	hypercholesterolemia. <i>N Engl J Med.</i> 2008 Apr 3;358(14):1431-43. Epub 2008 Mar 30.
11	Lieberman JA, Stroup TS, McEvoy JP, Swartz MS, Rosenheck RA, Perkins DO, Keefe RS, Davis SM, Davis CE, Lebowitz BD, Severe J, Hsiao JK; Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Investigators. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. <i>N Engl J Med.</i> 2005 Sep 22;353(12):1209-23.
12	MacLean C, Newberry S, Maglione M, McMahon M, Ranganath V, Suttorp M, Mojica W, Timmer M, Alexander A, McNamara M, Desai SB, Zhou A, Chen S, Carter J, Tringale C, Valentine D, Johnsen B, Grossman J. Systematic review: comparative effectiveness of treatments to prevent fractures in men and women with low bone density or osteoporosis. <i>Ann Intern Med.</i> 2008 Feb 5;148(3):197-213. Epub 2007 Dec 17.
13	Nissen SE, Wolski K. Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes. <i>N Engl J Med.</i> 2007 Jun 14;356(24):2457-71.
14	Peterson ED, Kaul P, Kaczmarek RG, Hammill BG, Armstrong PW, Bridges CR, Ferguson TB Jr; Society of Thoracic Surgeons. From controlled trials to clinical practice: monitoring transmyocardial revascularization use and outcomes. <i>J Am Coll Cardiol.</i> 2003 Nov 5;42(9):1611-6.
15	Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML, Jackson RD, Beresford SA, Howard BV, Johnson KC, Kotchen JM, Ockene J; Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. <i>JAMA.</i> 2002 Jul 17;288(3):321-33.
16	Rush AJ, Trivedi MH, Wisniewski SR, Nierenberg AA, Stewart JW, Warden D, Niederehe G, Thase ME, Lavori PW, Lebowitz BD, McGrath PJ, Rosenbaum JF, Sackeim HA, Kupfer DJ, Luther J, Fava M. Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR*D report. <i>Am J Psychiatry.</i> 2006 Nov;163(11):1905-17.
17	Shuldiner AR, O'Connell JR, Bliden KP, Gandhi A, Ryan K, Horenstein RB, Damcott CM, Pakyz R, Tantry US, Gibson Q, Pollin TI, Post W, Parsa A, Mitchell BD, Faraday N, Herzog W, Gurbel PA. Association of cytochrome P450 2C19 genotype with the antiplatelet effect and clinical efficacy of clopidogrel therapy. <i>JAMA.</i> 2009 Aug 26;302(8):849-57.
18	Seidenfeld J, Piper M, Bohlius J, et al: Comparative Effectiveness of Epoetin and Darbepoetin for Managing Anemia in Patients Undergoing Cancer Treatment. Comparative Effectiveness Review No. 3. (Prepared by Blue Cross and Blue Shield Association Technology Evaluation Center Evidence-based Practice Center under Contract No. 290-02-0026.) Agency for Healthcare Research and Quality, 2006.
19	Tan H, Sarawate C, Singer J, Elward K, Cohen RI, Smart BA, Busk MF, Lustig J, O'Brien JD, Schatz M. Impact of asthma controller medications on clinical, economic, and patient-reported outcomes. <i>Mayo Clin Proc.</i> 2009 Aug;84(8):675-84.
20	Taylor AJ, Kent SM, Flaherty PJ, Coyle LC, Markwood TT, Vernalis MN. ARBITER: Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol: a randomized trial comparing the effects of atorvastatin and pravastatin on carotid intima medial thickness. <i>Circulation.</i> 2002 Oct 15;106(16):2055-60.
21	Thompson IM Jr, Tangen CM, Paradelo J, Lucia MS, Miller G, Troyer D, Messing E, Forman J, Chin J, Swanson G, Canby-Hagino E, Crawford ED. Adjuvant radiotherapy for pathologically advanced prostate cancer: a randomized clinical trial. <i>JAMA.</i> 2006 Nov

	15;296(19):2329-35.
22	Warner E, Plewes DB, Hill KA, Causer PA, Zubovits JT, Jong RA, Cutrara MR, DeBoer G, Yaffe MJ, Messner SJ, Meschino WS, Piron CA, Narod SA. Surveillance of BRCA1 and BRCA2 mutation carriers with magnetic resonance imaging, ultrasound, mammography, and clinical breast examination. <i>JAMA</i> . 2004 Sep 15;292(11):1317-25.
23	Weinstein JN, Tosteson TD, Lurie JD, Tosteson AN, Hanscom B, Skinner JS, Abdu WA, Hilibrand AS, Boden SD, Deyo RA. Surgical vs nonoperative treatment for lumbar disk herniation: the Spine Patient Outcomes Research Trial (SPORT): a randomized trial. <i>JAMA</i> . 2006 Nov 22;296(20):2441-50.

eAppendix B

PRAVASTATIN OR ATORVASTATIN EVALUATION AND INFECTION THERAPY (PROVE-IT) (2004)

	Release Date	Citation
1	2004 (first publication of guideline after study)	Grundy SM, Cleeman JI, Merz CNB, et al. Implications of Recent Clinical Trials for the National Cholesterol Education Program Adult Treatment Panel III Guidelines. <i>J Am Coll Cardiol.</i> 2004 August 4;44(3):720-32.
2	2006	Smith, S. C., Feldman, T. E., Hirshfeld, J. W., Jacobs, A. K., Kern, M. J., King, S. B., ... & Riegel, B. (2006). ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update the 2001 Guidelines for Percutaneous Coronary Intervention). <i>J Am Coll Cardiol.</i> 2006;47(1):e1-e121.
3	2007	Anderson, J. L., Adams, C. D., Antman, E. M., Bridges, C. R., Califf, R. M., Casey, D. E., ... & Riegel, B. (2007). ACC/AHA 2007 Guidelines for the Management of Patients With Unstable Angina/Non–ST-Elevation Myocardial Infarction: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non–ST-Elevation Myocardial Infarction) Developed in Collaboration with the American College of Emergency Physicians, the Society for Cardiovascular Angiography and Interventions, and <i>J Am Coll Cardiol.</i> 2007;50(7):e1-e157.
4	2007	Califf, R. M., Chavey II, W. E., Fesmire, F. M., & Lincoff, A. M. (2007). ACC/AHA 2007 Guidelines for the Management of Patients With Unstable Angina/Non–ST-Elevation Myocardial Infarction. <i>J Am Coll Cardiol.</i> 2007;50(7):e1-e157.
5	2008 Jan, addendum; 2004 Jul, revised (original 1996 Nov 1)	(1) ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to revise the 1999 guidelines for the Management of Acute Myocardial Infarction). (2) 2007 focused update of the ACC/AHA 2004 guidelines for the management of patients with ST-elevation myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 1996 Nov 1 (revised 2004 Jul; addendum released 2008 Jan). [NGC Update Pending] NGC:006289. American College of Cardiology Foundation - Medical Specialty Society; American Heart Association - Professional Association.

6	2008 May, addendum released (original 2006 Feb)	(1) Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack. (2) Update to the AHA/ASA recommendations for the prevention of stroke in patients with stroke and transient ischemic attack. 2006 Feb (addendum released 2008 May). NGC:006659. American Heart Association - Professional Association; American Stroke Association - Disease Specific Society.
7	2008 Jul-Aug	American Association of Clinical Endocrinologists, The Obesity Society, and American Society for Metabolic & Bariatric Surgery medical guidelines for clinical practice for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient. 2008 Jul-Aug. NGC:006716. American Association of Clinical Endocrinologists - Medical Specialty Society; American Society for Metabolic and Bariatric Surgery - Professional Association; The Obesity Society - Disease Specific Society.
8	2008 Oct, revised (original 2003 Sep)	Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Sections 6-37: chemotherapy. 2003 Sep (revised 2008 Oct). NGC:007569. Children's Oncology Group - Medical Specialty Society.
9	2008	Rosenzweig, J. L., Ferrannini, E., Grundy, S. M., Haffner, S. M., Heine, R. J., Horton, E. S., & Kawamori, R. (2008). Primary prevention of cardiovascular disease and type 2 diabetes in patients at metabolic risk: an endocrine society clinical practice guideline. <i>J Clin Endocrinol Metab.</i> 2008;93(10):3671-3689.
10	2008	Sharma, K., & Eisenberg, M. J. (2008). Putting the benefits of percutaneous coronary revascularization into perspective: From trials to guidelines. <i>Curr Cardiol Rep.</i> 2008;10(5):393-401.
11	2008	Guide to the care of the hospitalized patient with ischemic stroke. 2nd edition. 2008. NGC:006947. American Association of Neuroscience Nurses - Professional Association.
12	2009 Feb, revised (original 2000 May)	Screening and management of lipids. 2000 May (revised 2009 Feb). NGC:007216. University of Michigan Health System - Academic Institution.
13	2009 Mar	Secondary prevention of coronary artery disease. 2009 Mar. NGC:007856. University of Michigan Health System - Academic Institution.
14	2009 Apr 14, revised (original 1995 Nov 1)	2009 focused update incorporated into the ACC/AHA 2005 guidelines for the diagnosis and management of heart failure in adults. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 1995 Nov 1 (revised 2009 Apr 14). NGC:008024. American College of Cardiology Foundation - Medical Specialty Society; American Heart Association - Professional Association; International Society for Heart and Lung Transplantation - Professional Association.

15	2009 Dec, revised (original 2004)	Adapting your practice: treatment and recommendations for homeless patients with hypertension, hyperlipidemia & heart failure. 2004 (revised 2009 Dec). NGC:007679. Health Care for the Homeless (HCH) Clinician's Network - Medical Specialty Society; National Health Care for the Homeless Council, Inc. - Nonprofit Organization.
16	2010 May	VA/DoD clinical practice guideline for management of bipolar disorder in adults. 2010 May. NGC:007865. Department of Defense - Federal Government Agency [U.S.]; Department of Veterans Affairs - Federal Government Agency [U.S.]; Veterans Health Administration - Federal Government Agency [U.S.].
17	2010 Jun, revised (original 1999)	Evaluation and therapy for heart failure in the setting of ischemic heart disease: HFSA 2010 comprehensive heart failure practice guideline. 1999 (revised 2010 Jun). NGC:007992. Heart Failure Society of America, Inc - Disease Specific Society.
18	2010 Jun, revised (original 2006 Jun)	Testosterone therapy in adult men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. 2006 Jun (revised 2010 Jun). NGC:007877. The Endocrine Society - Professional Association.
19	2010 Oct, revised (original 2009 Sep)	Perioperative protocol. Health care protocol. 2009 Sep (revised 2010 Oct). [NGC Update Pending] NGC:008119. Institute for Clinical Systems Improvement - Nonprofit Organization.
20	2010 Nov, revised (original 1995 Jun)	Hypertension diagnosis and treatment. 1995 Jun (revised 2010 Nov). [NGC Update Pending] NGC:008194. Institute for Clinical Systems Improvement - Nonprofit Organization.
21	2010 Dec	HIV/AIDS evidence-based nutrition practice guideline. 2010 Dec. NGC:008212. Academy of Nutrition and Dietetics - Professional Association.
22	2010, revised (original 1996)	Heart failure in the long-term care setting. 1996 (revised 2010). NGC:008399. American Medical Directors Association - Professional Association.
23	N/A	Diagnosis and Evaluation of Chronic Heart Failure (CHF) Compare Selected
24	N/A	The American Heart Association's "Get With The Guidelines" Program: Key Findings and Lessons Learned

MAMMOGRAPHY WITH MAGNETIC RESONANCE IMAGING (MRI) (2004)

	Release Date	Citation
1	2005	Smith, R. A., Cokkinides, V., & Eyre, H. J. (2005). American Cancer Society guidelines for the early detection of cancer, 2005 . <i>CA: a cancer journal for clinicians</i> , 55(1), 31-44.
2	2007 (first publication of guideline after study)	Saslow, D., Boetes, C., Burke, W., Harms, S., Leach, M. O., Lehman, C. D., ... & Russell, C. A. (2007). American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography . <i>CA Cancer J Clin.</i> 2007;57(2):75-89.
3	2007	Warner, E., Messersmith, H., Causer, P., Eisen, A., Shumak, R., & Plewes, D. (2007). Magnetic resonance imaging screening of women at high risk for breast cancer: a clinical practice guideline . <i>Review date: 2007-Apr.</i>
4	2008	Kaiser Permanente. (2008). Breast Cancer Screening Guideline .
5	2009 Nov, revised; Dec 2009, addendum released (original 1996)	1) Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. 2) December 2009 addendum . 1996 (revised 2009 Nov; addendum released 2009 Dec). NGC:007533. U.S. Preventive Services Task Force - Independent Expert Panel
6	2010 Aug	Breast cancer screening clinical practice guideline . 2010 Aug. NGC:008538. Kaiser Permanente Care Management Institute - Managed Care Organization
7	2010, revised (original 1995)	ACR Appropriateness Criteria® screening for pulmonary metastases . 1995 (revised 2010). [NGC Update Pending] NGC:008475. American College of Radiology - Medical Specialty Society
8	2010, revised (original 1995)	ACR Appropriateness Criteria® dyspnea — suspected cardiac origin . 1995 (revised 2010). NGC:007919. American College of Radiology - Medical Specialty Society
9	2010, revised (original 1996)	ACR–SPR practice guideline for the performance of tumor scintigraphy (with gamma cameras) . 1996 (revised 2010). NGC:008421. American College of Radiology - Medical Specialty Society; Society for Pediatric Radiology - Medical Specialty Society
10	2010, revised (original 1996)	ACR Appropriateness Criteria® local-regional recurrence (LR) and salvage surgery—breast cancer . 1996 (revised 2010). [NGC Update Pending] NGC:008446. American College of Radiology - Medical Specialty Society
11	2010, revised (original 1996)	ACR–ASTRO practice guideline for the performance of high-dose-rate brachytherapy . 1996 (revised 2010). NGC:008423. American College of Radiology - Medical Specialty Society; American Society for Radiation Oncology - Professional Association

12	2010, revised (original 1996)	ACR–ASTRO practice guideline for the performance of low-dose-rate brachytherapy. 1996 (revised 2010). NGC:008424. American College of Radiology - Medical Specialty Society; American Society for Radiation Oncology - Professional Association
13	2010, revised (original 1996)	ACR–ASTRO practice guideline for the performance of therapy with unsealed radiopharmaceutical sources. 1996 (revised 2010). NGC:008422. American College of Radiology - Medical Specialty Society; American Society for Radiation Oncology - Professional Association
14	2010, revised (original 1998)	ACR Appropriateness Criteria® liver lesion — initial characterization. 1998 (revised 2010). NGC:008445. American College of Radiology - Medical Specialty Society
15	2010, revised (original 1999)	ACR Appropriateness Criteria® follow-up of Hodgkin's lymphoma. 1999 (revised 2010). NGC:007943. American College of Radiology - Medical Specialty Society

SPINE PATIENT OUTCOMES RESEARCH TRIAL (SPORT) (2006)

	Release Date	Guideline
1	2007 (first publication of guideline after study)	Chou R, Qaseem A, Snow V, et al. Clinical Efficacy Assessment Subcommittee of the American College of Physicians; American College of Physicians; American Pain Society Low Back Pain Guidelines Panel. Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society. <i>Ann Intern Med.</i> 2007 Oct 2;147(7):478-91.
2	2010 Jan, revised (original 1997)	Acute low back pain. 1997 (revised 2010 Jan). NGC:008009. University of Michigan Health System - Academic Institution.
3	2010 Jan	Assessment: efficacy of transcutaneous electric nerve stimulation in the treatment of pain in neurologic disorders (an evidence-based review). Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. 2010 Jan. NGC:007678. American Academy of Neurology - Medical Specialty Society.
4	2010 Apr, revised (original 1997 Apr)	Practice guidelines for chronic pain management. An updated report by the American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine. 1997 Apr (revised 2010 Apr). NGC:007951. American Society of Anesthesiologists - Medical Specialty Society.

CLINICAL OUTCOMES UTILIZING REVASCULARIZATION AND AGGRESSIVE DRUG EVALUATION (COURAGE) (2007)

	Release Date	Citation
1	2007 (first publication of guideline after study)	Page, B. R., Tarkington, L. G., Yancy, C. W., Hunt, H. M. K., Kushner, F. G., Lytle, B. W., ... & King, S. B. (2007). 2007 Focused Update of the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. <i>Circulation.</i> 2008;117(2): 261-295.
2	2007	Anderson, J. L., Adams, C. D., Antman, E. M., Bridges, C. R., Califf, R. M., Casey, D. E., ... & Riegel, B. (2007). ACC/AHA 2007 Guidelines for the Management of Patients With Unstable Angina/Non–ST-Elevation Myocardial Infarction. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non–ST-Elevation Myocardial Infarction) Developed in Collaboration with the American College of Emergency Physicians, the Society for Cardiovascular Angiography and Interventions, and <i>J Am Coll Cardiol.</i> 2007;50(7):e1-e157.
3	2007	Califf, R. M., Chavey II, W. E., Fesmire, F. M., & Lincoff, A. M. (2007). ACC/AHA 2007 Guidelines for the Management of Patients With Unstable Angina/Non–ST-Elevation Myocardial Infarction. <i>J Am Coll Cardiol.</i> 2007;50(7):e1-e157.
4	2007	Cannon, C. P. (2007). ACS and Antiplatelet Management: Updated Guidelines and Current Trials. <i>J Am Coll Cardiol.</i> 2007;50(7):e1-e157.
5	2007	King III, S. B., Jacobs, A. K., Morrison, D. A., Williams, F. D. O., Kern, M. J., Buller, C. E., ... & Yancy, C. W. (2007). 2007 Focused update of the ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention. <i>Catheter Cardiovasc Interv.</i> 2008;71(1):E1-E40.
6	2008 Jan addendum released, 2004 Jul revised (original 1996 Nov 1)	(1) ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to revise the 1999 guidelines for the Management of Acute Myocardial Infarction). (2) 2007 focused update of the ACC/AHA 2004 guidelines for the management of patients with ST-elevation myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 1996 Nov 1 (revised 2004 Jul; addendum released 2008 Jan). [NGC Update Pending] NGC:006289. American College of Cardiology Foundation - Medical Specialty Society; American Heart Association - Professional Association.

7	2008	King, S. B., Smith, S. C., Hirshfeld, J. W., Jacobs, A. K., Morrison, D. A., & Williams, D. O. (2008). 2007 focused update of the ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention. <i>J Am Coll Cardiol.</i> 2008;51(2):172-209.
8	2008	King, S. B., Smith, S. C., Hirshfeld, J. W., Jacobs, A. K., Morrison, D. A., Williams, D. O., ... & Yancy, C. W. (2008). 2007 Focused Update of the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines: 2007 Writing Group to Review New Evidence and Update the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention, Writing on Behalf of the 2005 Writing Committee. <i>Circulation.</i> 2008;117(2):261-295.
9	2009 Nov 24, revised (original 1996)	2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 1996 Mar 15 (revised 2009 Nov 24). NGC:008025. American College of Cardiology Foundation - Medical Specialty Society; American Heart Association - Professional Association.
10	2010 Jun revised (original 1999)	Evaluation and therapy for heart failure in the setting of ischemic heart disease: HFSA 2010 comprehensive heart failure practice guideline. 1999 (revised 2010 Jun). NGC:007992. Heart Failure Society of America, Inc - Disease Specific Society.
11	2010	Hiratzka, L. F., Bakris, G. L., Beckman, J. A., Bersin, R. M., Carr, V. F., Casey, D. E., ... & Williams, D. M. (2010). 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the Diagnosis and Management of Patients With Thoracic Aortic Disease: Executive Summary A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional ... <i>Circulation.</i> 2010;121(13):1544-1579.
12	2010	Hiratzka, L. F., Bakris, G. L., Beckman, J. A., Bersin, R. M., Carr, V. F., Casey, D. E., ... & Williams, D. M. (2010). 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease. <i>J Am Coll Cardiol.</i> 2010;55(14):e27-e129.
13	2010 revised (original 1995)	ACR Appropriateness Criteria® chest pain, suggestive of acute coronary syndrome. 1995 (revised 2010). NGC:007917. American College of Radiology - Medical Specialty Society.

eAppendix C. Characteristics of All Enrollees, 2003-2010

Age Group	% of Total
0-17 years	13.7%
18-34 years	22.7%
35-44 years	17.7%
45-54 years	20.2%
55-64 years	17.9%
65 years and older	7.8%

Census Region	% of Total
Northeast	15.6%
North Central	23.3%
South	21.2%
West	39.3%
Unknown	0.6%

Characteristics of Enrollees Meeting the Inclusion Criteria for Each Case Study

	Study							
	PROVE-IT		Mammography with MRI		SPORT		COURAGE	
	N = 86,088		N = 5,159,253		N = 298,780		N = 50,960	
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD
Age (mean/SD), years	66	13.9	44	11.4	51	13.8	65	12.8
Age group (N, %)								
18-34 years	529	0.6%	1,263,457	24.5%	31,023	10.7%	429	0.8%
35-44 years	3726	4.3%	1,288,297	25.0%	63,294	21.8%	2199	4.3%
45-54 years	14,779	17.2%	1,408,359	27.3%	91,347	31.5%	8346	16.4%
55-64 years	28,118	32.7%	1,138,473	22.1%	63,196	21.8%	17,414	34.2%
65+ years	38,936	45.2%	60,667	1.2%	40,920	14.1%	22,572	44.3%
Sex (N, %)								
Male	56,905	66.1%	0	0.0%	134,993	46.6%	27,959	54.9%
Female	29,183	33.9%	5,159,253	100.0%	154,787	53.4%	23,001	45.1%
Employee class (N, %)								
Salaried	18,594	21.6%	1,021,864	19.8%	71,477	24.7%	12,326	24.2%
Hourly	26,229	30.5%	866,956	16.8%	59,681	20.6%	15,365	30.2%
Other/Unknown	41,265	47.9%	3,270,433	63.4%	158,622	54.7%	23,269	45.7%
Employee status (N, %)								
	24,667	28.7%	2,987,077	57.9%	163,061	56.3%	15,290	30.0%

Full-time								
Part-time	312	0.4%	53,463	1.0%	2383	0.8%	182	0.4%
Other/Unknown	61,109	71.0%	2,118,713	41.1%	124,336	42.9%	35,488	69.6%
Employee relationship (N, %)								
Employee	64,779	75.3%	2,968,957	57.6%	191,604	66.1%	36,040	70.7%
Spouse	21,144	24.6%	2,122,744	41.1%	93,557	32.3%	14,810	29.1%
Child/Other	165	0.2%	67,552	1.3%	4,619	1.6%	110	0.2%
Population density (N, %)								
Urban	66,723	77.5%	4,114,723	79.8%	229,247	79.1%	39,329	77.2%
Rural	19,268	22.4%	1,034,146	20.0%	59,911	20.7%	11,467	22.5%
Other/unknown	97	0.1%	10,384	0.2%	622	0.2%	164	0.3%
Geographic region (N, %)								
Northeast	8117	9.4%	420,524	8.2%	25,783	8.9%	4382	8.6%
North Central	33,176	38.5%	1,507,483	29.2%	82,029	28.3%	18,212	35.7%
South	30,826	35.8%	2,143,305	41.5%	130,898	45.2%	20,101	39.4%
West	13,804	16.0%	1,071,800	20.8%	50,076	17.3%	7935	15.6%
Other/Unknown	165	0.2%	16,141	0.3%	994	0.3%	330	0.7%

Note: Patient characteristics were measured the first time each patient met the inclusion criteria for a study

eAppendix D. Inclusion and Exclusion Criteria by Study

Inclusion Criteria – Original Study – PROVE-IT	Inclusion Criteria Requirements – Relaxed Study for Analysis ^{a,b}	Description
1. At least 18 years of age	Yes	Age on enrollment file
2. Hospitalized for an acute coronary syndrome—either acute myocardial infarction (with or without electrocardiographic evidence of ST-segment elevation) or high-risk unstable angina—in the preceding 10 days	Yes	<p>Hospitalization via inpatient admission; use discharge date (assumed to be stable and to have undergone percutaneous revascularization if necessary).</p> <p>Claims data available. (See below – PROVE-IT Inclusion Criteria).</p> <p>No way to show “with or without electrocardiographic evidence of ST-segment elevation or high-risk unstable angina in the preceding 10 days.”</p>
3. Stable condition	N/A	Not available on claims.
4. Enrolled after a percutaneous revascularization procedure if one was planned	N/A	Cannot determine if procedure was planned.
5. Total cholesterol level \leq 240 mg/dL, measured at the local hospital within the first 24 hours after the onset of the acute coronary syndrome or up to 6 months earlier if no sample had been obtained during the first 24 hours	N/A	Not available on claims.
6. For patients receiving long-term lipid-lowering therapy at the time of their index coronary syndrome had to have a total cholesterol level \leq 200 mg/dL at the time of screening in the	N/A	Not available on claims

local hospital		
----------------	--	--

^aYes indicates that the same criteria, as defined for original trial, are indicated for the relaxed analysis.

^bN/A indicates that the same criteria, as defined for original trial, are not applicable for the relaxed analysis.

Exclusion Criteria – Original Study – PROVE-IT	Exclusion Criteria Requirements – Relaxed Study for Analysis^{a,b,c} Analysis^{1,2,3}	Description
1. Coexisting condition that shortened expected survival to <2 years	N/A	No way to show (need to identify conditions of interest).
2. Were receiving therapy with an statin at a dose of 80 mg per day at the time of their index event or lipid-lowering therapy with fibric acid derivatives or niacin that could not be discontinued before randomization	No	Drug lists available from author.
3. Had received drugs that are strong inhibitors of cytochrome P450 3A4 within the month before randomization or were likely to require such treatment during the study period	Yes	Drug lists available from author.
4. Had undergone percutaneous coronary intervention within the previous 6 months (other than for the qualifying event) or coronary-artery bypass surgery within the previous 2 months or were scheduled to undergo bypass surgery in response to the index event.	N/A	No way to show “were scheduled to undergo bypass surgery in response to the index event.”
5. Had factors that might prolong the QT interval in 1 year prior to ACS hospitalization	Yes	Claims data available. (See below – PROVE-IT Exclusion Criteria). (Code for prolonged QT syndrome and drugs to treat long QT interval).

¹ Yes – indicates that the same criteria, as defined for original trial, are indicated for the relaxed analysis.

² No – indicates that the same criteria, as defined for original trial, are not indicated for the relaxed analysis.

³ N/A – indicates that the same criteria, as defined for original trial, are not applicable for the relaxed analysis.

6. Had obstructive hepatobiliary disease or other serious hepatic disease in 1 year prior to ACS hospitalization	Yes	Claims data available. (See below – PROVE-IT Exclusion Criteria).
7. Had an unexplained elevation in the creatine kinase level that was more than 3 times the upper limit of normal and that was not related to myocardial infarction	N/A	Not available on claims.
8. Had a creatinine level > 2.0 mg/dL in 1 year prior to ACS hospitalization	Yes	Not available on claims but use code list for renal disease as a proxy measure. (See below – PROVE-IT Exclusion Criteria).

PROVE-IT Inclusion Criteria – Clinical Codes, Relaxed Study Analysis		
Criteria Number		
2	Acute myocardial infarction or high-risk unstable angina:	
	ICD	Description
	410.xx	Acute myocardial infarction
	4111	Intermediate coronary syndrome
	41181	Acute coronary occlusion without myocardial infarction
4	Previous PTCA: (previous percutaneous revascularization procedure)	
	ICD	Description
	0066	Percutaneous transluminal coronary angioplasty [PTCA] or coronary atherectomy
	3601	Single vessel percutaneous transluminal coronary angioplasty [ptca] or coronary atherectomy without mention of thrombolytic agent
	3602	Single vessel percutaneous transluminal coronary angioplasty [ptca] or coronary atherectomy with mention of thrombolytic agent
	3603	Open chest coronary artery angioplasty

	3604	Intracoronary artery thrombolytic infusion
	3605	Multiple vessel percutaneous transluminal coronary angioplasty [ptca] or coronary atherectomy performed during the same operation, with or without mention of thrombolytic agent
	3606	Insertion of non-drug-eluting coronary artery stent(s)
	3607	Insertion of drug-eluting coronary artery stent(s)
	CPT/HCPCS	Description
	92973	Percutaneous transluminal coronary thrombectomy (List separately in addition to code for primary procedure)
	G0290	Transcatheter placement of a drug eluting intracoronary stent(s), percutaneous, with or without other therapeutic intervention, any method; single vessel
	G0291	Transcatheter placement of a drug eluting intracoronary stent(s), percutaneous, with or without other therapeutic intervention, any method; each additional vessel
	92980	Transcatheter placement of an intracoronary stent(s), percutaneous, with or without other therapeutic intervention, any method; single vessel
	92981	Transcatheter placement of an intracoronary stent(s), percutaneous, with or without other therapeutic intervention, any method; single vessel
	92982	Percutaneous transluminal coronary balloon angioplasty; single vessel
	92984	Percutaneous transluminal coronary balloon angioplasty; each additional vessel (List separately in addition to code for primary procedure)
	92995	Percutaneous transluminal coronary atherectomy, by mechanical or other method, with or without balloon angioplasty; single vessel
	92996	Percutaneous transluminal coronary atherectomy, by mechanical or other method, with or without balloon angioplasty; each additional vessel (List separately in addition to code for primary procedure)

PROVE-IT Exclusion Criteria – Clinical Codes, Relaxed Study Analysis		
Criteria Number		
4	Previous PTCA:	
	ICD	Description
	0066	Percutaneous transluminal coronary angioplasty [PTCA] or coronary atherectomy
	3601	Single vessel percutaneous transluminal coronary angioplasty [ptca] or coronary

		atherectomy without mention of thrombolytic agent
	3602	Single vessel percutaneous transluminal coronary angioplasty [ptca] or coronary atherectomy with mention of thrombolytic agent
	3603	Open chest coronary artery angioplasty
	3604	Intracoronary artery thrombolytic infusion
	3605	Multiple vessel percutaneous transluminal coronary angioplasty [ptca] or coronary atherectomy performed during the same operation, with or without mention of thrombolytic agent
	3606	Insertion of non-drug-eluting coronary artery stent(s)
	3607	Insertion of drug-eluting coronary artery stent(s)
	CPT/HCPCS	Description
	92973	Percutaneous transluminal coronary thrombectomy (List separately in addition to code for primary procedure)
	G0290	Transcatheter placement of a drug eluting intracoronary stent(s), percutaneous, with or without other therapeutic intervention, any method; single vessel
	G0291	Transcatheter placement of a drug eluting intracoronary stent(s), percutaneous, with or without other therapeutic intervention, any method; each additional vessel
	92980	Transcatheter placement of an intracoronary stent(s), percutaneous, with or without other therapeutic intervention, any method; single vessel
	92981	Transcatheter placement of an intracoronary stent(s), percutaneous, with or without other therapeutic intervention, any method; single vessel
	92982	Percutaneous transluminal coronary balloon angioplasty; single vessel
	92984	Percutaneous transluminal coronary balloon angioplasty; each additional vessel (List separately in addition to code for primary procedure)
	92995	Percutaneous transluminal coronary atherectomy, by mechanical or other method, with or without balloon angioplasty; single vessel
	92996	Percutaneous transluminal coronary atherectomy, by mechanical or other method, with or without balloon angioplasty; each additional vessel (List separately in addition to code for primary procedure)
4	Cardiac bypass:	
	Code	Description
	3611	(Aorto)coronary bypass of one coronary artery

	3612	(Aorto)coronary bypass of two coronary arteries
	3613	(Aorto)coronary bypass of three coronary arteries
	3614	(Aorto)coronary bypass of four or more coronary arteries
	3615	Single internal mammary-coronary artery bypass
	3616	Double internal mammary-coronary artery bypass
	3617	Abdominal-coronary artery bypass
	3619	Other bypass anastomosis for heart revascularization
	CPT/HCPCS	Description
	33510	Coronary artery bypass, vein only; single coronary venous graft
	33511	Coronary artery bypass, vein only; 2 coronary venous grafts
	33512	Coronary artery bypass, vein only; 3 coronary venous grafts
	33513	Coronary artery bypass, vein only; 4 coronary venous grafts
	33514	Coronary artery bypass, vein only; 5 coronary venous grafts
	33516	Coronary artery bypass, vein only; 6 or more coronary venous grafts
	33517	Coronary artery bypass, using venous graft(s) and arterial graft(s); single vein graft
	33518	Coronary artery bypass, using venous graft(s) and arterial graft(s); 2 venous grafts
	33519	Coronary artery bypass, using venous graft(s) and arterial graft(s); 3 venous grafts (
	33521	Coronary artery bypass, using venous graft(s) and arterial graft(s); 4 venous grafts
	33522	Coronary artery bypass, using venous graft(s) and arterial graft(s); 5 venous grafts
	33523	Coronary artery bypass, using venous graft(s) and arterial graft(s); 6 or more venous grafts (
	33533	Coronary artery bypass, using arterial graft(s); single arterial graft
	33534	Coronary artery bypass, using arterial graft(s); 2 coronary arterial grafts
	33535	Coronary artery bypass, using arterial graft(s); 3 coronary arterial grafts
	33536	Coronary artery bypass, using arterial graft(s); 4 or more coronary arterial grafts
	33572	Coronary endarterectomy, open, any method, of left anterior descending, circumflex, or right coronary artery performed in conjunction with coronary artery bypass graft procedure, each vessel (List separately in addition to primary procedure)
	S2205	Minimally invasive direct coronary artery bypass surgery involving mini-thoracotomy or mini-sternotomy surgery, performed under direct vision; using arterial graft(s), single coronary arterial graft

	S2206	Minimally invasive direct coronary artery bypass surgery involving mini-thoracotomy or mini-sternotomy surgery, performed under direct vision; using arterial graft(s), two coronary arterial grafts
	S2207	Minimally invasive direct coronary artery bypass surgery involving mini-thoracotomy or mini-sternotomy surgery, performed under direct vision; using venous graft only, single coronary venous graft
	S2208	Minimally invasive direct coronary artery bypass surgery involving mini-thoracotomy or mini-sternotomy surgery, performed under direct vision; using single arterial and venous graft(s), single venous graft
	S2209	Minimally invasive direct coronary artery bypass surgery involving mini-thoracotomy or mini-sternotomy surgery, performed under direct vision; using two arterial grafts and single venous graft
5	Factors that might prolong the QT interval :	
	ICD	Description
	42682	Long QT syndrome
6	Hepatobiliary disease or other serious hepatic disease:	
	ICD	Description
	1550	Malignant neoplasm of liver, primary
	1551	Malignant neoplasm of intrahepatic bile ducts
	1552	Malignant neoplasm of liver, not specified as primary or secondary
	1560	Malignant neoplasm of gallbladder
	1561	Malignant neoplasm of extrahepatic bile ducts
	1562	Malignant neoplasm of Ampulla of Vater
	1568	Malignant neoplasm of other specified sites of gallbladder and extrahepatic bile ducts
	1569	Malignant neoplasm of biliary tract, part unspecified
	570	Acute and subacute necrosis of liver
	5710	Alcoholic fatty liver
	5711	Acute alcoholic hepatitis
	5712	Alcoholic cirrhosis of liver

	5713	Alcoholic liver damage, unspecified
	57140	Chronic hepatitis, unspecified
	57141	Chronic persistent hepatitis
	57142	Autoimmune hepatitis
	57149	Other chronic hepatitis
	5715	Cirrhosis of liver without mention of alcohol
	5716	Biliary cirrhosis
	5718	Other chronic nonalcoholic liver disease
	5719	Unspecified chronic liver disease without mention of alcohol
	5720	Abscess of liver
	5721	Portal pyemia
	5722	Hepatic encephalopathy
	5723	Portal hypertension
	5724	Hepatorenal syndrome
	5728	Other sequelae of chronic liver disease
	5731	Hepatitis in viral diseases classified elsewhere
	5732	Hepatitis in other infectious diseases classified elsewhere
	5733	Hepatitis, unspecified
	5734	Hepatic infarction
	57401	Calculus of gallbladder with acute cholecystitis, with obstruction
	57411	Calculus of gallbladder with other cholecystitis, with obstruction
	57421	Calculus of gallbladder without mention of cholecystitis, with obstruction
	57431	Calculus of bile duct with acute cholecystitis, with obstruction
	57441	Calculus of bile duct with other cholecystitis, with obstruction
	57451	Calculus of bile duct without mention of cholecystitis, with obstruction
	57461	Calculus of gallbladder and bile duct, with acute cholecystitis with obstruction
	57471	Calculus of gallbladder and bile duct, with other cholecystitis with obstruction
	57481	Calculus of gallbladder and bile duct, with acute and chronic cholecystitis with obstruction

	57491	Calculus of gallbladder and bile duct, without cholecystitis with obstruction
	5761	Cholangitis
	5762	Obstruction of bile duct
	5763	Perforation of bile duct
	5764	Fistula of bile duct
	5765	Spasm of sphincter of Oddi
8	Serum creatinine equal to or greater than 2 mg/dL.	
	<i>ICD diagnosis codes 458.21, 585.3, 585.4, 585.5, 585.6, 792.5, 996.56, 996.68, 996.73, V45.1x, V56.0, V56.8; ICD procedure codes 39.95 and 54.98; CPT/HCPCS codes 90918-90925, 90935, 90937, 90940, 90945, 90947, 90951-90970, 90989, 90993, 90999, 99512, 4052F, 4053F, 4054F, 4055F, G0257, G0308-G0327, G8075-G8082, G8085, G8387, G8388, S9335, S9339 .</i>	
	ICD	Description
	458.21	Hypotension of hemodialysis
	585.3	Chronic kidney disease, Stage III (moderate)
	585.4	Chronic kidney disease, Stage IV (severe)
	585.5	Chronic kidney disease, Stage V
	585.6	End stage renal disease
	792.5	Cloudy (hemodialysis) (peritoneal) dialysis effluent
	996.56	Mechanical complications due to peritoneal dialysis catheter
	996.68	Infection and inflammatory reaction due to peritoneal dialysis catheter
	996.73	Other complications due to renal dialysis device, implant, and graft
	V4511	Renal dialysis status
	V4512	Noncompliance with renal dialysis
	V56.0	Extracorporeal dialysis encounter
	V56.8	Other dialysis encounter
	ICD Procedure	Description
	39.95	Hemodialysis

	54.98	Peritoneal dialysis
	CPT/HCPCS	Description
	90918	End stage renal disease (ESRD) related services per full month; for patients under two years of age to include monitoring for the adequacy of nutrition, assessment of growth and development, and counseling of parents
	90919	End-stage renal disease (ESRD) related services per full month; for patients between two and eleven years of age to include monitoring for the adequacy of nutrition, assessment of growth and development, and counseling of parents
	90920	End-stage renal disease (ESRD) related services per full month; for patients between twelve and nineteen years of age to include monitoring for the adequacy of nutrition, assessment of growth and development, and counseling of parents
	90921	End-stage renal disease (ESRD) related services per full month; for patients twenty years of age and older
	90922	End stage renal disease (ESRD) related services (less than full month), per day; for patients under two years of age
	90923	End-stage renal disease (ESRD) related services (less than full month), per day; for patients between two and eleven years of age
	90924	End-stage renal disease (ESRD) related services (less than full month), per day; for patients between twelve and nineteen years of age
	90925	End-stage renal disease (ESRD) related services (less than full month), per day; for patients twenty years of age and older
	90935	Hemodialysis procedure with single physician evaluation
	90937	Hemodialysis procedure requiring repeated evaluation(s) with or without substantial revision of dialysis prescription
	90940	Hemodialysis access flow study to determine blood flow in grafts and arteriovenous fistulae by an indicator method
	90945	Dialysis procedure other than hemodialysis (eg, peritoneal dialysis, hemofiltration, or other continuous renal replacement therapies), with single physician evaluation
	90947	Dialysis procedure other than hemodialysis (eg, peritoneal dialysis, hemofiltration, or other continuous renal replacement therapies) requiring repeated physician evaluations, with or without substantial revision of dialysis prescription
	90951	End-stage renal disease (ESRD) related services monthly, for patients younger than 2 years of age to include monitoring for the adequacy of nutrition, assessment of growth and development, and counseling of parents; with 4 or more face-to-face physician visits per month
	90970	End-stage renal disease (ESRD) related services for dialysis less than a full month of service, per day; for patients 20 years of age and older
	90989	Dialysis training, patient, including helper where applicable, any mode, completed course
	90993	Dialysis training, patient, including helper where applicable, any mode, course not

		completed, per training session
	90999	Unlisted dialysis procedure, inpatient or outpatient
	99512	Home visit for hemodialysis
	4052F	Hemodialysis via functioning arteriovenous (AV) fistula (ESRD) ¹
	4053F	Hemodialysis via functioning arteriovenous (AV) graft (ESRD) ¹
	4054F	Hemodialysis via catheter (ESRD) ¹
	4055F	Patient receiving peritoneal dialysis (ESRD) ¹
	G0257	Unscheduled or emergency dialysis treatment for an esrd patient in a hospital outpatient department that is not certified as an esrd facility
	G0308	End stage renal disease (esrd) related services during the course of treatment, for patients under 2 years of age to include monitoring for the adequacy of nutrition, assessment of growth and development, and counseling of parents; with 4 or more face-to-face physician visits per month
	G0309	End stage renal disease (esrd) related services during the course of treatment for patients under 2 years of age to include monitoring for the adequacy of nutrition, assessment of growth and development, and counseling of parents; with 2 or 3 face-to-face physician visits per month
	G0310	End stage renal disease (esrd) related services during the course of treatment, for patients under 2 years of age to include monitoring for the adequacy of nutrition, assessment of growth and development, and counseling of parents; with 1 face-to-face physician visit per month
	G0311	End stage renal disease (esrd) related services during the course of treatment, for patients between 2 and 11 years of age to include monitoring for the adequacy of nutrition, assessment of growth and development, and counseling of parents; with 4 or more face-to-face physician visits per month
	G0312	End stage renal disease (esrd) related services during the course of treatment, for patients between 2 and 11 years of age to include monitoring for the adequacy of nutrition, assessment of growth and development, and counseling of parents; with 2 or 3 face-to-face physician visits per month
	G0313	End stage renal disease (esrd) related services during the course of treatment, for patients between 2 and 11 years of age to include monitoring for the adequacy of nutrition, assessment of growth and development, and counseling of parents; with 1 face-to-face physician visit per month
	G0314	End stage renal disease (esrd) related services, during the course of treatment, for patients between 12 and 19 years of age to include monitoring for the adequacy of nutrition, assessment of growth and development, and counseling of parents; with 4 or more face-to-face physician visits per month
	G0315	End stage renal disease (esrd) related services during the course of treatment, for patients between 12 and 19 years of age to include monitoring for the adequacy of nutrition, assessment of growth and development, and counseling of parents; with 2 or 3 face-to-face physician visits per month

	G0316	End stage renal disease (esrd) related services during the course of treatment, for patients between 12 and 19 years of age to include monitoring for the adequacy of nutrition, assessment of growth and development, and counseling of parents; with 1 face-to-face physician visit per month
	G0317	End stage renal disease (esrd) related services during the course of treatment, for patients 20 years of age and over; with 4 or more face-to-face physician visits per month
	G0318	End stage renal disease (esrd) related services during the course of treatment, for patients 20 years of age and over; with 2 or 3 face-to-face physician visits per month
	G0319	End stage renal disease (esrd) related services during the course of treatment, for patients 20 years of age and over; with 1 face-to-face physician visit per month
	G0320	End stage renal disease (esrd) related services for home dialysis patients per full month; for patients under two years of age to include monitoring for adequacy of nutrition, assessment of growth and development, and counseling of parents
	G0321	End stage renal disease (esrd) related services for home dialysis patients per full month; for patients two to eleven years of age to include monitoring for adequacy of nutrition, assessment of growth and development, and counseling of parents
	G0322	End stage renal disease (esrd) related services for home dialysis patients per full month; for patients twelve to nineteen years of age to include monitoring for adequacy of nutrition, assessment of growth and development, and counseling of parents
	G0323	End stage renal disease (esrd) related services for home dialysis patients per full month; for patients twenty years of age and older
	G0324	End stage renal disease (esrd) related services less than full month, per day; for patients under two years of age
	G0325	End stage renal disease (esrd) related services less than full month, per day; for patients between two and eleven years of age
	G8075	End stage renal disease patient with documented dialysis dose of urr greater than or equal to 65% (or kt/v greater than or equal to 1.2)
	G8076	End stage renal disease patient with documented dialysis dose of urr less than 65% (or kt/v less than 1.2)
	G8077	Clinician documented that end stage renal disease patient was not an eligible candidate for urr or kt/v measure
	G8078	End stage renal disease patient with documented hematocrit greater than or equal to 33 (or hemoglobin greater than or equal to 11)
	G8079	End stage renal disease patient with documented hematocrit less than 33 (or hemoglobin less than 11)
	G8080	Clinician documented that end stage renal disease patient was not an eligible candidate for hematocrit (hemoglobin) measure
	G8081	End stage renal disease patient requiring hemodialysis vascular access documented to have received autogenous av fistula
	G8082	End stage renal disease patient requiring hemodialysis documented to have received

		vascular access other than autogenous av fistula
	G8085	End-stage renal disease patient requiring hemodialysis vascular access was not an eligible candidate for autogenous av fistula
	G8387	End-stage renal disease patient with a hematocrit or hemoglobin not documented
	G8388	End-stage renal disease patient with urr or kt/v value not documented, but otherwise eligible for measure
	S9335	Home therapy, hemodialysis; administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing services coded separately), per diem
	S9339	Home therapy; peritoneal dialysis, administrative services, professional pharmacy services, care coordination and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem
9	Pregnancy	
	ICD-9 Dx	Description
	630-679.14	Complications of pregnancy, childbirth and the puerperium
	<i>Other pregnancy status codes and postpartum codes:</i>	
	7965	Abnormal finding on antenatal screening
	V220	Supervision of normal first pregnancy
	V221	Supervision of other normal pregnancy
	V222	Pregnant state, incidental
	V230	Supervision of high-risk pregnancy with history of infertility
	V231	Supervision of high-risk pregnancy with history of trophoblastic disease
	V232	Supervision of high-risk pregnancy with history of abortion
	V233	Supervision of high-risk pregnancy with grand multiparity
	V234	Supervision of high-risk pregnancy with other poor obstetric history (prior to 10/1/2002)
	V2341	Supervision of high-risk pregnancy with history of pre-term labor
	V2349	Supervision of high-risk pregnancy with other poor obstetric history
	V235	Supervision of high-risk pregnancy with other poor reproductive history
	V237	Supervision of high-risk pregnancy with insufficient prenatal care
	V2382	Supervision of high-risk pregnancy of elderly multigravida

	V2383	Supervision of high-risk pregnancy of young primigravida
	V2384	Supervision of high-risk pregnancy of young multigravida
	V2385	Pregnancy resulting from assisted reproductive technology
	V2386	Pregnancy with history of in utero procedure during previous pregnancy
	V2389	Supervision of other high-risk pregnancy
	V270	Mother with single liveborn
	V271	Mother with single stillborn
	V272	Mother with twins, both liveborn
	V273	Mother with twins, one liveborn and one stillborn
	V274	Mother with twins, both stillborn
	V275	Mother with other multiple birth, all liveborn
	V276	Mother with other multiple birth, some liveborn
	V277	Mother with other multiple birth, all stillborn
	V279	Mother with unspecified outcome of delivery
	V280	Antenatal screening for chromosomal anomalies by amniocentesis
	V281	Antenatal screening for raised alpha-fetoprotein levels in amniotic fluid
	V282	Other antenatal screening based on amniocentesis
	V283	Encounter for routine screening for malformation using ultrasonics
	V284	Antenatal screening for fetal growth retardation using ultrasonics
	V285	Antenatal screening for isoimmunization
	V286	Antenatal screening for Streptococcus B
	V2881	Encounter for fetal anatomic survey
	V2882	Encounter for screening for risk of pre-term labor
	V2889	Other specified antenatal screening
	V289	Unspecified antenatal screening
	V616	Illegitimacy or illegitimate pregnancy
	V617	Other unwanted pregnancy
	V7242	Pregnancy examination or test, positive result

	V239	Supervision of unspecified high-risk pregnancy
	V240	Postpartum care and examination immediately after delivery
	V241	Postpartum care and examination of lactating mother
	V242	Routine postpartum follow-up

Mammography with MRI

Inclusion Criteria – Original Study – Mammography with MRI	Inclusion Criteria Requirements – Relaxed Study for Analysis^{1,2}	Description
1. Females aged 25 to 65 years old	Yes	Age on enrollment file
2. BRCA1 or BRCA2 mutation carrier	No	Claims data available. (See below – Mammography with MRI Inclusion Criteria) (Code added 10/1/2004, no way to code previously)
3. For women with a past history of unilateral breast cancer, eligible if the contralateral breast was intact	No	Claims data available. (See below – Mammography with MRI Inclusion Criteria) (No way to show unilateral vs bilateral)

¹ Yes – indicates that the same criteria, as defined for original trial, are indicated for the relaxed analysis.

² No – indicates that the same criteria, as defined for original trial, are not indicated for the relaxed analysis.

Exclusion Criteria – Original Study – Mammography with MRI	Exclusion Criteria Requirements – Relaxed Study for Analysis^{1,2,3}	Description
1. Currently pregnant or lactating	Yes	Claims data available. (See below – Mammography with MRI Exclusion Criteria)
2. History of bilateral breast cancer	No	Claims data available for breast cancer diagnoses. (See below – Mammography with MRI Exclusion Criteria) Patient will be excluded on date of bilateral or date of second unilateral. This may result in missing some outpatient double mastectomies.
3. Currently undergoing chemotherapy	Yes	Claims data available. (See below – Mammography with MRI Exclusion Criteria)
4. Known to have metastatic disease	Yes	Claims data available. (See below – Mammography with MRI Exclusion Criteria) (Clarification may be needed)
5. Weighed more than 91 kg	N/A	Not available on claims

Mammography with MRI Inclusion Criteria – Clinical Codes, Relaxed Study Analysis		
Inclusion		
Criteria		
2	BRCA1 or BRCA2 mutation carrier	
	ICD 9 DX	Description

¹ Yes – indicates that the same criteria, as defined for original trial, are indicated for the relaxed analysis.

² No – indicates that the same criteria, as defined for original trial, are not indicated for the relaxed analysis.

³ N/A – indicates that the same criteria, as defined for original trial, are not applicable for the relaxed analysis.

	V8401	Genetic susceptibility to malignant neoplasm of breast
3	Past history of unilateral breast cancer (no way to show unilateral vs bilateral)	
	ICD 9 DX	Description
	V103	Personal history of malignant neoplasm of breast

Mammography with MRI Exclusion Criteria – Clinical Codes, Relaxed Study Analysis		
Exclusion		
Criteria		
1	Pregnant or lactating women	
	ICD 9 DX	Description
	630-679.14	Complications of pregnancy, childbirth and the puerperium
	<i>Other pregnancy status codes and postpartum codes:</i>	
	7965	Abnormal finding on antenatal screening
	V220	Supervision of normal first pregnancy
	V221	Supervision of other normal pregnancy
	V222	Pregnant state, incidental
	V230	Supervision of high-risk pregnancy with history of infertility
	V231	Supervision of high-risk pregnancy with history of trophoblastic disease
	V232	Supervision of high-risk pregnancy with history of abortion
	V233	Supervision of high-risk pregnancy with grand multiparity
	V234	Supervision of high-risk pregnancy with other poor obstetric history (prior to 10/1/2002)
	V2341	Supervision of high-risk pregnancy with history of pre-term labor
	V2349	Supervision of high-risk pregnancy with other poor obstetric history
	V235	Supervision of high-risk pregnancy with other poor reproductive history
	V237	Supervision of high-risk pregnancy with insufficient prenatal care
	V2382	Supervision of high-risk pregnancy of elderly multigravida

	V2383	Supervision of high-risk pregnancy of young primigravida
	V2384	Supervision of high-risk pregnancy of young multigravida
	V2385	Pregnancy resulting from assisted reproductive technology
	V2386	Pregnancy with history of in utero procedure during previous pregnancy
	V2389	Supervision of other high-risk pregnancy
	V270	Mother with single liveborn
	V271	Mother with single stillborn
	V272	Mother with twins, both liveborn
	V273	Mother with twins, one liveborn and one stillborn
	V274	Mother with twins, both stillborn
	V275	Mother with other multiple birth, all liveborn
	V276	Mother with other multiple birth, some liveborn
	V277	Mother with other multiple birth, all stillborn
	V279	Mother with unspecified outcome of delivery
	V280	Antenatal screening for chromosomal anomalies by amniocentesis
	V281	Antenatal screening for raised alpha-fetoprotein levels in amniotic fluid
	V282	Other antenatal screening based on amniocentesis
	V283	Encounter for routine screening for malformation using ultrasonics
	V284	Antenatal screening for fetal growth retardation using ultrasonics
	V285	Antenatal screening for isoimmunization
	V286	Antenatal screening for Streptococcus B
	V2881	Encounter for fetal anatomic survey
	V2882	Encounter for screening for risk of pre-term labor
	V2889	Other specified antenatal screening
	V289	Unspecified antenatal screening
	V616	Illegitimacy or illegitimate pregnancy
	V617	Other unwanted pregnancy
	V7242	Pregnancy examination or test, positive result

	V239	Supervision of unspecified high-risk pregnancy
	V240	Postpartum care and examination immediately after delivery
	V241	Postpartum care and examination of lactating mother
	V242	Routine postpartum follow-up
2	History of bilateral breast cancer (no way to show laterality)	
	ICD 9 DX	Description
	1741	Malignant neoplasm of central portion of female breast
	1742	Malignant neoplasm of upper-inner quadrant of female breast
	1743	Malignant neoplasm of lower-inner quadrant of female breast
	1744	Malignant neoplasm of upper-outer quadrant of female breast
	1745	Malignant neoplasm of lower-outer quadrant of female breast
	1746	Malignant neoplasm of axillary tail of female breast
	1748	Malignant neoplasm of other specified sites of female breast
	1749	Malignant neoplasm of breast (female), unspecified
3	Currently undergoing chemotherapy	
	ICD 9 DX	Description
	V5811	Admission for antineoplastic chemotherapy
	V5812	
	ICD 9 PROC	Description
	9925	Injection or infusion of cancer chemotherapeutic substance
	0010	Implantation of chemotherapeutic agent
	0015	High dose infusion interleukin-2
	9928	Injection or infusion of biological response modifier, as antineoplastic agents. Please review for inclusion.
	CPT	Description
	96401	Chemotherapy administration, subcutaneous or intramuscular; non-hormonal anti-neoplastic
	96402	Chemotherapy administration, subcutaneous or intramuscular; hormonal anti-neoplastic
	96405	Chemotherapy administration; intralesional, up to and including 7 lesions

	96406	Chemotherapy administration; intralesional, more than 7 lesions
	96408	Chemotherapy administration, intravenous; push technique
	96409	Chemotherapy administration; intravenous, push technique, single or initial substance/drug
	96410	Chemotherapy administration; infusion technique, up to one hour
	96411	Chemotherapy administration; intravenous, push technique, each additional substance/drug (List separately in addition to code for primary procedure)
	96412	Chemotherapy administration, intravenous; infusion technique, one to 8 hours,
	96413	Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug
	96414	Chemotherapy administration, intravenous; infusion technique, initiation of prolon
	96415	Chemotherapy administration, intravenous infusion technique; each additional hour (List separately in addition to code for primary procedure)
	96416	Chemotherapy administration, intravenous infusion technique; initiation of prolonged chemotherapy infusion (more than 8 hours), requiring use of a portable or implantable pump
	96417	Chemotherapy administration, intravenous infusion technique; each additional sequential infusion (different substance/drug), up to 1 hour (List separately in addition to code for primary procedure)
	96420	Chemotherapy administration, intra-arterial; push technique
	96422	Chemotherapy administration, intra-arterial; infusion technique, up to 1 hour
	96423	Chemotherapy administration, intra-arterial; infusion technique, each additional hour (List separately in addition to code for primary procedure)
	96425	Chemotherapy administration, intra-arterial; infusion technique, initiation of prolonged infusion (more than 8 hours), requiring the use of a portable or implantable pump
	96440	Chemotherapy administration into pleural cavity, requiring and including thoracentesis
	96445	Chemotherapy administration into peritoneal cavity, requiring and including peritoneocentesis
	96450	Chemotherapy administration, into CNS (eg, intrathecal), requiring and including spinal puncture
	96520	Refilling and maintenance of portable pump
	96521	Refilling and maintenance of portable pump
	96522	Refilling and maintenance of implantable pump or reservoir for drug delivery, systemic (eg, intravenous, intra-arterial)
	96523	Irrigation of implanted venous access device for drug delivery systems
	96542	Chemotherapy injection, subarachnoid or intraventricular via subcutaneous reservoir, single or multiple agents

	96549	Unlisted chemotherapy procedure
	4179F	Tamoxifen or aromatase inhibitor (AI) prescribed (ONC)
	HCPCS	Description
	A9604	SAMARIUM SM-153 LEXIDRONAM, THERAPEUTIC, PER TREATMENT DOSE, UP TO 150
	A9605	SAMARIUM SM-153 LEXIDRONAM, THERAPEUTIC, PER 50 MILLICURIES
	J0128	INJECTION, ABARELIX, 10 MG
	J0594	INJECTION, BUSULFAN, 1 MG
	J0894	INJECTION, DECITABINE, 1 MG
	J2562	INJECTION, PLERIXAFOR, 1 MG
	J3315	INJECTION, TRIPTORELIN PAMOATE, 3.75 MG
	J8510	BUSULFAN; ORAL, 2 MG
	J8515	CABERGOLINE, ORAL, 0.25 MG
	J8520	CAPECITABINE, ORAL, 150 MG
	J8521	CAPECITABINE, ORAL, 500 MG
	J8530	CYCLOPHOSPHAMIDE; ORAL, 25 MG
	J8560	ETOPOSIDE; ORAL, 50 MG
	J8565	GEFITINIB, ORAL, 250 MG
	J8600	MELPHALAN; ORAL, 2 MG
	J8610	METHOTREXATE; ORAL, 2.5 MG
	J8700	TEMOZOLOMIDE, ORAL, 5 MG
	J8705	TOPOTECAN, ORAL, 0.25 MG
	J8999	PRESCRIPTION DRUG, ORAL, CHEMOTHERAPEUTIC, NOS
	J9000	INJECTION, DOXORUBICIN HYDROCHLORIDE, 10 MG
	J9001	INJECTION, DOXORUBICIN HYDROCHLORIDE, ALL LIPID FORMULATIONS, 10 MG
	J9010	INJECTION, ALEMTUZUMAB, 10 MG
	J9015	INJECTION, ALDESLEUKIN, PER SINGLE USE VIAL
	J9017	INJECTION, ARSENIC TRIOXIDE, 1 MG

	J9020	INJECTION, ASPARAGINASE, 10,000 UNITS
	J9025	INJECTION, AZACITIDINE, 1 MG
	J9027	INJECTION, CLOFARABINE, 1 MG
	J9031	BCG (INTRAVESICAL) PER INSTILLATION
	J9033	INJECTION, BENDAMUSTINE HCL, 1 MG
	J9035	INJECTION, BEVACIZUMAB, 10 MG
	J9040	INJECTION, BLEOMYCIN SULFATE, 15 UNITS
	J9041	INJECTION, BORTEZOMIB, 0.1 MG
	J9045	INJECTION, CARBOPLATIN, 50 MG
	J9050	INJECTION, CARMUSTINE, 100 MG
	J9055	INJECTION, CETUXIMAB, 10 MG
	J9060	INJECTION, CISPLATIN, POWDER OR SOLUTION, 10 MG
	J9062	CISPLATIN, 50 MG
	J9065	INJECTION, CLADRIBINE, PER 1 MG
	J9070	CYCLOPHOSPHAMIDE, 100 MG
	J9080	CYCLOPHOSPHAMIDE, 200 MG
	J9090	CYCLOPHOSPHAMIDE, 500 MG
	J9091	CYCLOPHOSPHAMIDE, 1.0 GRAM
	J9092	CYCLOPHOSPHAMIDE, 2.0 GRAM
	J9093	CYCLOPHOSPHAMIDE, LYOPHILIZED, 100 MG
	J9094	CYCLOPHOSPHAMIDE, LYOPHILIZED, 200 MG
	J9095	CYCLOPHOSPHAMIDE, LYOPHILIZED, 500 MG
	J9096	CYCLOPHOSPHAMIDE, LYOPHILIZED, 1.0 GRAM
	J9097	CYCLOPHOSPHAMIDE, LYOPHILIZED, 2.0 GRAM
	J9098	INJECTION, CYTARABINE LIPOSOME, 10 MG
	J9100	INJECTION, CYTARABINE, 100 MG
	J9110	INJECTION, CYTARABINE, 500 MG
	J9120	INJECTION, DACTINOMYCIN, 0.5 MG

	J9130	DACARBAZINE, 100 MG
	J9140	DACARBAZINE, 200 MG
	J9150	INJECTION, DAUNORUBICIN, 10 MG
	J9151	INJECTION, DAUNORUBICIN CITRATE, LIPOSOMAL FORMULATION, 10 MG
	J9155	INJECTION, DEGARELIX, 1 MG
	J9160	INJECTION, DENILEUKIN DIFTITOX, 300 MICROGRAMS
	J9165	INJECTION, DIETHYLSTILBESTROL DIPHOSPHATE, 250 MG
	J9170	INJECTION, DOCETAXEL, 20 MG
	J9171	INJECTION, DOCETAXEL, 1 MG
	J9175	INJECTION, ELLIOTTS' B SOLUTION, 1 ML
	J9178	INJECTION, EPIRUBICIN HCL, 2 MG
	J9181	INJECTION, ETOPOSIDE, 10 MG
	J9182	ETOPOSIDE, 100 MG
	J9185	INJECTION, FLUDARABINE PHOSPHATE, 50 MG
	J9190	INJECTION, FLUOROURACIL, 500 MG
	J9200	INJECTION, FLOXURIDINE, 500 MG
	J9201	INJECTION, GEMCITABINE HYDROCHLORIDE, 200 MG
	J9202	GOSERELIN ACETATE IMPLANT, PER 3.6 MG
	J9206	INJECTION, IRINOTECAN, 20 MG
	J9207	INJECTION, IXABEPILONE, 1 MG
	J9208	INJECTION, IFOSFAMIDE, 1 GRAM
	J9209	INJECTION, MESNA, 200 MG
	J9211	INJECTION, IDARUBICIN HYDROCHLORIDE, 5 MG
	J9212	INJECTION, INTERFERON ALFACON-1, RECOMBINANT, 1 MICROGRAM
	J9213	INJECTION, INTERFERON, ALFA-2A, RECOMBINANT, 3 MILLION UNITS
	J9214	INJECTION, INTERFERON, ALFA-2B, RECOMBINANT, 1 MILLION UNITS
	J9215	INJECTION, INTERFERON, ALFA-N3, (HUMAN LEUKOCYTE DERIVED), 250,000 IU
	J9216	INJECTION, INTERFERON, GAMMA 1-B, 3 MILLION UNITS

	J9217	LEUPROLIDE ACETATE (FOR DEPOT SUSPENSION), 7.5 MG
	J9218	LEUPROLIDE ACETATE, PER 1 MG
	J9219	LEUPROLIDE ACETATE IMPLANT, 65 MG
	J9225	HISTRELIN IMPLANT (VANTAS), 50 MG
	J9226	HISTRELIN IMPLANT (SUPPRELIN LA), 50 MG
	J9230	INJECTION, MECHLORETHAMINE HYDROCHLORIDE, (NITROGEN MUSTARD), 10 MG
	J9245	INJECTION, MELPHALAN HYDROCHLORIDE, 50 MG
	J9250	METHOTREXATE SODIUM, 5 MG
	J9260	METHOTREXATE SODIUM, 50 MG
	J9261	INJECTION, NELARABINE, 50 MG
	J9263	INJECTION, OXALIPLATIN, 0.5 MG
	J9264	INJECTION, PACLITAXEL PROTEIN-BOUND PARTICLES, 1 MG
	J9265	INJECTION, PACLITAXEL, 30 MG
	J9266	INJECTION, PEGASPARGASE, PER SINGLE DOSE VIAL
	J9268	INJECTION, PENTOSTATIN, 10 MG
	J9270	INJECTION, PLICAMYCIN, 2.5 MG
	J9280	MITOMYCIN, 5 MG
	J9290	MITOMYCIN, 20 MG
	J9291	MITOMYCIN, 40 MG
	J9293	INJECTION, MITOXANTRONE HYDROCHLORIDE, PER 5 MG
	J9300	INJECTION, GEMTUZUMAB OZOGAMICIN, 5 MG
	J9302	INJECTION, OFATUMUMAB, 10 MG
	J9303	INJECTION, PANITUMUMAB, 10 MG
	J9305	INJECTION, PEMETREXED, 10 MG
	J9307	INJECTION, PRALATREXATE, 1 MG
	J9310	INJECTION, RITUXIMAB, 100 MG
	J9315	INJECTION, ROMIDEPSIN, 1 MG

	J9320	INJECTION, STREPTOZOCIN, 1 GRAM
	J9328	INJECTION, TEMOZOLOMIDE, 1 MG
	J9330	INJECTION, TEMSIROLIMUS, 1 MG
	J9340	INJECTION, THIOTEPA, 15 MG
	J9350	INJECTION, TOPOTECAN, 4 MG
	J9351	INJECTION, TOPOTECAN, 0.1 MG
	J9355	INJECTION, TRASTUZUMAB, 10 MG
	J9357	INJECTION, VALRUBICIN, INTRAVESICAL, 200 MG
	J9360	INJECTION, VINBLASTINE SULFATE, 1 MG
	J9370	VINCRISTINE SULFATE, 1 MG
	J9375	VINCRISTINE SULFATE, 2 MG
	J9380	VINCRISTINE SULFATE, 5 MG
	J9390	INJECTION, VINORELBINE TARTRATE, 10 MG
	J9395	INJECTION, FULVESTRANT, 25 MG
	J9600	INJECTION, PORFIMER SODIUM, 75 MG
	J9999	NOT OTHERWISE CLASSIFIED, ANTINEOPLASTIC DRUGS
	Q0083	CHEMOTHERAPY ADMINISTRATION BY OTHER THAN INFUSION TECHNIQUE ONLY (EG SUBCUTANEOUS, INTRAMUSCULAR, PUSH), PER VISIT
	Q0084	CHEMOTHERAPY ADMINISTRATION BY INFUSION TECHNIQUE ONLY, PER VISIT
	Q0085	CHEMOTHERAPY ADMINISTRATION BY BOTH INFUSION TECHNIQUE AND OTHER TECHIQUE(S) (EG SUBCUTANEOUS, INTRAMUSCULAR, PUSH), PER VISIT
	S0088	IMATINIB, 100 MG
	S0108	MERCAPTOPYRINE, ORAL, 50 MG
	S0170	ANASTROZOLE, ORAL, 1MG
	S0172	CHLORAMBUCIL, ORAL, 2MG
	S0175	FLUTAMIDE, ORAL, 125MG
	S0176	HYDROXYUREA, ORAL, 500MG
	S0177	LEVAMISOLE HYDROCHLORIDE, ORAL, 50MG
	S0178	LOMUSTINE, ORAL, 10MG

	S0182	PROCARBAZINE HYDROCHLORIDE, ORAL, 50MG
	S0187	TAMOXIFEN CITRATE, ORAL, 10MG
	S9329	HOME INFUSION THERAPY, CHEMOTHERAPY INFUSION; ADMINISTRATIVE SERVICES, PROFESSIONAL PHARMACY SERVICES, CARE COORDINATION, AND ALL NECESSARY SUPPLIES AND EQUIPMENT (DRUGS AND NURSING VISITS CODED SEPARATELY), PER DIEM (DO NOT USE THIS CODE WITH S9330 OR S9331)
	S9330	HOME INFUSION THERAPY, CONTINUOUS (TWENTY-FOUR HOURS OR MORE) CHEMOTHERAPY INFUSION; ADMINISTRATIVE SERVICES, PROFESSIONAL PHARMACY SERVICES, CARE COORDINATION, AND ALL NECESSARY SUPPLIES AND EQUIPMENT (DRUGS AND NURSING VISITS CODED SEPARATELY), PER DIEM
	S9331	HOME INFUSION THERAPY, INTERMITTENT (LESS THAN TWENTY-FOUR HOURS) CHEMOTHERAPY INFUSION; ADMINISTRATIVE SERVICES, PROFESSIONAL PHARMACY SERVICES, CARE COORDINATION, AND ALL NECESSARY SUPPLIES AND EQUIPMENT (DRUGS AND NURSING VISITS CODED SEPARATELY), PER DIEM
4	Metastatic disease from breast would require the reporting of history of breast cancer or current breast cancer codes with a code from the following secondary carcinoma codes:	
	ICD 9 DX	Description
	1960	Secondary and unspecified malignant neoplasm of lymph nodes of head, face, and neck
	1961	Secondary and unspecified malignant neoplasm of intrathoracic lymph nodes
	1962	Secondary and unspecified malignant neoplasm of intra-abdominal lymph nodes
	1969	Secondary and unspecified malignant neoplasm of lymph nodes, site unspecified
	1970	Secondary malignant neoplasm of lung
	1972	Secondary malignant neoplasm of pleura
	1973	Secondary malignant neoplasm of other respiratory organs
	1974	Secondary malignant neoplasm of small intestine including duodenum
	1975	Secondary malignant neoplasm of large intestine and rectum
	1976	Secondary malignant neoplasm of retroperitoneum and peritoneum
	1977	Malignant neoplasm of liver, specified as secondary
	1978	Secondary malignant neoplasm of other digestive organs and spleen
	1980	Secondary malignant neoplasm of kidney
	1981	Secondary malignant neoplasm of other urinary organs

	1982	Secondary malignant neoplasm of skin
	1983	Secondary malignant neoplasm of brain and spinal cord
	1984	Secondary malignant neoplasm of other parts of nervous system
	1985	Secondary malignant neoplasm of bone and bone marrow
	1986	Secondary malignant neoplasm of ovary
	1987	Secondary malignant neoplasm of adrenal gland
	19881	Secondary malignant neoplasm of breast
	19882	Secondary malignant neoplasm of genital organs
	19889	Secondary malignant neoplasm of other specified sites

Inclusion Criteria – Original Study – SPORT	Inclusion Criteria Requirements – Relaxed	Description
--	--	--------------------

SPORT

	Study for Analysis^{1,2,3}	
1. At least 18 years of age	Yes	Age on enrollment file
2. Diagnosed by participating physicians during the study enrollment period as having intervertebral disk herniation and persistent symptoms despite some nonoperative treatment for at least 6 weeks (INDEX EVENT)	Dx of disk herniation, Yes. Nonoperative treatment, No	Claims data available. (See below – SPORT Inclusion Criteria)
3. A surgical candidate who underwent advanced vertebral imaging showing disk herniation (protrusion, extrusion or sequestered fragment) at a level and side corresponding to the clinical symptoms	No	Claims data available. (See below – SPORT Inclusion Criteria) (Procedures not routinely coded in ICD-9-CM)
4. Among patients with multiple herniations, included if only one of the herniations was considered symptomatic	N/A	Not available on claims
5. At least one of the symptoms at enrollment:	Yes	See below
a. Radicular pain (below the knee for lower lumbar herniations, into the anterior thigh for upper lumbar herniations)	Yes	Claims data available. (See below – SPORT Inclusion Criteria) (Only coded if not part of disease process, would not be coded for patients with lumbar herniation)
b. Evidence of nerve-root irritation with a positive nerve-root tension sign (straight leg raise-positive between 30° and 70° or positive femoral tension sign)	N/A	Not available on claims
c. Corresponding neurologic deficit (asymmetrical depressed reflex, decreased sensation in a dermatomal distribution, or weakness in a	N/A	Not available on claims

¹ Yes – indicates that the same criteria, as defined for original trial, are indicated for the relaxed analysis.

² No – indicates that the same criteria, as defined for original trial, are not indicated for the relaxed analysis.

³ N/A – indicates that the same criteria, as defined for original trial, are not applicable for the relaxed analysis.

myotomal distribution		
-----------------------	--	--

Exclusion Criteria – Original Study – SPORT	Exclusion Criteria Requirements – Relaxed Study for Analysis^{1,2,3}	Description
1. Prior lumbar surgery	No	Claims data available. (See below – SPORT Exclusion Criteria) (Clarification may be required to classify “lumbar” surgery)
2. Cauda equina syndrome	Yes	Claims data available. (See below – SPORT Exclusion Criteria)
3. Scoliosis greater than 15°	No	Claims data available. (See below – SPORT Exclusion Criteria)
4. Segmental instability (> 10° angular motion or > 4 mm translation)	N/A	Not available on claims
5. Vertebral fractures	Yes	Claims data available. (See below – SPORT Exclusion Criteria)
6. Spine infection or tumor	Yes	Claims data available. (See below – SPORT Exclusion Criteria)
7. Inflammatory spondyloarthropathy	No	Claims data available. (See below – SPORT Exclusion Criteria)
8. Pregnancy	Yes	Claims data available. (See below – SPORT Exclusion Criteria)

¹ Yes – indicates that the same criteria, as defined for original trial, are indicated for the relaxed analysis.

² No – indicates that the same criteria, as defined for original trial, are not indicated for the relaxed analysis.

³ N/A – indicates that the same criteria, as defined for original trial, are not applicable for the relaxed analysis.

		Criteria)
9. Comorbid conditions contraindicating surgery	N/A	Identification of comorbid conditions is not necessary due to rarity of such conditions
10. Inability or unwillingness to have surgery within 6 months	N/A	Not available on claims

SPORT Inclusion Criteria – Clinical Codes, Relaxed Study Analysis		
Criteria Number		
2	Intervertebral disk herniation:	
	ICD-9 Dx	Description
	7220	Displacement of cervical intervertebral disc without myelopathy
	72210	Displacement of lumbar intervertebral disc without myelopathy
	72211	Displacement of thoracic intervertebral disc without myelopathy
	7222	Displacement of intervertebral disc, site unspecified, without myelopathy
	72270	Intervertebral disc disorder with myelopathy, unspecified region
	72271	Intervertebral disc disorder with myelopathy, cervical region
	72272	Intervertebral disc disorder with myelopathy, thoracic region
	72273	Intervertebral disc disorder with myelopathy, lumbar region
	Education/Counseling:	
	<i>procedures not routinely coded in ICD-9-CM</i>	
	ICD-9 Dx	Description
	9449	Other counselling
	CPT	Description
	90887	Interpretation or explanation of results of psychiatric, other medical examinations and procedures, or other accumulated data to family or other responsible persons, or advising them how to assist patient

	96152	Health and behavior intervention, each 15 minutes, face-to-face; individual
	96153	Health and behavior intervention, each 15 minutes, face-to-face; group (2 or more patients)
	96154	Health and behavior intervention, each 15 minutes, face-to-face; family (with the patient present)
	96155	Health and behavior intervention, each 15 minutes, face-to-face; family (without the patient present)
	97802	Medical nutrition therapy; initial assessment and intervention, individual, face-to-face with the patient, each 15 minutes
	97803	Medical nutrition therapy; re-assessment and intervention, individual, face-to-face with the patient, each 15 minutes
	97804	Medical nutrition therapy; group (2 or more individual(s)), each 30 minutes
	Physical therapy:	
	<i>procedures not routinely coded in ICD-9-CM</i>	
	ICD-9 Dx	Description
	9301	Functional evaluation
	9302	Orthotic evaluation
	9303	Prosthetic evaluation
	9304	Manual testing of muscle function
	9305	Range of motion testing
	9306	Measurement of limb length
	9307	Body measurement
	9308	Electromyography
	9309	Other diagnostic physical therapy procedure
	9311	Assisting exercise
	9312	Other active musculoskeletal exercise
	9313	Resistive exercise
	9314	Training in joint movements
	9315	Mobilization of spine
	9316	Mobilization of other joints

	9317	Other passive musculoskeletal exercise
	9318	Breathing exercise
	9319	Exercise, not elsewhere classified
	9321	Manual and mechanical traction
	9322	Ambulation and gait training
	9323	Fitting of orthotic device
	9324	Training in use of prosthetic or orthotic device
	9325	Forced extension of limb
	9326	Manual rupture of joint adhesions
	9327	Stretching of muscle or tendon
	9328	Stretching of fascia
	9329	Other forcible correction of musculoskeletal deformity
	9331	Assisted exercise in pool
	9332	Whirlpool treatment
	9333	Other hydrotherapy
	9334	Diathermy
	9335	Other heat therapy
	9336	Cardiac retraining
	9337	Prenatal training
	9338	Combined physical therapy without mention of the components
	9339	Other physical therapy
	CPT	Description
	97001	Physical therapy evaluation
	97002	Physical therapy re-evaluation
	97003	Occupational therapy evaluation
	97004	Occupational therapy re-evaluation
	97005	Athletic training evaluation
	97006	Athletic training re-evaluation

	97010	Application of a modality to 1 or more areas; hot or cold packs
	97012	Application of a modality to 1 or more areas; traction, mechanical
	97014	Application of a modality to 1 or more areas; electrical stimulation (unattended)
	97016	Application of a modality to 1 or more areas; vasopneumatic devices
	97018	Application of a modality to 1 or more areas; paraffin bath
	97022	Application of a modality to 1 or more areas; whirlpool
	97024	Application of a modality to 1 or more areas; diathermy (eg, microwave)
	97026	Application of a modality to 1 or more areas; infrared
	97028	Application of a modality to 1 or more areas; ultraviolet
	97032	Application of a modality to one or more areas; electrical stimulation (manual), each 15 minutes
	97033	Application of a modality to one or more areas; iontophoresis, each 15 minutes
	97034	Application of a modality to one or more areas; contrast baths, each 15 minutes
	97035	Application of a modality to one or more areas; ultrasound, each 15 minutes
	97036	Application of a modality to one or more areas; Hubbard tank, each 15 minutes
	97039	Unlisted modality (specify type and time if constant attendance)
	97110	Therapeutic procedure, one or more areas, each 15 minutes; therapeutic exercises to develop strength and endurance, range of motion and flexibility
	97112	Therapeutic procedure, one or more areas, each 15 minutes; neuromuscular reeducation of movement, balance, coordination, kinesthetic sense, posture, and/or proprioception for sitting and/or standing activities
	97113	Therapeutic procedure, one or more areas, each 15 minutes; aquatic therapy with therapeutic exercises
	97116	Therapeutic procedure, one or more areas, each 15 minutes; gait training (includes stair climbing)
	97124	Therapeutic procedure, one or more areas, each 15 minutes; massage, including effleurage, petrissage and/or tapotement (stroking, compression, percussion)
	97139	Unlisted therapeutic procedure (specify)
	97140	Manual therapy techniques (eg, mobilization/ manipulation, manual lymphatic drainage, manual traction), one or more regions, each 15 minutes
	97150	Therapeutic procedure(s), group (2 or more individuals)
	97530	Therapeutic activities, direct (one-on-one) patient contact by the provider (use of dynamic activities to improve functional performance), each 15 minutes

	97532	Development of cognitive skills to improve attention, memory, problem solving (includes compensatory training), direct (one-on-one) patient contact by the provider, each 15 minutes
	97533	Sensory integrative techniques to enhance sensory processing and promote adaptive responses to environmental demands, direct (one-on-one) patient contact by the provider, each 15 minutes
	97535	Self-care/home management training (eg, activities of daily living (ADL) and compensatory training, meal preparation, safety procedures, and instructions in use of assistive technology devices/adaptive equipment) direct one-on-one contact by provider, each 15 minutes
	97537	Community/work reintegration training (eg, shopping, transportation, money management, avocational activities and/or work environment/modification analysis, work task analysis, use of assistive technology device/adaptive equipment), direct one-on-one contact by provider, each 15 minutes
	97542	Wheelchair management (eg, assessment, fitting, training), each 15 minutes
	97545	Work hardening/conditioning; initial 2 hours
	97546	Work hardening/conditioning; each additional hour (List separately in addition to code for primary procedure)
	97750	Physical performance test or measurement (eg, musculoskeletal, functional capacity), with written report, each 15 minutes
	97755	Assistive technology assessment (eg, to restore, augment or compensate for existing function, optimize functional tasks and/or maximize environmental accessibility), direct one-on-one contact by provider, with written report, each 15 minutes
	97760	Orthotic(s) management and training (including assessment and fitting when not otherwise reported), upper extremity(s), lower extremity(s) and/or trunk, each 15 minutes
	97761	Prosthetic training, upper and/or lower extremity(s), each 15 minutes
	97762	Checkout for orthotic/prosthetic use, established patient, each 15 minutes
	97799	Unlisted physical medicine/rehabilitation service or procedure
	Epidural injections:	
	<i>procedures not routinely coded in ICD-9-CM</i>	
	ICD-9 Dx	Description
	0391	Injection of anesthetic into spinal canal for analgesia
	0392	Injection of other agent into spinal canal
	CPT	Description
	61055	Cisternal or lateral cervical (C1-C2) puncture; with injection of medication or other substance for diagnosis or treatment (eg, C1-C2)

	62310	Injection, single (not via indwelling catheter), not including neurolytic substances, with or without contrast (for either localization or epidurography), of diagnostic or therapeutic substance(s) (including anesthetic, antispasmodic, opioid, steroid, oth
	62311	Injection, single (not via indwelling catheter), not including neurolytic substances, with or without contrast (for either localization or epidurography), of diagnostic or therapeutic substance(s) (including anesthetic, antispasmodic, opioid, steroid, oth
	62318	Injection, including catheter placement, continuous infusion or intermittent bolus, not including neurolytic substances, with or without contrast (for either localization or epidurography), of diagnostic or therapeutic substance(s) (including anesthetic,
	62319	Injection, including catheter placement, continuous infusion or intermittent bolus, not including neurolytic substances, with or without contrast (for either localization or epidurography), of diagnostic or therapeutic substance(s) (including anesthetic,
	64479	Injection, anesthetic agent and/or steroid, transforaminal epidural; cervical or thoracic, single level
	64480	Injection, anesthetic agent and/or steroid, transforaminal epidural; cervical or thoracic, each additional level (List separately in addition to code for primary procedure)
	64483	Injection, anesthetic agent and/or steroid, transforaminal epidural; lumbar or sacral, single level
	64484	Injection, anesthetic agent and/or steroid, transforaminal epidural; lumbar or sacral, each additional level (List separately in addition to code for primary procedure)
5a	Chiropractic therapy:	
	<i>procedures not routinely coded in ICD-9-CM</i>	
	ICD-9 Dx	Description
	9361	Osteopathic manipulative treatment for general mobilization
	9362	Osteopathic manipulative treatment using high-velocity, low-amplitude forces
	9363	Osteopathic manipulative treatment using low-velocity, high-amplitude forces
	9364	Osteopathic manipulative treatment using isotonic, isometric forces
	9365	Osteopathic manipulative treatment using indirect forces
	9366	Osteopathic manipulative treatment to move tissue fluids
	9367	Other specified osteopathic manipulative treatment
	CPT	Description
3	98940	Chiropractic manipulative treatment (CMT); spinal, 1-2 regions
	98941	Chiropractic manipulative treatment (CMT); spinal, 3-4 regions

	98942	Chiropractic manipulative treatment (CMT); spinal, 5 regions
	98943	Chiropractic manipulative treatment (CMT); extraspinal, 1 or more regions
	Radicular pain:	
	<i>only coded if not part of disease process, would not be coded for patients with lumbar herniation</i>	
	ICD-9 Dx	Description
	7220	Displacement of cervical intervertebral disc without myelopathy
	72210	Displacement of lumbar intervertebral disc without myelopathy
	72211	Displacement of thoracic intervertebral disc without myelopathy
	7222	Displacement of intervertebral disc, site unspecified, without myelopathy
	72270	Intervertebral disc disorder with myelopathy, unspecified region
	72271	Intervertebral disc disorder with myelopathy, cervical region
	72272	Intervertebral disc disorder with myelopathy, thoracic region
	72273	Intervertebral disc disorder with myelopathy, lumbar region
	7234	Brachial neuritis or radiculitis NOS
	7243	Sciatica
	7244	Thoracic or lumbosacral neuritis or radiculitis, unspecified
	7292	Neuralgia, neuritis, and radiculitis, unspecified
	7292	Neuralgia, neuritis, and radiculitis, unspecified
	3531	Lumbosacral plexus lesions
3	3532	Cervical root lesions, not elsewhere classified
	3533	Thoracic root lesions, not elsewhere classified
	3534	Lumbosacral root lesions, not elsewhere classified
	Magnetic resonance imaging :	
	ICD-9 Dx	Description
	8893	Magnetic resonance imaging of spinal canal
	CPT	Description
	72141	Magnetic resonance (eg, proton) imaging, spinal canal and contents, cervical; without

		contrast material
	72142	Magnetic resonance (eg, proton) imaging, spinal canal and contents, cervical; with contrast material(s)
	72146	Magnetic resonance (eg, proton) imaging, spinal canal and contents, thoracic; without contrast material
	72147	Magnetic resonance (eg, proton) imaging, spinal canal and contents, thoracic; with contrast material(s)
	72148	Magnetic resonance (eg, proton) imaging, spinal canal and contents, lumbar; without contrast material
	72149	Magnetic resonance (eg, proton) imaging, spinal canal and contents, lumbar; with contrast material(s)
	72156	Magnetic resonance (eg, proton) imaging, spinal canal and contents, without contrast material, followed by contrast material(s) and further sequences; cervical
	72157	Magnetic resonance (eg, proton) imaging, spinal canal and contents, without contrast material, followed by contrast material(s) and further sequences; thoracic
	72158	Magnetic resonance (eg, proton) imaging, spinal canal and contents, without contrast material, followed by contrast material(s) and further sequences; lumbar
Computed tomography :		
	ICD-9 Dx	Description
	8838	Other computerized axial tomography
	CPT	Description
	72125	Computed tomography, cervical spine; without contrast material
	72126	Computed tomography, cervical spine; with contrast material
	72127	Computed tomography, cervical spine; without contrast material, followed by contrast material(s) and further sections
	72128	Computed tomography, thoracic spine; without contrast material
	72129	Computed tomography, thoracic spine; with contrast material
	72130	Computed tomography, thoracic spine; without contrast material, followed by contrast material(s) and further sections
	72131	Computed tomography, lumbar spine; without contrast material
	72132	Computed tomography, lumbar spine; with contrast material
	72133	Computed tomography, lumbar spine; without contrast material, followed by contrast material(s) and further sections

SPORT Exclusion Criteria - Clinical Codes. Relaxed Study Analysis

Criteria Number		
1	Lumbar surgery:	
	ICD-9 Dx	Description
	8050	Excision or destruction of intervertebral disc, unspecified
	8051	Excision of intervertebral disc
	8052	Intervertebral chemonucleolysis
	8053	Repair of the annulus fibrosus with graft or prosthesis
	8054	Other and unspecified repair of the annulus fibrosus
	8059	Other destruction of intervertebral disc
	8104	Dorsal and dorsolumbar fusion, anterior technique
	8105	Dorsal and dorsolumbar fusion, posterior technique
	8106	Lumbar and lumbosacral fusion, anterior technique
	8107	Lumbar and lumbosacral fusion, lateral transverse process technique
	8108	Lumbar and lumbosacral fusion, posterior technique
	8134	Refusion of dorsal and dorsolumbar spine, anterior technique
	8135	Refusion of dorsal and dorsolumbar spine, posterior technique
	8136	Refusion of lumbar and lumbosacral spine, anterior technique
	8137	Refusion of lumbar and lumbosacral spine, lateral transverse process technique
	8138	Refusion of lumbar and lumbosacral spine, posterior technique
	8165	Percutaneous vertebroplasty
	8166	Percutaneous vertebral augmentation
	8451	Insertion of interbody spinal fusion device
	8459	Insertion of other spinal devices
	8464	Insertion of partial spinal disc prosthesis, lumbosacral
	8465	Insertion of total spinal disc prosthesis, lumbosacral
	8468	Revision or replacement of artificial spinal disc prosthesis, lumbosacral

	8480	Insertion or replacement of interspinous process device(s)
	8481	Revision of interspinous process device(s)
	8482	Insertion or replacement of pedicle-based dynamic stabilization device(s)
	8483	Revision of pedicle-based dynamic stabilization device(s)
	8484	Insertion or replacement of facet replacement device(s)
	8485	Revision of facet replacement device(s)
	CPT	Description
	0062T	Percutaneous intradiscal annuloplasty, any method except electrothermal, unilateral or bilateral including fluoroscopic guidance; single level
	0063T	Percutaneous intradiscal annuloplasty, any method except electrothermal, unilateral or bilateral including fluoroscopic guidance; 1 or more additional levels (List separately in addition to 0062T for primary procedure)
	22015	Incision and drainage, open, of deep abscess (subfascial), posterior spine; lumbar, sacral, or lumbosacral
	22102	Partial excision of posterior vertebral component (eg, spinous process, lamina or facet) for intrinsic bony lesion, single vertebral segment; lumbar
	22114	Partial excision of vertebral body, for intrinsic bony lesion, without decompression of spinal cord or nerve root(s), single vertebral segment; lumbar
	22207	Osteotomy of spine, posterior or posterolateral approach, three columns, one vertebral segment (eg, pedicle/vertebral body subtraction); lumbar
	22214	Osteotomy of spine, posterior or posterolateral approach, one vertebral segment; lumbar
	22224	Osteotomy of spine, including discectomy, anterior approach, single vertebral segment; lumbar
	22305	Closed treatment of vertebral process fracture(s)
	22310	Closed treatment of vertebral body fracture(s), without manipulation, requiring and including casting or bracing
	22315	Closed treatment of vertebral fracture(s) and/or dislocation(s) requiring casting or bracing, with and including casting and/or bracing, with or without anesthesia, by manipulation or traction
	22325	Open treatment and/or reduction of vertebral fracture(s) and/or dislocation(s), posterior approach, one fractured vertebra or dislocated segment; lumbar
	22521	Percutaneous vertebroplasty, one vertebral body, unilateral or bilateral injection; lumbar
	22524	Percutaneous vertebral augmentation, including cavity creation (fracture reduction and bone biopsy included when performed) using mechanical device, one vertebral body, unilateral or bilateral cannulation (eg, kyphoplasty); lumbar

	22526	Percutaneous intradiscal electrothermal annuloplasty, unilateral or bilateral including fluoroscopic guidance; single level
	22533	Arthrodesis, lateral extracavitary technique, including minimal discectomy to prepare interspace (other than for decompression); lumbar
	22558	Arthrodesis, anterior interbody technique, including minimal discectomy to prepare interspace (other than for decompression); lumbar
	22612	Arthrodesis, posterior or posterolateral technique, single level; lumbar (with or without lateral transverse technique)
	22630	Arthrodesis, posterior interbody technique, including laminectomy and/or discectomy to prepare interspace (other than for decompression), single interspace; lumbar
	22800	Arthrodesis, posterior, for spinal deformity, with or without cast; up to 6 vertebral segments
	22802	Arthrodesis, posterior, for spinal deformity, with or without cast; 7 to 12 vertebral segments
	22804	Arthrodesis, posterior, for spinal deformity, with or without cast; 13 or more vertebral segments
	22808	Arthrodesis, anterior, for spinal deformity, with or without cast; 2 to 3 vertebral segments
	22810	Arthrodesis, anterior, for spinal deformity, with or without cast; 4 to 7 vertebral segments
	22812	Arthrodesis, anterior, for spinal deformity, with or without cast; 8 or more vertebral segments
	22830	Exploration of spinal fusion
	22840	Posterior non-segmental instrumentation (eg, Harrington rod technique, pedicle fixation across one interspace, atlantoaxial transarticular screw fixation, sublaminar wiring at C1, facet screw fixation) (List separately in addition to code for primary procedure)
	22841	Internal spinal fixation by wiring of spinous processes (List separately in addition to code for primary procedure)
	22842	Posterior segmental instrumentation (eg, pedicle fixation, dual rods with multiple hooks and sublaminar wires); 3 to 6 vertebral segments (List separately in addition to code for primary procedure)
	22843	Posterior segmental instrumentation (eg, pedicle fixation, dual rods with multiple hooks and sublaminar wires); 7 to 12 vertebral segments (List separately in addition to code for primary procedure)
	22844	Posterior segmental instrumentation (eg, pedicle fixation, dual rods with multiple hooks and sublaminar wires); 13 or more vertebral segments (List separately in addition to code for primary procedure)
	22845	Anterior instrumentation; 2 to 3 vertebral segments (List separately in addition to code for primary procedure)
	22846	Anterior instrumentation; 4 to 7 vertebral segments (List separately in addition to code for primary procedure)

	22847	Anterior instrumentation; 8 or more vertebral segments (List separately in addition to code for primary procedure)
	22849	Reinsertion of spinal fixation device
	22850	Removal of posterior nonsegmental instrumentation (eg, Harrington rod)
	22851	Application of intervertebral biomechanical device(s) (eg, synthetic cage(s), threaded bone dowel(s), methylmethacrylate) to vertebral defect or interspace (List separately in addition to code for primary procedure)
	22852	Removal of posterior segmental instrumentation
	22855	Removal of anterior instrumentation
	22857	Total disc arthroplasty (artificial disc), anterior approach, including discectomy to prepare interspace (other than for decompression), single interspace, lumbar
	22862	Revision including replacement of total disc arthroplasty (artificial disc), anterior approach, single interspace; lumbar
	22865	Removal of total disc arthroplasty (artificial disc), anterior approach, single interspace; lumbar
	62263	Percutaneous lysis of epidural adhesions using solution injection (eg, hypertonic saline, enzyme) or mechanical means (eg, catheter) including radiologic localization (includes contrast when administered), multiple adhesiolysis sessions; 2 or more days
	62264	Percutaneous lysis of epidural adhesions using solution injection (eg, hypertonic saline, enzyme) or mechanical means (eg, catheter) including radiologic localization (includes contrast when administered), multiple adhesiolysis sessions; 1 day
	62282	Injection/infusion of neurolytic substance (eg, alcohol, phenol, iced saline solutions), with or without other therapeutic substance; epidural, lumbar, sacral (caudal)
	62287	Decompression procedure, percutaneous, of nucleus pulposus of intervertebral disc, any method, single or multiple levels, lumbar (eg, manual or automated percutaneous discectomy, percutaneous laser discectomy)
	62292	Injection procedure for chemonucleolysis, including discography, intervertebral disc, single or multiple levels, lumbar
	62311	Injection, single (not via indwelling catheter), not including neurolytic substances, with or without contrast (for either localization or epidurography), of diagnostic or therapeutic substance(s) (including anesthetic, antispasmodic, opioid, steroid, other solution), epidural or subarachnoid; lumbar, sacral (caudal)
	62319	Injection, including catheter placement, continuous infusion or intermittent bolus, not including neurolytic substances, with or without contrast (for either localization or epidurography), of diagnostic or therapeutic substance(s) (including anesthetic, antispasmodic, opioid, steroid, other solution), epidural or subarachnoid; lumbar, sacral (caudal)
	62350	Implantation, revision or repositioning of tunneled intrathecal or epidural catheter, for long-term medication administration via an external pump or implantable reservoir/infusion pump; without laminectomy

	62351	Implantation, revision or repositioning of tunneled intrathecal or epidural catheter, for long-term medication administration via an external pump or implantable reservoir/infusion pump; with laminectomy
	63005	Laminectomy with exploration and/or decompression of spinal cord and/or cauda equina, without facetectomy, foraminotomy or discectomy (eg, spinal stenosis), 1 or 2 vertebral segments; lumbar, except for spondylolisthesis
	63012	Laminectomy with removal of abnormal facets and/or pars inter-articularis with decompression of cauda equina and nerve roots for spondylolisthesis, lumbar (Gill type procedure)
	63017	Laminectomy with exploration and/or decompression of spinal cord and/or cauda equina, without facetectomy, foraminotomy or discectomy (eg, spinal stenosis), more than 2 vertebral segments; lumbar
	63030	Laminotomy (hemilaminectomy), with decompression of nerve root(s), including partial facetectomy, foraminotomy and/or excision of herniated intervertebral disc, including open and endoscopically-assisted approaches; 1 interspace, lumbar
	63042	Laminotomy (hemilaminectomy), with decompression of nerve root(s), including partial facetectomy, foraminotomy and/or excision of herniated intervertebral disc, reexploration, single interspace; lumbar
	63044	Laminotomy (hemilaminectomy), with decompression of nerve root(s), including partial facetectomy, foraminotomy and/or excision of herniated intervertebral disc, reexploration, single interspace; each additional lumbar interspace (List separately in addition to code for primary procedure)
	63047	Laminectomy, facetectomy and foraminotomy (unilateral or bilateral with decompression of spinal cord, cauda equina and/or nerve root[s], [eg, spinal or lateral recess stenosis]), single vertebral segment; lumbar
	63056	Transpedicular approach with decompression of spinal cord, equina and/or nerve root(s) (eg, herniated intervertebral disc), single segment; lumbar (including transfacet, or lateral extraforaminal approach) (eg, far lateral herniated intervertebral disc)
	63087	Vertebral corpectomy (vertebral body resection), partial or complete, combined thoracolumbar approach with decompression of spinal cord, cauda equina or nerve root(s), lower thoracic or lumbar; single segment
	63090	Vertebral corpectomy (vertebral body resection), partial or complete, transperitoneal or retroperitoneal approach with decompression of spinal cord, cauda equina or nerve root(s), lower thoracic, lumbar, or sacral; single segment
	63102	Vertebral corpectomy (vertebral body resection), partial or complete, lateral extracavitary approach with decompression of spinal cord and/or nerve root(s) (eg, for tumor or retropulsed bone fragments); lumbar, single segment
	63170	Laminectomy with myelotomy (eg, Bischof or DREZ type), cervical, thoracic, or thoracolumbar
	63185	Laminectomy with rhizotomy; 1 or 2 segments
	63190	Laminectomy with rhizotomy; more than 2 segments
	63200	Laminectomy, with release of tethered spinal cord, lumbar

	63252	Laminectomy for excision or occlusion of arteriovenous malformation of spinal cord; thoracolumbar
	63267	Laminectomy for excision or evacuation of intraspinal lesion other than neoplasm, extradural; lumbar
	63272	Laminectomy for excision of intraspinal lesion other than neoplasm, intradural; lumbar
	63277	Laminectomy for biopsy/excision of intraspinal neoplasm; extradural, lumbar
	63282	Laminectomy for biopsy/excision of intraspinal neoplasm; intradural, extramedullary, lumbar
	63287	Laminectomy for biopsy/excision of intraspinal neoplasm; intradural, intramedullary, thoracolumbar
	63290	Laminectomy for biopsy/excision of intraspinal neoplasm; combined extradural-intradural lesion, any level
	63303	Vertebral corpectomy (vertebral body resection), partial or complete, for excision of intraspinal lesion, single segment; extradural, lumbar or sacral by transperitoneal or retroperitoneal approach
	63307	Vertebral corpectomy (vertebral body resection), partial or complete, for excision of intraspinal lesion, single segment; intradural, lumbar or sacral by transperitoneal or retroperitoneal approach
	63600	Creation of lesion of spinal cord by stereotactic method, percutaneous, any modality including stimulation and/or recording
	63655	Laminectomy for implantation of neurostimulator electrodes, plate/paddle, epidural
	63664	Revision including replacement, when performed, of spinal neurostimulator electrode plate/paddle(s) placed via laminotomy or laminectomy, including fluoroscopy, when performed
	63740	Creation of shunt, lumbar, subarachnoid-peritoneal, -pleural, or other; including laminectomy
2	Cauda equina syndrome:	
	ICD-9 Dx	Description
	34460	Cauda equina syndrome without mention of neurogenic bladder
	34461	Cauda equina syndrome with neurogenic bladder
3	Scoliosis:	
	ICD-9 Dx	Description
	73730	Scoliosis [and kyphoscoliosis], idiopathic

	73731	Resolving infantile idiopathic scoliosis
	73732	Progressive infantile idiopathic scoliosis
	73733	Scoliosis due to radiation
	73734	Thoracogenic scoliosis
	73739	Other kyphoscoliosis and scoliosis
5	Vertebral fractures:	
	ICD-9 Dx	Description
	73313	Pathologic fracture of vertebrae
	80500	Closed fracture of cervical vertebra without mention of spinal cord injury, unspecified level
	80501	Closed fracture of first cervical vertebra without mention of spinal cord injury
	80502	Closed fracture of second cervical vertebra without mention of spinal cord injury
	80503	Closed fracture of third cervical vertebra without mention of spinal cord injury
	80504	Closed fracture of fourth cervical vertebra without mention of spinal cord injury
	80505	Closed fracture of fifth cervical vertebra without mention of spinal cord injury
	80506	Closed fracture of sixth cervical vertebra without mention of spinal cord injury
	80507	Closed fracture of seventh cervical vertebra without mention of spinal cord injury
	80508	Closed fracture of multiple cervical vertebrae without mention of spinal cord injury
	80510	Open fracture of cervical vertebra without mention of spinal cord injury, unspecified level
	80511	Open fracture of first cervical vertebra without mention of spinal cord injury
	80512	Open fracture of second cervical vertebra without mention of spinal cord injury
	80513	Open fracture of third cervical vertebra without mention of spinal cord injury
	80514	Open fracture of fourth cervical vertebra without mention of spinal cord injury
	80515	Open fracture of fifth cervical vertebra without mention of spinal cord injury
	80516	Open fracture of sixth cervical vertebra without mention of spinal cord injury
	80517	Open fracture of seventh cervical vertebra without mention of spinal cord injury
	80518	Open fracture of multiple cervical vertebrae without mention of spinal cord injury

	8052	Closed fracture of dorsal [thoracic] vertebra without mention of spinal cord injury
	8053	Open fracture of dorsal [thoracic] vertebra without mention of spinal cord injury
	8054	Closed fracture of lumbar vertebra without mention of spinal cord injury
	8055	Open fracture of lumbar vertebra without mention of spinal cord injury
	8056	Closed fracture of sacrum and coccyx without mention of spinal cord injury
	8057	Open fracture of sacrum and coccyx without mention of spinal cord injury
	8058	Closed fracture of unspecified part of vertebral column without mention of spinal cord injury
	8059	Open fracture of unspecified part of vertebral column without mention of spinal cord injury
	80600	Closed fracture of C1-C4 level with unspecified spinal cord injury
	80601	Closed fracture of C1-C4 level with complete lesion of cord
	80602	Closed fracture of C1-C4 level with anterior cord syndrome
	80603	Closed fracture of C1-C4 level with central cord syndrome
	80604	Closed fracture of C1-C4 level with other specified spinal cord injury
	80605	Closed fracture of C5-C7 level with unspecified spinal cord injury
	80606	Closed fracture of C5-C7 level with complete lesion of cord
	80607	Closed fracture of C5-C7 level with anterior cord syndrome
	80608	Closed fracture of C5-C7 level with central cord syndrome
	80609	Closed fracture of C5-C7 level with other specified spinal cord injury
	80610	Open fracture of C1-C4 level with unspecified spinal cord injury
	80611	Open fracture of C1-C4 level with complete lesion of cord
	80612	Open fracture of C1-C4 level with anterior cord syndrome
	80613	Open fracture of C1-C4 level with central cord syndrome
	80614	Open fracture of C1-C4 level with other specified spinal cord injury
	80615	Open fracture of C5-C7 level with unspecified spinal cord injury
	80616	Open fracture of C5-C7 level with complete lesion of cord
	80617	Open fracture of C5-C7 level with anterior cord syndrome
	80618	Open fracture of C5-C7 level with central cord syndrome

	80619	Open fracture of C5-C7 level with other specified spinal cord injury
	80620	Closed fracture of T1-T6 level with unspecified spinal cord injury
	80621	Closed fracture of T1-T6 level with complete lesion of cord
	80622	Closed fracture of T1-T6 level with anterior cord syndrome
	80623	Closed fracture of T1-T6 level with central cord syndrome
	80624	Closed fracture of T1-T6 level with other specified spinal cord injury
	80625	Closed fracture of T7-T12 level with unspecified spinal cord injury
	80626	Closed fracture of T7-T12 level with complete lesion of cord
	80627	Closed fracture of T7-T12 level with anterior cord syndrome
	80628	Closed fracture of T7-T12 level with central cord syndrome
	80629	Closed fracture of T7-T12 level with other specified spinal cord injury
	80630	Open fracture of T1-T6 level with unspecified spinal cord injury
	80631	Open fracture of T1-T6 level with complete lesion of cord
	80632	Open fracture of T1-T6 level with anterior cord syndrome
	80633	Open fracture of T1-T6 level with central cord syndrome
	80634	Open fracture of T1-T6 level with other specified spinal cord injury
	80635	Open fracture of T7-T12 level with unspecified spinal cord injury
	80636	Open fracture of T7-T12 level with complete lesion of cord
	80637	Open fracture of T7-T12 level with anterior cord syndrome
	80638	Open fracture of T7-T12 level with central cord syndrome
	80639	Open fracture of T7-T12 level with other specified spinal cord injury
	8064	Closed fracture of lumbar spine with spinal cord injury
	8065	Open fracture of lumbar spine with spinal cord injury
	80660	Closed fracture of sacrum and coccyx with unspecified spinal cord injury
	80661	Closed fracture of sacrum and coccyx with complete cauda equina lesion
	80662	Closed fracture of sacrum and coccyx with other cauda equina injury
	80669	Closed fracture of sacrum and coccyx with other spinal cord injury
	80670	Open fracture of sacrum and coccyx with unspecified spinal cord injury

	80671	Open fracture of sacrum and coccyx with complete cauda equina lesion
	80672	Open fracture of sacrum and coccyx with other cauda equina injury
	80679	Open fracture of sacrum and coccyx with other spinal cord injury
	8068	Closed fracture of unspecified vertebra with spinal cord injury
	8069	Open fracture of unspecified vertebra with spinal cord injury
6	Spine infection:	
	ICD-9 Dx	Description
	3200	Hemophilus meningitis
	3201	Pneumococcal meningitis
	3202	Streptococcal meningitis
	3203	Staphylococcal meningitis
	3207	Meningitis in other bacterial diseases classified elsewhere
	32081	Meningitis due to anaerobic bacteria
	32082	Meningitis due to gram-negative bacteria, not elsewhere classified
	32089	Meningitis due to other specified bacteria
	3209	Meningitis due to unspecified bacterium
	3210	Cryptococcal meningitis
	3211	Meningitis in other fungal diseases
	3212	Meningitis due to viruses not elsewhere classified
	3213	Meningitis due to trypanosomiasis
	3214	Meningitis in sarcoidosis
	3218	Meningitis due to other nonbacterial organisms classified elsewhere
	3220	Nonpyogenic meningitis
	3221	Eosinophilic meningitis
	3222	Chronic meningitis
	3229	Meningitis, unspecified
	3230	Encephalitis in viral diseases classified elsewhere (prior to 10/1/2006)

	32301	Encephalitis and encephalomyelitis in viral diseases classified elsewhere
	32302	Myelitis in viral diseases classified elsewhere
	3231	Encephalitis, myelitis, and encephalomyelitis in rickettsial diseases classified elsewhere
	3232	Encephalitis, myelitis, and encephalomyelitis in protozoal diseases classified elsewhere
	3234	Other encephalitis due to infection classified elsewhere (prior to 10/1/2006)
	32341	Other encephalitis and encephalomyelitis due to infection classified elsewhere
	32342	Other myelitis due to infection classified elsewhere
	32351	Encephalitis and encephalomyelitis following immunization procedures
	32352	Myelitis following immunization procedures
	3235	Encephalitis following immunization procedures (prior to 10/1/2006)
	3236	Postinfectious encephalitis (prior to 10/1/2006)
	32361	Infectious acute disseminated encephalomyelitis [ADEM]
	32362	Other postinfectious encephalitis and encephalomyelitis
	32363	Postinfectious myelitis
	3237	Toxic encephalitis (prior to 10/1/2006)
	32371	Toxic encephalitis and encephalomyelitis
	32372	Toxic myelitis
	3238	Other causes of encephalitis (prior to 10/1/2006)
	32381	Other causes of encephalitis and encephalomyelitis
	32382	Other causes of myelitis
	3239	Unspecified causes of encephalitis, myelitis, and encephalomyelitis
	3241	Intraspinal abscess
	00321	Salmonella meningitis
	01300	Tuberculous meningitis, unspecified examination
	01301	Tuberculous meningitis, bacteriological or histological examination not done
	01302	Tuberculous meningitis, bacteriological or histological examination unknown (at present)
	01303	Tuberculous meningitis, tubercle bacilli found (in sputum) by microscopy
	01304	Tuberculous meningitis, tubercle bacilli not found (in sputum) by microscopy, but found

		by bacterial culture
	01305	Tuberculous meningitis, tubercle bacilli not found by bacteriological examination, but tuberculosis confirmed histologically
	01306	Tuberculous meningitis, tubercle bacilli not found by bacteriological or histological examination, but tuberculosis confirmed by other methods (inoculation of animals)
	01310	Tuberculoma of meninges, unspecified examination
	01311	Tuberculoma of meninges, bacteriological or histological examination not done
	01312	Tuberculoma of meninges, bacteriological or histological examination unknown (at present)
	01313	Tuberculoma of meninges, tubercle bacilli found (in sputum) by microscopy
	01314	Tuberculoma of meninges, tubercle bacilli not found (in sputum) by microscopy, but found by bacterial culture
	01315	Tuberculoma of meninges, tubercle bacilli not found by bacteriological examination, but tuberculosis confirmed histologically
	01316	Tuberculoma of meninges, tubercle bacilli not found by bacteriological or histological examination, but tuberculosis confirmed by other methods (inoculation of animals)
	01340	Tuberculoma of spinal cord, unspecified examination
	01341	Tuberculoma of spinal cord, bacteriological or histological examination not done
	01342	Tuberculoma of spinal cord, bacteriological or histological examination unknown (at present)
	01343	Tuberculoma of spinal cord, tubercle bacilli found (in sputum) by microscopy
	01344	Tuberculoma of spinal cord, tubercle bacilli not found (in sputum) by microscopy, but found by bacterial culture
	01345	Tuberculoma of spinal cord, tubercle bacilli not found by bacteriological examination, but tuberculosis confirmed histologically
	01346	Tuberculoma of spinal cord, tubercle bacilli not found by bacteriological or histological examination, but tuberculosis confirmed by other methods (inoculation of animals)
	01350	Tuberculous abscess of spinal cord, unspecified examination
	01351	Tuberculous abscess of spinal cord, bacteriological or histological examination not done
	01352	Tuberculous abscess of spinal cord, bacteriological or histological examination unknown (at present)
	01353	Tuberculous abscess of spinal cord, tubercle bacilli found (in sputum) by microscopy
	01354	Tuberculous abscess of spinal cord, tubercle bacilli not found (in sputum) by microscopy, but found by bacterial culture
	01355	Tuberculous abscess of spinal cord, tubercle bacilli not found by bacteriological

		examination, but tuberculosis confirmed histologically
	01356	Tuberculous abscess of spinal cord, tubercle bacilli not found by bacteriological or histological examination, but tuberculosis confirmed by other methods (inoculation of animals)
	01360	Tuberculous encephalitis or myelitis, unspecified examination
	01361	Tuberculous encephalitis or myelitis, bacteriological or histological examination not done
	01362	Tuberculous encephalitis or myelitis, bacteriological or histological examination unknown (at present)
	01363	Tuberculous encephalitis or myelitis, tubercle bacilli found (in sputum) by microscopy
	01364	Tuberculous encephalitis or myelitis, tubercle bacilli not found (in sputum) by microscopy, but found by bacterial culture
	01365	Tuberculous encephalitis or myelitis, tubercle bacilli not found by bacteriological examination, but tuberculosis confirmed histologically
	01366	Tuberculous encephalitis or myelitis, tubercle bacilli not found by bacteriological or histological examination, but tuberculosis confirmed by other methods (inoculation of animals)
	01500	Tuberculosis of vertebral column, unspecified examination
	01501	Tuberculosis of vertebral column, bacteriological or histological examination not done
	01502	Tuberculosis of vertebral column, bacteriological or histological examination unknown (at present)
	01503	Tuberculosis of vertebral column, tubercle bacilli found (in sputum) by microscopy
	01504	Tuberculosis of vertebral column, tubercle bacilli not found (in sputum) by microscopy, but found by bacterial culture
	01505	Tuberculosis of vertebral column, tubercle bacilli not found by bacteriological examination, but tuberculosis confirmed histologically
	01506	Tuberculosis of vertebral column, tubercle bacilli not found by bacteriological or histological examination, but tuberculosis confirmed by other methods (inoculation of animals)
	0360	Meningococcal meningitis
	0470	Meningitis due to Coxsackie virus
	0471	Meningitis due to ECHO virus
	0478	Other specified viral meningitis
	0479	Unspecified viral meningitis
	0490	Non-arthropod borne lymphocytic choriomeningitis
	0491	Non-arthropod borne meningitis due to adenovirus

	0530	Herpes zoster with meningitis
	05314	Herpes zoster myelitis
	05472	Herpes simplex meningitis
	05474	Herpes simplex myelitis
	0721	Mumps meningitis
	09042	Congenital syphilitic meningitis
	09181	Acute syphilitic meningitis (secondary)
	0942	Syphilitic meningitis
	09882	Gonococcal meningitis
	10081	Leptospiral meningitis (aseptic)
	11283	Candidal meningitis
	1142	Coccidioidal meningitis
	11501	Histoplasma capsulatum meningitis
	11511	Histoplasma duboisii meningitis
	11591	Histoplasmosis meningitis
	73008	Acute osteomyelitis, other specified sites
	73018	Chronic osteomyelitis, other specified sites
	73028	Unspecified osteomyelitis, other specified sites
	73038	Periostitis, without mention of osteomyelitis, other specified sites
	73088	Other infections involving bone diseases classified elsewhere, other specified sites
	73098	Unspecified infection of bone of other specified sites
6	Spinal tumor:	
	ICD-9 Dx	Description
	1702	Malignant neoplasm of vertebral column, excluding sacrum and coccyx
	1706	Malignant neoplasm of pelvic bones, sacrum, and coccyx
	1922	Malignant neoplasm of spinal cord
	1923	Malignant neoplasm of spinal meninges

	1983	Secondary malignant neoplasm of brain and spinal cord
	1984	Secondary malignant neoplasm of other parts of nervous system
	1985	Secondary malignant neoplasm of bone and bone marrow
	2132	Benign neoplasm of vertebral column, excluding sacrum and coccyx
	2136	Benign neoplasm of pelvic bones, sacrum, and coccyx
	2253	Benign neoplasm of spinal cord
	2254	Benign neoplasm of spinal meninges
	2375	Neoplasm of uncertain behavior of brain and spinal cord
	2376	Neoplasm of uncertain behavior of meninges
	2380	Neoplasm of uncertain behavior of bone and articular cartilage
	2381	Neoplasm of uncertain behavior of connective and other soft tissue
	2392	Neoplasm of unspecified nature of bone, soft tissue, and skin
	2397	Neoplasm of unspecified nature of endocrine glands and other parts of nervous system
7	Inflammatory spondyloarthropathy:	
	ICD-9 Dx	Description
	7200	Ankylosing spondylitis
	72081	Inflammatory spondylopathies in diseases classified elsewhere
	72089	Other inflammatory spondylopathies
	7209	Unspecified inflammatory spondylopathy
8	Pregnancy:	
	ICD-9 Dx	Description
	630-679.14	Complications of pregnancy, childbirth and the puerperium
	<i>Other pregnancy status codes and postpartum codes:</i>	
	7965	Abnormal finding on antenatal screening
	V220	Supervision of normal first pregnancy
	V221	Supervision of other normal pregnancy
	V222	Pregnant state, incidental

	V230	Supervision of high-risk pregnancy with history of infertility
	V231	Supervision of high-risk pregnancy with history of trophoblastic disease
	V232	Supervision of high-risk pregnancy with history of abortion
	V233	Supervision of high-risk pregnancy with grand multiparity
	V234	Supervision of high-risk pregnancy with other poor obstetric history (prior to 10/1/2002)
	V2341	Supervision of high-risk pregnancy with history of pre-term labor
	V2349	Supervision of high-risk pregnancy with other poor obstetric history
	V235	Supervision of high-risk pregnancy with other poor reproductive history
	V237	Supervision of high-risk pregnancy with insufficient prenatal care
	V2382	Supervision of high-risk pregnancy of elderly multigravida
	V2383	Supervision of high-risk pregnancy of young primigravida
	V2384	Supervision of high-risk pregnancy of young multigravida
	V2385	Pregnancy resulting from assisted reproductive technology
	V2386	Pregnancy with history of in utero procedure during previous pregnancy
	V2389	Supervision of other high-risk pregnancy
	V270	Mother with single liveborn
	V271	Mother with single stillborn
	V272	Mother with twins, both liveborn
	V273	Mother with twins, one liveborn and one stillborn
	V274	Mother with twins, both stillborn
	V275	Mother with other multiple birth, all liveborn
	V276	Mother with other multiple birth, some liveborn
	V277	Mother with other multiple birth, all stillborn
	V279	Mother with unspecified outcome of delivery
	V280	Antenatal screening for chromosomal anomalies by amniocentesis
	V281	Antenatal screening for raised alpha-fetoprotein levels in amniotic fluid
	V282	Other antenatal screening based on amniocentesis
	V283	Encounter for routine screening for malformation using ultrasonics

	V284	Antenatal screening for fetal growth retardation using ultrasonics
	V285	Antenatal screening for isoimmunization
	V286	Antenatal screening for Streptococcus B
	V2881	Encounter for fetal anatomic survey
	V2882	Encounter for screening for risk of pre-term labor
	V2889	Other specified antenatal screening
	V289	Unspecified antenatal screening
	V616	Illegitimacy or illegitimate pregnancy
	V617	Other unwanted pregnancy
	V7242	Pregnancy examination or test, positive result
	V239	Supervision of unspecified high-risk pregnancy
	V240	Postpartum care and examination immediately after delivery
	V241	Postpartum care and examination of lactating mother
	V242	Routine postpartum follow-up

COURAGE

Inclusion Criteria – Original Study – COURAGE	Inclusion Criteria Requirements – Relaxed Study for Analysis – Stable Angina^{1,2,3}	Description
1. Patients with a >70% lesion in >1 vessel subtending a large area of myocardium with one of the following:	See below	See below
a. Prior PCI or coronary artery bypasses grafting (CABG) with evidence of ischemia.	No	Claims data available. (See below – COURAGE)

¹ Yes – indicates that the same criteria, as defined for original trial, are indicated for the relaxed analysis.

² No – indicates that the same criteria, as defined for original trial, are not indicated for the relaxed analysis.

³ N/A – indicates that the same criteria, as defined for original trial, are not applicable for the relaxed analysis.

		Inclusion Criteria) Note, most definitions of PCI include PTCA and coronary stent insertion
b. Chronic stable angina, Canadian Cardiovascular Society (CCS) class I-III	Yes	Claims data available. (See below – COURAGE Inclusion Criteria)
c. Post-MI patients without class IV angina, severe LV dysfunction, or arrhythmia	N/A	Not available on claims
d. Asymptomatic ischemia detected by exercise or perfusion scintigraphy or 24-hour ambulatory electrocardiogram (ECG) recording.	N/A	Not available on claims
2. Patients who meet criteria adapted from one of the existing AHA/ACC Joint Task force Class I or II indications for PCI:		
a. Patients with single-vessel CAD who are asymptomatic to severely symptomatic and who have a large area of ischemic myocardium subtending a significant (>50% diameter reduction) coronary stenosis (AHA/ACC Class I indication) or a moderate area of ischemia (AHA/ACC Class II indication)	Yes	Claims data available. (See below – COURAGE Inclusion Criteria)
b. Patients with multivessel CAD who are asymptomatic to severely symptomatic. Asymptomatic or minimally symptomatic patients must have a large ischemic area or moderate ischemic area (AHA/ACC Class II indication) to qualify.	Yes	Claims data available. (See below – COURAGE Inclusion Criteria)
3. Has at least 1 vessel for angioplasty meeting one of the following criteria: a. Right coronary artery: proximal to the posterior descending artery in a right dominant vessel b. Left circumflex coronary artery: proximal to 1 or 2 obtuse marginal (OM) branches or proximal to the posterior descending artery and posterolateral branches in a left dominant vessel c. Left anterior descending coronary artery (LAD): proximal or mid vessel d. Saphenous vein graft (SVG) or left internal mammary artery (LIMA): graft must supply the same regions as outlined previously or, in the opinion of the interventionalist, the coronary stenosis subtends a major mass of myocardium	N/A	Not available on claims
4. Has objective evidence of myocardial ischemia or severe symptoms with marked coronary stenosis including one of the following:	N/A	Not available on claims

<p>a. Spontaneous new ST-T changes on resting ECG defined as either >1.0 mm ST-segment deviation from the baseline (80 mm from J point) or >2.0 mm T-wave inversion (or pseudonormalization, if T waves were previously inverted) in a minimum of 2 contiguous leads within 1 of 3 ECG lead groups (anterior V1-V4; inferior II, III, aVF; lateral I, aVL, V5-V6)</p> <p>b. Objective evidence of stress-induced myocardial ischemia as detected by standard 12-lead exercise stress test, exercise or pharmacologic stress (adenosine or dipyridamole) coupled with perfusion scintigraphy, exercise or pharmacologic stress (dobutamine) coupled with 2-dimensional echocardiography, or exercise radionuclide ventriculography, based on one of the following:</p> <ul style="list-style-type: none"> i. >1.0 mm ST-segment deviation from baseline on standard treadmill exercise using 12-lead ECG ii. >1 Scintigraphic perfusion defects during exercise technetium 99m sestamibi or thallium-based isotope imaging iii. >1 Perfusion defects (reversible or partial reversible) with pharmacologic stress (dipyridamole, adenosine) during technetium 99m sestamibi or thallium imaging iv. >1 Wall motion abnormalities during exercise radionuclide ventriculography v. 2-Dimensional echocardiography (exercise or dobutamine) vi. Severe angina (CCS class III) and coronary stenosis $\geq 80\%$ 		
---	--	--

Exclusion Criteria – Original Study – COURAGE	Exclusion Criteria Requirements – Relaxed Study for Analysis – Stable Angina ^{1,2,3}	Description
---	---	-------------

¹ Yes – indicates that the same criteria, as defined for original trial, are indicated for the relaxed analysis.

² No – indicates that the same criteria, as defined for original trial, are not indicated for the relaxed analysis.

³ N/A – indicates that the same criteria, as defined for original trial, are not applicable for the relaxed analysis.

1. Unstable angina and symptoms refractory to maximal oral and intravenous medical therapy (persistent CCS class IV)	Yes	Claims data available. (See below – COURAGE Exclusion Criteria)
2. Post-MI course complicated by persistent rest angina, shock, and persistent CHF for which the need or likelihood of urgent myocardial revascularization is high Note, per NPC should include all CHF patients unless they meet strict exclusion criteria	No	Claims data available. (See below – COURAGE Exclusion Criteria)
3. Coronary angiographic exclusions: a. Patients with no prior CABG and left main coronary disease >50% b. Coronary arteries technically unsuitable or hazardous for PCI c. Patients with nonsignificant CAD in whom PCI would not be considered appropriate or indicated d. Patients with restenosis of a lesion previously treated with PCI and no other target lesion	No	Claims data available for a) no prior CABG. (See below – COURAGE Exclusion Criteria) All others (b,c,d) Not available on claims
4. EF <30% (<35% if patient has 3-vessel disease including >70% LAD proximal stenosis)	N/A	Not available on claims
5. Cardiogenic shock	Yes	Claims data available. (See below – COURAGE Exclusion Criteria)
6. Pulmonary edema or heart failure unresponsive to standard medical therapy	Yes	Claims data available. (See below – COURAGE Exclusion Criteria)
7. CABG or PCI within the last 6 months	Yes	Claims data available. (See below – COURAGE Exclusion Criteria) Enrollment criteria (below)
8. Concomitant valvular heart disease likely to require surgery or affect prognosis during follow-up	Yes	Claims data available. (See below – COURAGE Exclusion Criteria)

9. Congenital or primary cardiac muscle disease likely to affect prognosis during follow-up	Yes	Claims data available. (See below – COURAGE Exclusion Criteria)
10. Resuscitated out-of-hospital sudden death or symptomatic sustained or nonsustained ventricular tachycardia	Yes	Claims data available. (See below – COURAGE Exclusion Criteria)
11. Significant systemic hypertension (BP >200/100 mm Hg) unresponsive to medical therapy – Per NPC, should include all hypertension patients unless they meet strict exclusion criteria	No	Claims data available. (See below – COURAGE Exclusion Criteria) No way to show severity
12. Markedly positive stress test (significant ST segment depressions or hypotensive response during stage I of the Bruce protocol)	Yes	Claims data available. (See below – COURAGE Exclusion Criteria)
13. Severe noncardiovascular comorbidity limiting survival	N/A	Not available on Claims

COURAGE Inclusion Criteria – Clinical Codes, Relaxed Study Analysis		
Criteria Number		
CAD	Coronary artery disease is indexed to coronary atherosclerosis:	
	ICD 9 Dx	Description
	410.xx	Acute myocardial infarction
	411.xx	Other acute and subacute forms of ischemic heart disease
	412	Old myocardial infarction
	413.xx	Angina pectoris
	414.xx	Other forms of chronic ischemic heart disease
	429.7x	Certain sequelae of myocardial infarction, not elsewhere classified
Stable Angina	Angina	
	ICD 9 Dx	Description

	413.0	Angina decubitis
	413.1	Prinzmetal angina
	413.9	Other unspecified angina pectoris

COURAGE Exclusion Criteria – Clinical Codes, Relaxed Study Analysis		
Criteria Number		
1	Unstable angina	
	ICD 9 Dx	Description
	411.1	Intermediate coronary syndrome
5	Cardiogenic shock	
	ICD 9 Dx	Description
	785.50	Shock, unspecified
	785.51	Cardiogenic shock
6	Pulmonary edema or heart failure	
	ICD 9 Dx	Description
	514	Pulmonary congestion and hypostasis
	518.4	Acute edema of lung, unspecified
	398.91	Rheumatic heart failure (congestive).
	402.01	Hypertensive heart disease, malignant, with heart failure
	402.11	Hypertensive heart disease, benign, with heart failure
	402.91	Hypertensive heart disease, unspecified, with heart failure
	404.01	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
	404.03	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic

		kidney disease stage V or end stage renal disease
	404.11	Hypertensive heart and chronic kidney disease, benign, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
	404.13	Hypertensive heart and chronic kidney disease, benign, with heart failure and chronic kidney disease stage V or end stage renal disease
	404.91	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
	404.93	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and chronic kidney disease stage V or end stage renal disease
	428.0	Congestive heart failure, unspecified
	428.1	Left heart failure
	428.20	Unspecified systolic heart failure
	428.21	Acute systolic heart failure
	428.22	Chronic systolic heart failure
	428.23	Acute on chronic systolic heart failure
	428.30	Unspecified diastolic heart failure
	428.31	Acute diastolic heart failure
	428.32	Chronic diastolic heart failure
	428.33	Acute on chronic diastolic heart failure
	428.40	Unspecified combined systolic and diastolic heart failure
	428.41	Acute combined systolic and diastolic heart failure
	428.42	Chronic combined systolic and diastolic heart failure
	428.43	Acute on chronic combined systolic and diastolic heart failure
	428.9	Heart failure, unspecified
7	Prior CABG or PCI	
	ICD 9 Proc	Description
	V4582	Percutaneous transluminal coronary angioplasty status
	V4581	Aortocoronary bypass status

	00.66	Percutaneous transluminal coronary angioplasty [PTCA] or coronary atherectomy
	36.01	Single vessel PTCA/atherectomy w/o thrombolytic agent
	36.02	Single vessel PTCA/atherectomy w thrombolytic agent
	36.04	Intracoronary artery thrombolytic infusion
	36.05	Multiple vessel PTCA w or w/o thrombolytic agent
	36.06	Insertion of non-drug-eluting coronary artery stent(s)
	36.07	Insertion of drug-eluting coronary artery stent(s)
	36.09	Other specified removal of coronary artery obstruction
	36.10	Aortocoronary bypass for heart revascularization, not otherwise specified
	36.11	(Aorto)coronary bypass of one coronary artery
	36.12	(Aorto)coronary bypass of two coronary arteries
	36.13	(Aorto)coronary bypass of three coronary arteries
	36.14	(Aorto)coronary bypass of four or more coronary arteries
	36.15	Single internal mammary-coronary artery bypass
	36.16	Double internal mammary-coronary artery bypass
	36.17	Abdominal-coronary artery bypass
	36.19	Other bypass anastomosis for heart revascularization
	36.2	Heart revascularization by arterial implant
	36.31	Open chest transmyocardial revascularization
	36.32	Other transmyocardial revascularization
	36.33	Endoscopic transmyocardial revascularization
	36.34	Percutaneous transmyocardial revascularization
	36.39	Other heart revascularization
	CPT/HCPCS	Description
	G0290	Transcatheter placement of a drug eluting intracoronary stent(s), percutaneous, with or without other therapeutic intervention, any method; single vessel
	G0291	Transcatheter placement of a drug eluting intracoronary stent(s), percutaneous, with or without other therapeutic intervention, any method; each additional vessel

	92973	Percutaneous transluminal coronary thrombectomy (List separately in addition to code for primary procedure)
	92980	Transcatheter placement of an intracoronary stent(s), percutaneous, with or without other therapeutic intervention, any method; single vessel
	92981	Transcatheter placement of an intracoronary stent(s), percutaneous, with or without other therapeutic intervention, any method; each additional vessel (list separately in addition to code for primary procedure)
	92982	Percutaneous transluminal coronary balloon angioplasty; single vessel
	92984	Percutaneous transluminal coronary balloon angioplasty; each additional vessel (List separately in addition to code for primary procedure)
	92995	Percutaneous transluminal coronary atherectomy, by mechanical or other method, with or without balloon angioplasty; single vessel
	92996	Percutaneous transluminal coronary atherectomy, by mechanical or other method, with or without balloon angioplasty; each additional vessel (List separately in addition to code for primary procedure)
	33140	Transmyocardial laser revascularization, by thoracotomy; (separate procedure)
	33141	Transmyocardial laser revascularization, by thoracotomy; performed at the time of other open cardiac procedure(s)
	33510	Coronary artery bypass, vein only; single coronary venous graft
	33511	Coronary artery bypass, vein only; 2 coronary venous grafts
	33512	Coronary artery bypass, vein only; 3 coronary venous grafts
	33513	Coronary artery bypass, vein only; 4 coronary venous grafts
	33514	Coronary artery bypass, vein only; 5 coronary venous grafts
	33516	Coronary artery bypass, vein only; 6 or more coronary venous grafts
	33517	Coronary artery bypass, using venous graft(s) and arterial graft(s); single vein graft
	33518	Coronary artery bypass, using venous graft(s) and arterial graft(s); 2 venous grafts
	33519	Coronary artery bypass, using venous graft(s) and arterial graft(s); 3 venous grafts
	33521	Coronary artery bypass, using venous graft(s) and arterial graft(s); 4 venous grafts
	33522	Coronary artery bypass, using venous graft(s) and arterial graft(s); 5 venous grafts
	33523	Coronary artery bypass, using venous graft(s) and arterial graft(s); 6 or more venous grafts
	33533	Coronary artery bypass, using arterial graft(s); single arterial graft
	33534	Coronary artery bypass, using arterial graft(s); 2 coronary arterial grafts
	33535	Coronary artery bypass, using arterial graft(s); 3 coronary arterial grafts

	33536	Coronary artery bypass, using arterial graft(s); 4 or more coronary arterial grafts
	S2205	Minimally invasive direct coronary artery bypass surgery involving mini-thoracotomy or mini-sternotomy surgery, performed under direct vision; using arterial graft(s), single coronary arterial graft
	S2206	Minimally invasive direct coronary artery bypass surgery involving mini-thoracotomy or mini-sternotomy surgery, performed under direct vision; using arterial graft(s), two coronary arterial grafts
	S2207	Minimally invasive direct coronary artery bypass surgery involving mini-thoracotomy or mini-sternotomy surgery, performed under direct vision; using venous graft only, single coronary venous graft
	S2208	Minimally invasive direct coronary artery bypass surgery involving mini-thoracotomy or mini-sternotomy surgery, performed under direct vision; using single arterial and venous graft(s), single venous graft
	S2209	Minimally invasive direct coronary artery bypass surgery involving mini-thoracotomy or mini-sternotomy surgery, performed under direct vision; using two arterial grafts and single venous graft
8	Valvular heart disease:	
	ICD 9 Dx	Description
	093.21	Cardiovascular syphilis, mitral valve
	424.0	Mitral valve disorders
	424.1	Aortic valve disorders
	424.2	Tricuspid valve disorders, specified as nonrheumatic
	424.3	Pulmonary valve disorders
	424.90	Endocarditis, valve unspecified, unspecified cause
	424.91	Endocarditis in diseases classified elsewhere
	424.99	Other endocarditis, valve unspecified
	391.1	Acute rheumatic endocarditis
	394.0	Mitral stenosis
	394.1	Rheumatic mitral insufficiency
	394.2	Mitral stenosis with insufficiency
	394.9	Other and unspecified mitral valve diseases
	395.0	Rheumatic aortic stenosis

	395.1	Rheumatic aortic insufficiency
	395.2	Rheumatic aortic stenosis with insufficiency
	395.9	Other and unspecified rheumatic aortic diseases
	396.0	Mitral valve stenosis and aortic valve stenosis
	396.1	Mitral valve stenosis and aortic valve insufficiency
	396.2	Mitral valve insufficiency and aortic valve stenosis
	396.3	Mitral valve insufficiency and aortic valve insufficiency
	396.8	Multiple involvement of mitral and aortic valves
	396.9	Mitral and aortic valve diseases, unspecified
	397.0	Diseases of tricuspid valve
	397.1	Rheumatic diseases of pulmonary valve
	397.9	Rheumatic diseases of endocardium, valve unspecified
	746.0	Anomalies of pulmonary valve
	746.00	Congenital pulmonary valve anomaly, unspecified
	746.01	Atresia of pulmonary valve, congenital
	746.02	Stenosis of pulmonary valve, congenital
	746.09	Other congenital anomalies of pulmonary valve
	746.1	Tricuspid atresia and stenosis, congenital
	746.2	Ebstein's anomaly
	746.3	Congenital stenosis of aortic valve
	746.4	Congenital insufficiency of aortic valve
	746.5	Congenital mitral stenosis
	746.6	Congenital mitral insufficiency
	746.7	Hypoplastic left heart syndrome
	996.02	Mechanical complication due to heart valve prosthesis
	996.71	Other complications due to heart valve prosthesis
9	Cardiac muscle disease:	

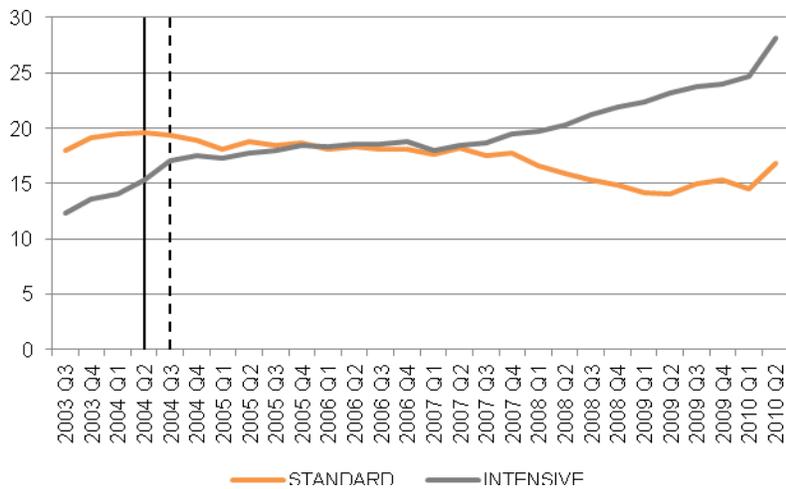
	ICD 9 Dx	Description
	425.x	Cardiomyopathy
	429.0	Myocarditis, unspecified
	429.1	Myocardial degeneration
	429.6	Rupture of papillary muscle
	429.81	Other disorders of papillary muscle
10	Ventricular tachycardia:	
	ICD 9 Dx	Description
	427.1	Paroxysmal ventricular tachycardia
12	Positive stress test	
	ICD 9 Dx	Description
	794.39	Other nonspecific abnormal function study of cardiovascular system

eAppendix E.

We conducted a separate analysis and replicated the study results using a stricter set of criteria described in the clinical trial (without relaxation) to analyze quarterly trends among a smaller group of enrollees. Results from this analysis are shown for reference purposes only, below.

PROVE-IT

Prescription Utilization Rate (Days Supplied per Enrollee): Standard and Intensive Statin Therapy



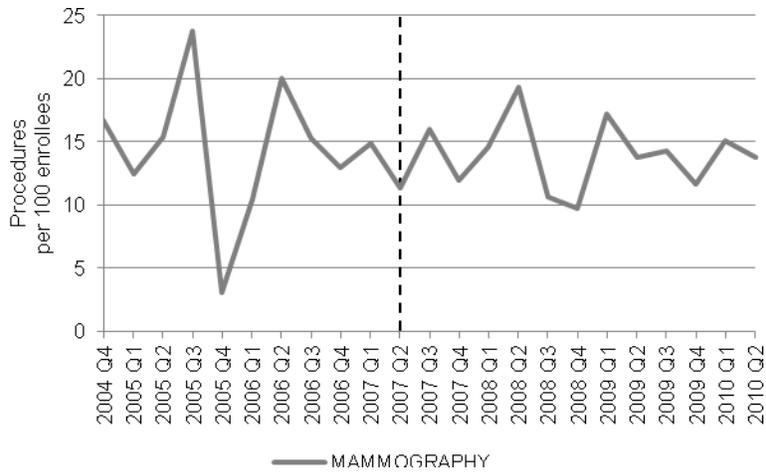
Study Published: 2004 Q2 (Cannon, et al)
Guideline Published: 2004 Q3 (Grundy, et al)

Quarter	2003 Q4	2004 Q2	2004 Q4	2005 Q2	2005 Q4	2006 Q2	2006 Q4	2007 Q2	2007 Q4	2008 Q2	2008 Q4	2009 Q2	2009 Q4	2010 Q2
Months since publication	-6	0	6	12	18	24	30	36	42	48	54	60	66	72
Months since guideline	-9	-3	3	9	15	21	27	33	39	45	51	57	63	69
Intensive	13.57	15.34	17.49	17.74	18.39	18.56	18.78	18.43	19.50	20.28	21.87	23.20	23.97	28.17
Standard	19.17	19.56	18.92	18.78	18.64	18.28	18.10	18.17	17.75	15.92	14.91	14.04	15.35	16.79
% change Intensive		13.0	14.0	1.4	3.7	0.9	1.2	-1.9	5.8	4.0	7.9	6.1	3.3	17.5
% change Standard		2.0	-3.2	-0.8	-0.7	-1.9	-1.0	0.4	-2.3	-10.3	-6.3	-5.8	9.3	9.4

MAMMOGRAPHY WITH MRI

Mammography with MRI Utilization Rate (Procedures per 100 Enrollees)

Panel A. – Mammography Utilization

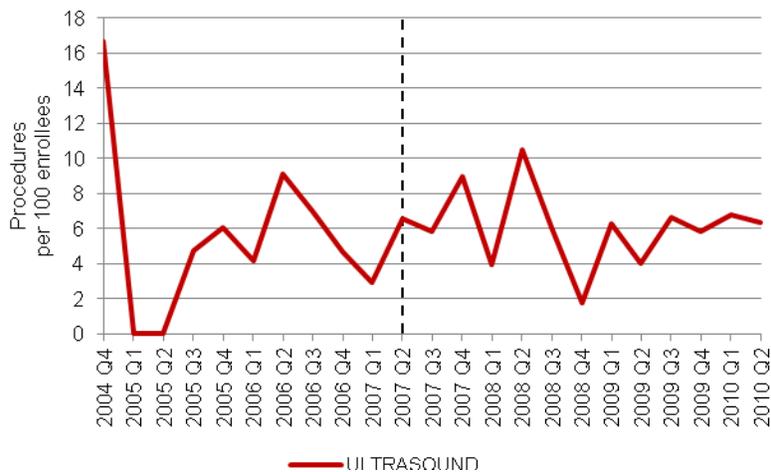


Study Published: 2004 Q3 (Warner, et al)

Guideline Published: 2007 Q2 (Saslow, et al)

The code for BRCA sensitivity was added in October 2004. No way to code previously.

Panel B – Breast Ultrasound Utilization

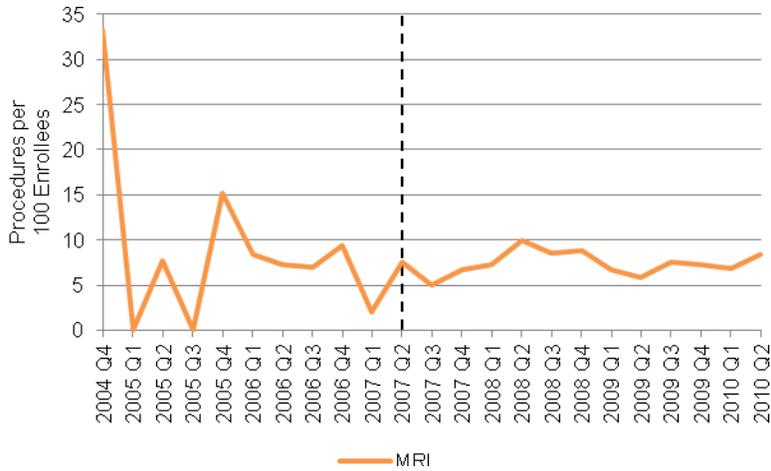


Study Published: 2004 Q3 (Warner, et al)

Guideline Published: 2007 Q2 (Saslow, et al)

The code for BRCA sensitivity was added in October 2004. No way to code previously.

Panel C – Breast MRI Utilization



Study Published: 2004 Q3 (Warner, et al)

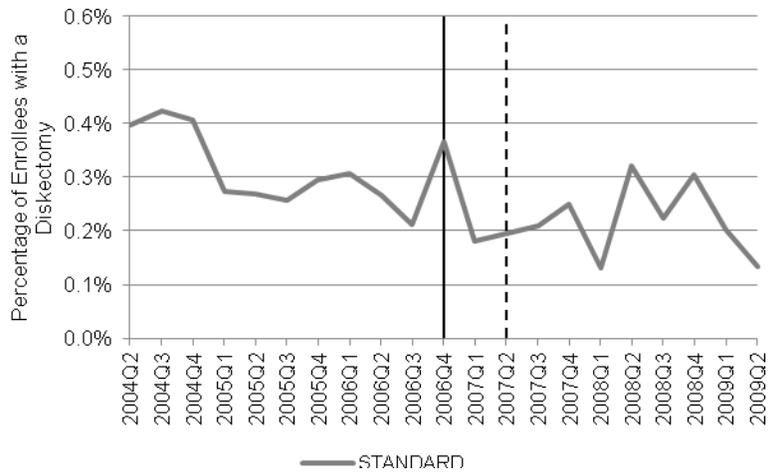
Guideline Published: 2007 Q2 (Saslow, et al)

The code for BRCA sensitivity was added in October 2004. No way to code previously.

Quarter	2005 Q2	2006 Q1	2006 Q4	2007 Q3	2008 Q2	2009 Q1	2009 Q4
Months since publication	9	18	27	36	45	54	63
Months since guideline	-24	-15	-6	3	12	21	30
MRI	7.69	8.33	9.41	5.04	9.94	6.64	7.24
Mammography	15.38	10.42	12.94	15.97	19.34	17.19	11.70
Ultrasound	0.00	4.17	4.71	5.88	10.50	6.25	5.85
% change MRI		8.3	12.9	-46.4	97.2	-33.2	9.1
% change Mammography		-32.3	24.2	23.4	21.1	-11.1	-31.9
% change Ultrasound		0.0	12.9	25.0	78.5	-40.5	-6.4

SPORT

Standard Discectomy Utilization Rate (Percent of Enrollees with Procedure)



Study Published: 2006 Q4 (Weinstein, et al)
 Guideline Published: 2007 Q2 (Chou, et al)

Quarter	2004 Q2	2004 Q4	2005 Q2	2005 Q4	2006 Q2	2006 Q4	2007 Q2	2007 Q4	2008 Q2	2008 Q4	2009 Q2	2009 Q4
Months since publication	-30	-24	-18	-12	-6	0	6	12	18	24	30	36
Months since guideline	-36	-30	-24	-18	-12	-6	0	6	12	18	24	30
Standard	0.40	0.41	0.27	0.29	0.27	0.37	0.20	0.25	0.32	0.30	0.13	0.33
% change		2.7	-33.9	9.3	-9.2	36.7	-46.6	27.8	28.5	-5.2	-56.1	147.6

COURAGE
Utilization Rate of Percutaneous Coronary Intervention (PCI) (Procedures per 100 Enrollees)



Study Published: 2007 Q2 (Boden, et al)

Guideline Published: 2007 (American College of Cardiology)

Note: OMT is administered on an outpatient basis therefore cannot be fully observed in claims data.

Quarter	2004 Q2	2004 Q4	2005 Q2	2005 Q4	2006 Q2	2006 Q4	2007 Q2	2007 Q4	2008 Q2	2008 Q4	2009 Q2	2009 Q4
Months since publication	-36	-30	-24	-18	-12	-6	0	6	12	18	24	30
Months since guideline	-44	-38	-32	-26	-20	-14	-8	-2	4	10	16	22
PCI	1.57	1.38	1.27	1.09	1.22	1.30	1.11	1.13	1.26	1.28	1.67	1.42
% change		-12.2	-8.1	-13.7	11.5	6.3	-14.7	2.5	11.1	1.4	30.8	-14.7