Comment

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The US Patent Office issued the first patent for a drug-eluting stenting (DES) device in 1997. By 2004, the new technology had transformed the way that patients with coronary artery disease were managed in the United States and elsewhere. The new technology built on an existing technology—coronary artery catheterization and stenting. The DES are now a commonly applied technology, with over a half million patients having a DES placed each year (Roger et al. 2012). In this chapter, Chandra, Malenka, and Skinner ask an important series of questions—which providers were most likely to adopt drug-eluting stents, what motive best explains adoption, and how did the diffusion process affect the welfare of patients? These are important questions because the diffusion of new medical technology plays such a pivotal role in explaining both why American health care is so expensive and why it is broadly seen as providing cutting edge care.

Medical Background

To understand the economics underlying the diffusion of DES devices, a bit of background medicine is necessary. The heart is a muscle, and like any muscle, requires a steady supply of oxygenated blood to survive. The heart muscle is supplied by multiple coronary arteries to perform this function. With each heartbeat, healthy coronary arteries guarantee that the heart receives the oxygen it needs to keep beating.

Unfortunately, the coronary arteries are prone to becoming clogged with atherosclerotic plaques. These plaques impede the flow of blood into the heart muscle and promote the development of blood clots that further reduce blood flow. If these plaques and clots entirely obstruct blood flow within a coronary artery, the muscle tissue normally supplied by that artery is deprived of oxygen and starts to die. A heart attack (or acute myocardial infarction) is what happens when part of the heart muscle dies due to constricted blood flow from the coronary arteries. Coronary artery disease is one of the most common causes of death in the United States.

The prevention and treatment of heart disease follows from this basic biology. Daily low-dose aspirin, for instance, prevents clot formation and hence reduces heart disease risk. A healthy diet reduces the substrates that promote atherosclerotic plaque formation. For patients with substantial blockage of one or more coronary arteries, treatment is focused on restoring clear blood flow to heart muscles. Coronary artery bypass grafts (CABG), for instance, involve open heart surgery to directly replace diseased coronary arteries with vessels that have no plaque. A less invasive procedure, coronary
angioplasty, involves inserting a catheter (or long narrow tube) into the coronary artery and taking action to clear the plaque from within the artery itself.

A major problem with both CABG and coronary angioplasty is that the coronary arteries tend not to stay clear of atherosclerotic plaque forever. Restenosis is the process of the cleared coronary arteries becoming blocked again, placing a patient at risk of a heart attack. If restenosis is detected, patients may need to undergo a repeat CABG or angioplasty.

Stents are small metal tubes, placed during angioplasty at the site of the blocked artery, to prevent restenosis. While bare-metal stents can be effective in reducing restenosis rates, even with such stents, restenosis can happen. One reason for this is that the cell lining of coronary arteries (called endothelium) plays a key role in the development of atherosclerotic plaques and in restenosis. Healthy endothelial cells prevent atherosclerotic plaque formation, while diseased cells—and scar tissue caused by stent placement—promote restenosis.

Drug-eluting stents (DES) prevent restenosis by incorporating powerful immunosuppressive drugs (like sirolimus or everolimus) or chemotherapeutic agents (like paclitaxel) into the stent. These drugs, which are delivered over time to coronary artery endothelial cells, for various reasons, prevent or slow the process of the coronary arteries becoming blocked again. At the same time, the process of placing a DES can itself cause damage to the endothelial lining and promote clot formation, so DES patients often need to take powerful anticlotting drugs for years after stent placement.

**A Brief Timeline**

Given this medical background, the rapid adoption of DES into medical practice should not be surprising. The following is a brief timeline of events that are crucial to understanding the dissemination of DES into practice in the United States.1 The key events involve clinical science and regulatory action. Crucially, between 2002 and 2008, Medicare paid the same fee for patients undergoing DES placement in multiple coronary arteries as it paid for patients undergoing DES placement in one coronary artery.

- 1997: First patent filed for sirolimus-eluting stents.
- 2001–2002: First randomized evidence shows that DES could reduce restenosis rates relative to coronary angiography using bare-metal stents (BMS) (e.g., Morice et al. 2002).
- 2002: The Center for Medicare and Medicaid Services (CMS) authorizes higher reimbursement for angioplasty with drug-eluting stents; no separate codes, though, for multivessel DES placement.

1. This timeline is based in part on Stefanini and Holmes’s (2013) review of the literature on DES.
• 2004: The FDA approves paclitaxel DES.
• 2006–2007: New evidence emerges that sirolimus and paclitaxel stents increase the rate of clot formation at the site of the stent (e.g., Dae-men et al. 2007); physicians start putting DES patients on long-term anticlotting agents.
• 2007: The FDA approves zotarolimus-eluting stents. Physicians switch away from sirolimus stents.
• 2008: CMS introduces new billing codes to reimburse providers a higher amount for multivessel stenting.
• 2012: More than 500,000 DES placed in American patients with coronary artery disease per year.

Theories of Technological Diffusion

Chandra, Malenka, and Skinner offer three different, though not mutually exclusive, possible mechanisms for the spread of DES technology into practice. Their delineation of the possible mechanisms provides a helpful way to think about the ways in which the process of technological dissemination in medicine is helpful and harmful to patients, both from a medical and from an economic point of view. They also test the four mechanisms against Medicare data to measure the empirical importance of them. They rely on data from 2003 to 2004, a period of time when DES technology was popular but had not yet matured into practice. This is a particularly interesting period to study for technology diffusion because it focuses attention on early adopters. Though none of their empirical tests are definitive, they are all interesting and point toward ways to generate better information.

The first mechanism Chandra, Malenka, and Skinner explore is the profit motive. The idea is simple: health care providers will adopt a new technology if and only if doing so improves the bottom line. There is undoubtedly a lot of truth to this idea; health care providers, whatever their charitable instincts, cannot afford to stay in business indefinitely losing money, and there is a wealth of evidence in the health economics literature in supporting. In Italy, for instance, Grilli, Guastaroba, and Taroni (2007) argue that private hospitals with highly profitable open heart surgical suites have little incentive to provide DES to patients in lieu of a CABG, while the opposite is true in public hospitals. Accordingly, they find that public hospitals in Italy were much quicker to adopt DES than private hospitals.

Chandra, Malenka, and Skinner employ a similar empirical strategy in the American context—they compare the adoption rate of DES by for-profit hospitals against the adoption rate by nonprofit hospitals. Unlike the Italian context, however, it is not true that the placement of DES during this period was always profitable. DES placement for Medicare patients with multivessel coronary artery disease, for instance, was most likely unprofitable for hospitals, since Medicare’s billing codes during that period did not
The second mechanism that Chandra, Malenka, and Skinner explore is also simple and persuasive: hospitals that were most likely to have experience with DES during its development and testing periods before FDA approval in 2003 are also the ones most likely to adopt the technology quickly. They test this idea by comparing the adoption rates of teaching hospitals against nonteaching hospitals. They reason correctly that the former were more likely to have prior experience with DES placement. The adoption data do in fact confirm that teaching hospitals adopted DES faster than nonteaching hospitals. Perhaps a future analysis could directly measure which teaching hospitals participated in the testing of DES on patients in the pre–2003 era, and compare their uptake against teaching hospitals that did not.

The third mechanism is one of knowledge spillovers—a hospital is more likely to adopt DES technology if doctors in a nearby hospital adopt DES technology. In principle, this could happen for many reasons. For instance, some doctors have admitting privileges to several hospitals. This would induce a mechanical correlation between the hospital-level adoption rates of DES, as long as doctors practice the same way at every hospital. Another possibility is that providers adopt the technology to gain a competitive advantage over the other providers in a market. Or finally, perhaps there is direct transfer of knowledge and expertise from doctor to doctor within a community about the use of the new technology. All of these stories are consistent with Chandra, Malenka, and Skinner's finding of a correlation between a hospital's adoption rate of DES and the adoption rate of other hospitals in a market.

Allocation of New Technologies to Patients

In a separate analysis, Chandra, Malenka, and Skinner study the effects of rapid diffusion of DES on patient outcomes. This complements a prominent earlier study involving two of the three authors, which found that the spread of DES technology decreased restenosis rates in the Medicare population (Malenka et al. 2008). Here, Chandra, Malenka, and Skinner study whether hospitals located in places where DES diffusion was slow had worse outcomes than those located in places where diffusion was fast. This is an important question because, like many new medical technologies, supplies of drug-eluting stents were limited in the 2002–2003 period when they were first introduced. A rational allocation process would send those limited supplies to areas where there are patients who stand to benefit the most from the new technology.

Chandra et al. divide up their sample into quintiles based on the rate of adoption of DES. Table 11C.1 reorganizes the point estimates from the
Chandra et al. logistic regression analyzing the probability of a repeat angioplasty procedure for hospitals in the various diffusion quintiles. The table reports odds ratios of a repeat angiography relative to a hospital in a rapid adoption quintile. Table 11C.2 does the same for the probability of patient death or heart attack following coronary angioplasty.

There are two striking findings. First, even before the introduction of DES, patients treated at hospitals that ultimately were slow to adopt DES had lower odds of a repeat coronary angiography, but higher odds of death or a heart attack. Second, the fastest adopting hospitals had the largest improvements in patient outcomes. Together, these findings suggest that the allocation process of new technologies appropriately started with the best-prepared providers.

This is an optimistic take-home message about the American health care system, but this optimism should be tempered when considering the welfare of the early adopting patients. In 2003, when DES diffused into medical practice, there was much that was not known about how best to manage patients with drug-eluting stents. For instance, the fact that many patients should be placed on anticlotting drugs for an extended period after the DES placement was not known. Further, the drug used (sirolimus) has subsequently been replaced by other immunosuppressive agents that apparently produce better outcomes. Any comprehensive welfare analysis of technological spread should account for the fact that early adopters serve as test subjects for the development of the technology, even after it has been approved for use by the various regulatory authorities.

### Table 11C.1 Odds ratios from patient-level regression of repeat coronary angiography

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<th>Pre-DES</th>
<th>Post-DES</th>
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<tr>
<td>Q1 (low diffusion)</td>
<td>0.971</td>
<td>1.014</td>
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<tr>
<td>Q2</td>
<td>0.97</td>
<td>0.812</td>
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<tr>
<td>Q3</td>
<td>0.99</td>
<td>0.891</td>
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<tr>
<td>Q4</td>
<td>1.026</td>
<td>0.909</td>
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<tr>
<td>Q5 (high diffusion)</td>
<td>1</td>
<td>0.866</td>
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### Table 11C.2 Odds ratios from patient-level regression of death or heart attack

<table>
<thead>
<tr>
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<th>Pre-DES</th>
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</thead>
<tbody>
<tr>
<td>Q1 (low diffusion)</td>
<td>1.199</td>
<td>1.161</td>
</tr>
<tr>
<td>Q2</td>
<td>1.034</td>
<td>1.081</td>
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<tr>
<td>Q3</td>
<td>1.121</td>
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<tr>
<td>Q4</td>
<td>1.018</td>
<td>1.008</td>
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<tr>
<td>Q5 (high diffusion)</td>
<td>1</td>
<td>0.918</td>
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*Note: Technically, Chandra, Malenka, and Skinner study ST-elevation myocardial infarctions.*
References


