SAN ANTONIO — There is little that Dr. Lindsay Irvin has not done for the children’s vaccines in her office refrigerator: She remortgaged her home to afford their rising prices. She packed them in ice chests and moved them when her office flooded this year. She pays a company to monitor the fridge in case the temperature rises.

“The security company can call me any time of the day or night so I can go save my vaccines,” said Dr. Irvin, a pediatrician. Those in the refrigerator recently cost $70,000, she said — “more than I
paid for four years of medical school.”

Vaccination prices have gone from single digits to sometimes triple digits in the last two decades, creating dilemmas for doctors and their patients as well as straining public health budgets. Here in San Antonio and elsewhere, some doctors have stopped offering immunizations because they say they cannot afford to buy these potentially lifesaving preventive treatments that insurers often reimburse poorly, sometimes even at a loss.

Childhood immunizations are so vital to public health that the Affordable Care Act mandates their coverage at no out-of-pocket cost and they are generally required for school entry. Once a loss leader for manufacturers, because they are often more expensive to produce than conventional drugs, vaccines now can be very profitable.

Old vaccines have been reformulated with higher costs. New ones have entered the market at once-unthinkable prices. Together, since 1986, they have pushed up the average cost to fully vaccinate a child with private insurance to the age of 18 to $2,192 from $100, according to data from the Centers for Disease Control and Prevention. Even with deep discounts, the costs for the federal government, which buys half of all vaccines for the nation’s children, have increased 15-fold during that period. The most expensive shot for young children in Dr. Irvin’s refrigerator is Prevnar 13, which prevents diseases caused by pneumococcal bacteria, from ear infections to pneumonia.

Like many vaccines, Prevnar requires multiple jabs. Each shot is priced at $136, and most states require children to get four doses before entering day care or preschool. Pfizer, the sole manufacturer, had revenues of nearly $4 billion from its Prevnar vaccine line last year, about double what it made from high-profile drugs like Lipitor and Viagra, which now face generic competitors.
A Fort Knox of Vaccines
Dr. Lindsay Irvin keeps about 20 different vaccines, worth about $34,000, in this refrigerator. This represents her current supply, which is about half the value that would be present at the start of the camp season or before school starts. A few of the most expensive and common vaccines are listed.

Dr. Irvin
ON THE DIFFICULTIES OF AFFORDING VACCINES

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Description</th>
<th>Dose/Price</th>
</tr>
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<tbody>
<tr>
<td>DTaP</td>
<td>Diphtheria, tetanus, pertussis</td>
<td>48 doses $25</td>
</tr>
<tr>
<td>Prevnar 13</td>
<td>Pneumococcal disease</td>
<td>10 doses $135</td>
</tr>
<tr>
<td><strong>TOP SHELF TOTAL</strong></td>
<td></td>
<td><strong>$6,864</strong></td>
</tr>
<tr>
<td>Menactra</td>
<td>Meningitis and others</td>
<td>20 doses $112</td>
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<tr>
<td>MMR</td>
<td>Measles, mumps, rubella</td>
<td>23 doses $56</td>
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<tr>
<td><strong>2ND SHELF TOTAL</strong></td>
<td></td>
<td><strong>$9,302</strong></td>
</tr>
<tr>
<td>FluMist</td>
<td>These were not used, and their value is a total loss. 90 doses at $22</td>
<td></td>
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<tr>
<td><strong>3RD SHELF TOTAL</strong></td>
<td></td>
<td><strong>$11,610</strong></td>
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<tr>
<td>Varicella</td>
<td>Chickenpox. 43 doses at $94</td>
<td></td>
</tr>
<tr>
<td><strong>FREEZER TOTAL</strong></td>
<td></td>
<td><strong>$4,048</strong></td>
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</table>

Source: Centers for Disease Control and Prevention
Photograph by Ben Sklar for The New York Times

Michael Haydock, an analyst at the London-based consulting firm Datamonitor Healthcare, said no vaccine had ever been such a big seller. “It’s expensive in part because it’s a very effective vaccine,” he said. “And also because they’re exploiting their monopoly.”

That does not sit well with many doctors. Even though the vaccine has not changed, the price of the current version, Prevnar 13 (it protects against 13 strains), has gone up an average of 6 percent each year since it
was approved by the Food and Drug Administration in 2010.

“You have to make back your investment and pay your shareholders, but at what point do you say, ‘Look, you’ve had your steak, gravy and potatoes and this is enough?’” said Dr. Steven Black, a vaccine expert at Cincinnati Children’s Hospital who served on the government committee that recommended all children get Prevnar 7, an earlier version of the vaccine.

To deal with the rising prices, some doctors, who say they lose money on every vaccination, reserve their shots for longstanding patients. A survey of family-practice doctors, who along with pediatricians are among the lowest-earning physicians, found that about one-third were considering giving up immunizations because of the expense. Another survey found that 40 percent do not offer at least some required childhood immunizations.

That is why Breanna Farris, a San Antonio mother, had to call 10 pediatricians in April before she found Dr. Irvin to vaccinate her son, Traven, who is entering kindergarten this fall. The family’s usual doctors do not offer vaccinations, and referred Ms. Farris to local pharmacies (which do not vaccinate children) or the city health clinic (which would not take Traven’s insurance).

“I was like, ‘Where should I go?’” Ms. Farris said. “They say vaccines are covered, but that isn’t really true if doctors aren’t giving them.”

Business Decisions

To many pediatricians, not providing vaccines is as unthinkable as a baker not selling bread. Before they became widely available in the mid-20th century, tens of thousands of American children died each year from diseases like polio, whooping cough and diphtheria. “It’s up there with finding fire and the invention of the wheel,” said Dr. Irvin, 51, of vaccines.

Vaccines work by stimulating the body to develop immunity to a particular disease. The process involves injecting a molecule under the skin that mimics the virus or bacteria to prime the immune system to attack the real thing when it arrives. Vaccines can contain a fragment of the pathogen or a
Weakened version that can teach the immune system to recognize a germ, without itself causing the disease.

The earliest vaccines were not patented, in part because the law at the time held that natural products could not be so protected. And vaccines like polio were developed through a large infusion of government and foundation funds, not by a company. Even when commercialized by the 1960s, vaccines were made by small specialty manufacturers, instead of big pharmaceutical firms, since producing them involved particular challenges: using live organisms, some of them dangerous. Indeed, huge liability payouts and aggressive mergers had, by the 1990s, meant that more than half of the country’s vaccine makers had closed down. With low retail prices, no one regarded vaccine making as a lucrative business.

When he started his pediatric practice in 1982 in San Antonio, Dr. Michael Ozer remembers, he charged $22 for a 2-month well-child checkup, with $8 added on for the polio vaccine and another $8 for the vaccine against diphtheria, pertussis and tetanus. “And I’m sure we were making money on it,” he said.

But one by one, various barriers eroded: Drug manufacturers discovered new ways to protect their products, like patenting the manufacturing process. The number of vaccine patent applications rose tenfold in the 1990s to more than 10,000. In 1988, the federal government set up the Vaccine Injury Compensation Program, effectively shielding manufacturers and doctors.

And the acceptable list price for drugs was rising. Vaccines, which families often used to pay for out of pocket, are now typically covered by insurance, and patients often do not notice the prices.

There are, of course, some good reasons vaccines like Prevnar are more expensive than previous offerings. Vaccine trials, which once included thousands of volunteers, must now include tens, if not hundreds of thousands of people, as fears about side effects like autism have grown, even
though many studies have concluded that such worries are unfounded. Some of the newer vaccines are complicated to manufacture.

Prevnar, for example, involves attaching a piece of a dangerous bacterium’s outer layer to a protein that renders it better able to provoke a protective immune reaction in babies. And because it covers 13 strains of the disease, it is in some ways 13 vaccines in one.

Pfizer maintains that Prevnar’s prices are justified because of its investment in “one of the most complex biologic products ever developed and manufactured,” said Sally Beatty, a company spokeswoman. She noted that it takes five years and costs $600 million to build a vaccine manufacturing site, and that one batch of Prevnar 13 takes two years to create, with more than 500 quality control tests. Development of the first Prevnar vaccine took 14 years, Ms. Beatty said, from the initiation of research to licensing. (That work occurred before Pfizer acquired the Prevnar brand in 2009 when it bought Wyeth Laboratories, which had in turn acquired it from smaller companies.)

“It’s a risky business developing vaccines, so you can explain — if not necessarily justify — the higher costs of vaccination,” said Dr. Alan Hinman, a former head of the immunization division of the C.D.C. and now a senior scientist at the Task Force for Global Health in Georgia. “A more difficult question is, after the research and development costs are recouped, why don’t prices come down?”

For a 2-month well-child checkup in 2014, Dr. Ozer charges $115. And the vaccine charges have grown to $725, for which insurers like Blue Cross/Blue Shield reimburse $613.79.

Cost vs. Benefit

For most prescription medicines, the crucial hurdle to marketing is to win Food and Drug Administration approval. But for vaccines, the prize is the imprimatur of the federal Advisory Committee on Immunization Practices.
Once the committee recommends a shot for all children, states usually require children to get it before entering day care or school; insurers have to cover it, at least nominally. (Many states require home-schooled children to be vaccinated as well.) “We have to give it to every kid, so it’s a golden ticket,” Dr. Irvin said.

That requirement is a powerful incentive: Last year, Ms. Farris’s older child, Lenna, missed the first week of school as Ms. Farris, then new to Texas, searched for a provider willing to vaccinate the girl. Desperate, Ms. Farris took her daughter to a public health clinic and lied, saying she had no insurance. She found Dr. Irvin to immunize her son only this year.

WHERE SHOULD I GO? Breanna Farris searched frantically for doctors to immunize her children, Traven, left, and Lenna. Ben Sklar for The New York Times

The value of that “school mandate” is also apparent in the pricing. When Singapore’s national vaccine advisory group evaluated Prevnar 7 for mandated use, its price was about $80, said Karen Tyo, a researcher from
Brandeis University, who was advising the government. After the government included it in the required national schedule, “the price jumped immediately” to about $120, she said. “Nothing had changed,” she noted. “It didn’t make any sense.”

To evaluate new vaccines for inclusion on mandated lists, national vaccine panels assess a vaccine’s cost benefit ratio. (F.D.A. approval requires that companies show vaccines are “safe and effective.” Cost is not considered.) Will the cost of buying and administering the vaccine result in a substantial payback for patients and society at large? That is a complicated, often nebulous, calculation.

Even before the advent of Prevnar, children under 5 rarely died of pneumococcal illness — about 200 in the United States annually, according to the C.D.C. So, in urging countries to adopt Prevnar 13, Pfizer produced extensive studies emphasizing the vaccine’s broad indirect benefits, such as reductions in a parent’s lost work time as well as the fact that the grandparent of an immunized baby is less likely to contract the disease. The company also factored in the ear infections Prevnar might prevent in children, even though most of those could be treated with antibiotics.

A C.D.C. economic review based on data from earlier studies estimated that in 2009, Prevnar prevented 2.3 million cases of pneumococcal disease including ear infections, 5,056 deaths of all ages, and saved $965 million in direct costs and $2.7 billion in societal costs in the United States.

But when Prevnar 7 was first evaluated in 2000 for universal vaccination of children in the United States, the vaccine advisory committee concluded it was not likely to be cost effective, said Dr. Black, who was on the panel. In a study around that time, Dr. Black and colleagues concluded that the vaccine would result in cost saving for society only if each dose was priced at $46. It entered the market, though, at $58 a shot.

The committee decided to approve it anyway because it would save a few families from the tragedy of an infant’s death; the vaccine later proved more effective than the study had anticipated.

Most other developed countries demand better cost-effectiveness numbers before approval and can use that to negotiate for discounts, said Anthony Newall, a health economist at the University of New South Wales in Australia.
The Swiss Agency for Therapeutic Products pays $101, a price that has not changed over time. In Britain, the small private health care market sells prefilled syringes of Prevnar 13 for an average of $82 at pharmacies; the National Health Service pays even less, experts say. Prefilled syringes cost an average of $136 in the United States, and even the C.D.C. — which buys vaccines for the Medicaid program at a discount — pays $112.84.

Other countries have also diverged from the United States in how they deploy Prevnar 13, generally giving only three shots instead of four. Studies have shown that the protection is almost as good, particularly against the serious forms of the disease. “There’s virtually no benefit,” Dr. Black said. “We’re basically paying an extra $100-plus per child for nothing.”

The Vaccine Market

Every week or two, Dr. Irvin sits down at her computer to buy vaccines. With more than 3,000 patients in her practice, she estimates that it would cost her $70,860 a month to be fully stocked with vaccines for any patient who walked in the door. Instead, she buys sparingly for scheduled appointments and looks for manufacturers’ bargains.

Online, there are back-to-school sales, closeout sales on last year’s models and discounts for early booking. Dr. Irvin buys vaccines for polio, whooping cough, tetanus and hemophilus meningitis from Sanofi-Pasteur on a site called the Vaccine Shoppe. “I feel like I’m going to a boutique,” she commented while completing a recent purchase.

Because Dr. Irvin belongs to a purchasing cooperative of Texas pediatricians, the prices are often discounted 5 to 10 percent from the list price. But rates often fluctuate: On the Merck website, she noticed that the price of the vaccine against human papillomavirus had gone up from the previous week. She decided to buy vials rather than prefilled syringes.
because she would save about $1.50 a dose on a price of $132.46 a shot. “That’s make or break it,” she noted.

Likewise she buys vials, rather than syringes, for the measles, mumps, rubella vaccine to lower the cost to $51.20 a dose. In 2002, the same vaccine was $27.70 for private doctors. Because some companies require that each physician sign a legal agreement not to disclose the price he or she paid, there is little informed shopping. “I was kind of aghast, I didn’t think it could be legal, but it is,” said Dr. Gary L. Freed, a pediatrician at the University of Michigan School of Public Health who has studied vaccine purchases. “And it’s certainly a very inefficient market since it means physicians don’t have information to bargain.”

The result is much like that in other aspects of American medicine: Huge price variations for the same item or service. Large group practices that have purchasing clout with drug makers and insurers may make a profit from providing vaccines, while solo practices, like Dr. Irvin’s, can incur losses. Some doctors pay three times as much as others in the same city, Dr. Freed’s studies have found. One large practice was yielding $39 per dose of Prevnar, while 11 percent of practices were losing money on it.

Private insurers pay doctors a median of $145 for Prevnar, according to data compiled by Athena Health. Dr. Jeffrey J. Cain, the board chairman of the American Academy of Family Physicians, noted that reimbursement from insurers runs between 40 and 100 percent of the vaccine’s purchase cost, which often does not allow for overhead such as insurance, storage
and the computer record-keeping systems required by the federal government.

Dr. Irvin says she loses money every time she gives a shot.

A Wide World of Prices

It is not clear how much Pfizer is profiting from Prevnar in the United States. But one measure is to look at the price at which Pfizer sells Prevnar for use in the poorest countries through a World Health Organization initiative: $3.30 a dose. Even at those prices, “I do not think pharmaceutical manufacturers are losing money,” said Dr. Hinman, the former C.D.C. official.

Since Pfizer bought Wyeth Pharmaceuticals and acquired Prevnar, its most visible research efforts have involved studies to prove its value. Company scientists have shown, for example, that Prevnar 13 is more cost effective than Synflorix, a competing vaccine made by GlaxoSmithKline that is far cheaper, but is effective against only 10 strains. It is not available in the United States.

This year, Pfizer submitted a new study to the C.D.C. showing that Prevnar 13 is effective in preventing pneumonia in people over 65, and is hoping that the vaccination committee will recommend it for all Americans over 50. People in that age group typically get a different type of vaccine against pneumococcal bacteria that has been around for decades and is only $30, but is not effective in babies.

Dr. Hinman said Prevnar 13 is a “really good vaccine” that is probably more effective than the older version, and he himself hopes to get it once it is available. But in 2012, when Pfizer tried to get Prevnar 13 recommended for use in adults in Britain, the Joint Committee on Vaccination and Immunization said no because of the cost. If the United States recommends it for use in all healthy adults, analysts say it will mean an additional $1 billion in annual sales for Pfizer.
The C.D.C., which declined an interview for this article, must walk a delicate line pressing drug companies to modulate prices: When there is one manufacturer, as with Prevnar 13, the company could raise charges or slow production, creating disastrous shortages.

“What leverage does the C.D.C. have really?” Dr. Freed asked. “They’re in a terrible bind and it will only get worse as prices rise.”

Rising Vaccine Prices
The cost of recommended vaccines from birth to age 18 has risen sharply.

$1,255
Eight new vaccines added since 1986

Note: Adjusted for inflation
Source: Centers for Disease Control and Prevention
The New York Times

Meanwhile, Dr. Irvin feels the pressure as other doctors stop offering shots, and parents like Ms. Farris go searching.

Clark Petty, who runs a public immunization clinic in San Antonio, said his store of vaccines from the C.D.C. are meant for the poor and people without insurance. Patients with private insurance must pay full list price and an administration fee and would have to apply for reimbursement themselves.

The family practice doctor downstairs in Dr. Irvin’s office building has stopped immunizing children. A local obstetrician recently told her in tears that she cannot afford to give pregnant patients a shot recommended to boost the mother’s immunity to whooping cough, protection that is transferred to her unborn baby for the first months of after birth.

Nationally less than 10 percent of pregnant women are getting this recommended shot. Though there are many reasons women go unvaccinated, studies show that patients are far less likely to get a vaccine if their doctors do not offer it. And the consequences can be grave: Last year, two babies, each a month old, died of whooping cough here in San Antonio. Their mothers had not been vaccinated during pregnancy.

Correction: July 8, 2014
An article on Thursday about the high costs of vaccines for children contained several errors. The federal Advisory Committee on Immunization Practices recommends vaccines; it does not mandate them. (It is up to states to mandate vaccines for school entry.) Most states require vaccination with Prevnar, which protects against pneumonia and other diseases, before children can enter preschool or daycare; not all
states do. Additionally, the entity that produced an economic review that estimated the benefits of Prevnar was misidentified. It was the Centers for Disease Control and Prevention, not Pfizer, which manufactures the vaccine. The article also referred imprecisely to requirements by drug companies that physicians not disclose prices of medicines and vaccines. While many companies require doctors to sign such agreements, Pfizer does not require it for Prevnar.

For a continuing conversation about health care costs and pricing in the United States, please join our Facebook group, Paying Till It Hurts.

A version of this article appears in print on July 3, 2014, on page A1 of the New York edition with the headline: The Price of Prevention: Vaccine Costs Soaring. Order Reprints | Today's Paper | Subscribe