To the Gerald Loeb judges:

“Dangerous Doses” was an innovative, two-year investigation into the dangers of prescription drug combinations. The series prompted major reforms in corporate and government policies that will impact millions of people, with the potential to save lives for years to come.

America’s biggest pharmacy chains plan to take significant steps to improve patient safety at stores nationwide. The changes cover 22,000 drugstores and involve additional training for 123,000 pharmacists and technicians.

The series also sparked Illinois Gov. Bruce Rauner to take numerous safety measures and, in the field of science, created a new method to discover fatal drug interactions.

Experts say the moves represent the biggest steps in a generation to safeguard the public against the dangers of prescription drug interactions.

We set out with ambitious goals: to conduct the research Big Pharma wasn’t doing and to assess how well pharmacies perform one of their fundamental duties.

Work on the project began when investigative reporter Sam Roe received a tip that two well-known prescription drugs were interacting in dangerous ways. While researching the issue, Roe started to wonder whether there were other popular drug pairs that, unbeknownst to anyone, were causing sudden death. And if so, how could one possibly find them?

Intrigued by novel data-mining algorithms developed by scientist Nicholas Tatonetti of Columbia University Medical Center, Roe proposed that the two team up to search for drug combinations that might cause a potentially fatal heart condition. Roe also recruited Dr. Ray Woosley, the leading authority on that condition, to the team.

To orchestrate the project, Roe traveled to New York 12 times to meet with Tatonetti, brainstorm and analyze data. Tatonetti had access to Columbia’s vast patient archive, which was crucial to executing the experiment and validating the results. Several of Tatonetti’s graduate students joined the team, as did Columbia cellular researchers.

We believe that this was a fresh approach to investigative reporting – bringing people together to solve difficult problems and make discoveries. Roe wrote about his approach for the Columbia Journalism Review: http://tinyurl.com/zpux6nf Columbia University also embraced the collaboration: http://tinyurl.com/gqmk829

The Tribune’s pharmacy testing story — the largest and most comprehensive of its kind — was also inventive. Reporters Karisa King, Ray Long and Roe led the project, with 15 other journalists from seven newsroom departments participating. The logistics were daunting. What drug pairs should be used? How would tests be conducted? What would constitute a pass or fail?
The paper also meticulously considered the ethical and legal issues raised by testing pharmacies and working with a physician to obtain prescriptions. The team conducted a legal review; interviewed scientists who have used similar research methods; and consulted the Tribune’s ethics policy and ethical guidelines from the Poynter Institute.

Testing did not begin until top editors were confident that the process met the highest journalistic standards. The Tribune went to such lengths because everyone believed deeply in the public service mission. The team’s reporting suggested that if the paper didn’t pursue the story, patients might be harmed unnecessarily. CJR wrote about the project: https://tinyurl.com/jepg2et

The series achieved results, including:

**Broad industry reforms:** CVS said it will alter policies and computer systems at 9,600 stores; require pharmacists to warn about serious drug interactions, and mandate more transparent communication with patients on every prescription filled, roughly 1 billion a year. Walgreens said it will provide additional training for pharmacists at 8,175 stores. Wal-Mart said it will improve its alert system and require more training at 4,500 stores.

**Scientific discoveries:** The Tribune-Columbia team uncovered four drug pairs associated with a heart condition and, just as important, demonstrated an innovative model to detect dangerous interactions and save lives. Two scientific papers resulted, including one in a top cardiovascular journal. https://www.ncbi.nlm.nih.gov/pubmed/27737742

**Government action:** Illinois Governor Rauner ordered regulators to clamp down on pharmacy errors and proposed changes in code to ensure pharmacists discuss safety issues with customers. A leading Illinois state lawmaker introduced ambitious legislation; hearings are planned. Both U.S. Sen. Richard Durbin of Illinois and the head of the nation’s top association of pharmacy regulators called for new laws and policies.

The entire series, including reaction articles, editorials and videos, can be found at http://www.chicagotribune.com/news/watchdog/druginteractions/

Response from grateful readers poured in. “Truly astonishing,” tweeted one. Emailed another: “That is journalism at its absolute finest. Your reporting has literally saved lives.”

For their innovative, bold and collaborative approach to reporting, one that greatly impacted the pharmacy industry and will improve safety for millions of people, we proudly nominate Sam Roe, Karisa King and Ray Long for the Gerald Loeb Award for Investigative Reporting.

Sincerely,

George Papajohn
Associate Managing Editor for Investigations
“Dangerous Doses” by the Chicago Tribune

Investigative Reporting

List of elements:


Note to judges:

Entire series, including reaction articles, editorials and videos, can be found at http://www.chicagotribune.com/news/watchdog/druginteractions/

Reporter Sam Roe wrote about the innovative reporting approach for Columbia Journalism Review: http://tinyurl.com/zpxu6nf

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The Tribune-Columbia collaboration resulted in two published peer-reviewed scientific papers, including one in the Journal of the American College of Cardiology, a leading cardiovascular journal. https://www.ncbi.nlm.nih.gov/pubmed/27737742

The other paper was published in Drug Safety https://www.ncbi.nlm.nih.gov/pubmed/26860921
TRIBUNE WATCHDOG
DANGEROUS DOSES

Half of pharmacies fail to alert customers about serious drug interactions, Tribune testing found. Now major chains are promising safety fixes.

By Sam Roe, Ray Long and Karla Kimb | Chicago Tribune

The Tribune reporters dropped off prescriptions for two medications that can be harmful or even fatal if taken together. Other, pharmacists did not say a word about the risk.

Reporters dropped off prescriptions for two medications that can be harmful or even fatal if taken together. Other, pharmacists did not say a word about the risk.

Filled without warning

Cabdrivers struggle as ride-sharing raises

Medallions’ value plunges to $66K from $349K peak

By Lance Turner

Chicago Tribune

Chicago cab drivers and medallion owners are feeling the pinch of what they say is unfair competition from ride-sharing apps.

"We're struggling," said Randy Al, who has been driving a cab for a decade in the city. "It's the same thing as the Uber and Lyft drivers are doing, and it makes it difficult for us to do medallions in the city."

 dados de plataforma de transporte compartido, como Uber y Lyft, que competen con los taxistas en el número de pasajeros, lo que afecta a la demanda de cab alientos en la ciudad.

El número total de viajes que ha realizado la plataforma Uber es de más de 4,000, lo que representa un aumento de casi un 40% en comparación con los viajes realizados en la ciudad el año pasado, según el informe de la ciudad de Chicago.

The city also has taken steps to address the issue, including a recent vote to increase the number of medallions available for purchase.

Los taxistas han respondido a estas medidas con una serie de protestas y campañas para proteger su relatioship con la ciudad.

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Road out of Aleppo paved with pain

Thousands have left their war-torn home to find safety in the remotes of Europe.

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Filled without warning

Half of pharmacies fail to alert customers about serious drug interactions, Tribune testing found. Now major chains are promising safety fixes.

By Sam Roe, Ray Long and Karisa King

The Tribune reporter walked into an Evanston CVS pharmacy carrying two prescriptions: one for a common antibiotic, the other for a popular anti-cholesterol drug.

Taken alone, these two drugs, clarithromycin and simvastatin, are relatively safe. But taken together they can cause a severe breakdown in muscle tissue and lead to kidney failure and death.

When the reporter tried to fill the prescriptions, the pharmacist should have warned him of the dangers. But that’s not what happened. The two medications were packaged, labeled and sold within minutes, without a word of caution.

The same thing happened when a reporter presented prescriptions for a different potentially deadly drug pair at a Walgreens on the Magnificent Mile.

And at a Wal-Mart in Evergreen Park, a Jewel-Osco in River Forest and a Kmart in Springfield.
In the largest and most comprehensive study of its kind, the Tribune tested 255 pharmacies to see how often stores would dispense dangerous drug pairs without warning patients. Fifty-two percent of the pharmacies sold the medications without mentioning the potential interaction, striking evidence of an industrywide failure that places millions of consumers at risk.

CVS, the nation’s largest pharmacy retailer by store count, had the highest failure rate of any chain in the Tribune tests, dispensing the medications with no warning 63 percent of the time. Walgreens, one of CVS’ main competitors, had the lowest failure rate at 30 percent — but that’s still missing nearly 1 in 3 interactions.

In response to the Tribune tests, CVS, Walgreens and Wal-Mart said they would take significant steps to improve patient safety at stores nationwide. Combined, the actions affect 22,000 drugstores and involve additional training for 123,000 pharmacists and technicians.

“There is a very high sense of urgency to pursue this issue and get to the root cause,” said Tom Davis, CVS’ vice president of pharmacy professional services.

CVS, which filled about 1 billion prescriptions last year, said the company would improve policies and its computer system to “dramatically” increase warnings to patients.

Walgreens said it would, among other changes, increase training for pharmacists. “We take this very seriously,” said Rex Swords, Walgreens’ vice president of pharmacy and retail operations and planning.

Dangerous drug combinations are a major public health problem, hospitalizing tens of thousands of people each year. Pharmacists are the last line of defense, and their role is growing as Americans use more prescription drugs than ever. One in 10 people take five or more drugs — twice the percentage seen in 1994.

Some pharmacists who were tested got it right, coming to the counter to issue stern warnings. “You’ll be on the floor. You can’t have the two together,” said one pharmacist at a Walgreens on Chicago’s Northwest Side. Said a Kmart pharmacist in Rockford: “I’ve seen people go to the hospital on this combination.”

But in test after test, other pharmacists dispensed dangerous drug pairs at a fast-food pace, with little attention paid to customers. They failed to catch combinations that could trigger a stroke, result in kidney failure, deprive the body of oxygen or lead to unexpected pregnancy with a risk of birth defects.

Location didn’t matter: Failures occurred in poor neighborhoods on the South Side as well as in affluent suburbs and the Gold Coast. Even the Walgreens at Northwestern Memorial Hospital in downtown Chicago failed its test.

The newspaper also tested independent pharmacies, many of which take pride in providing personalized care. As a group, they had a higher failure rate than any retail chain, missing risky drug interactions 72 percent of the time. Chains overall failed 49 percent of their tests.

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**PHARMACIES’ OVERALL FAILURE RATE: 52 PERCENT**

Thirty tests were conducted at each of these Chicago-area chains. Independent pharmacies performed even worse, failing 72 percent of the time.
The Tribune study, two years in the making, exposes fundamental flaws in the pharmacy industry. Safety laws are not being followed, computer alert systems designed to flag drug interactions either don’t work or are ignored, and some pharmacies emphasize fast service over patient safety. Several chain pharmacists, in interviews, described assembly-line conditions in which staff hurried to fill hundreds of prescriptions a day.

Wal-Mart, operator of 4,500 U.S. pharmacies, failed 43 percent of its tests. The company said it would update and improve its pharmacy alert system and train pharmacists on the changes.

Kmart failed 60 percent of the tests. Phil Keough, pharmacy president for Sears Holdings, which owns Kmart, said he was disappointed with the results. “While not happy, we also take this as an opportunity to look in the mirror and see where we can get better,” he said.

Costco, a membership warehouse club whose pharmacies are open to the general public, failed 60 percent of the tests; the company declined to comment.

The Tribune also tested two Chicago-area chains: Jewel-Osco, which failed 43 percent of the time, and Mariano’s, 37 percent.

Jewel-Osco declined an interview request and instead emailed the Tribune a one-sentence written statement: “Osco pharmacists have a history of providing knowledgeable, exemplary care to our customers and their health, well-being and safety is our primary concern.”

Mariano’s also declined to answer questions. The chain said in a written statement: “None of our pharmacists are intentionally disregarding drug interactions or patient safety.”

The chain wrote, “Our pharmacists look at each patient profile which includes patient history, allergy profile, pre-existing conditions and other factors such as age, all of which must be considered when assessing the potential for a drug interaction.”

But in the Tribune tests, pharmacists at Mariano’s stores rarely asked for all of that information.

Last line of defense

In the fight to protect patients from dangerous drug interactions, doctors shoulder significant responsibility. They are the ones who write the prescriptions.
But one physician may not know what another has prescribed, and research has found that doctors’ knowledge about specific interactions is often poor.

In filling prescriptions, pharmacists are uniquely positioned to detect potential drug interactions, warn patients and prevent harm. Pharmacists themselves say that is one of their primary duties.

Yet little data exists about how well they perform in real-world situations.

The Tribune set out to find the answer. To select drug pairs to be used in the tests, the newspaper enlisted the help of two leading experts on drug interactions: pharmacy professors Daniel Malone of the University of Arizona and John Horn of the University of Washington. Five pairs were chosen, three of which posed life-threatening risks. Another could cause patients to pass out. A fifth included an oral contraceptive and could lead to unplanned pregnancies.

According to the two experts, all of the drugs had been on the market for years, and the pairs presented well-established interactions that pharmacists should easily catch. “No-brainers,” Horn called them.

Writing the prescriptions was Dr. Steven C. Fox, a Chicago physician who treats many elderly patients on multiple medications. He knew the risks of interactions firsthand.

Fox wrote the prescriptions in the names of 18 Tribune journalists, 15 of whom conducted tests in the field. They presented the prescriptions written in their names or, in some instances, their colleagues’ names. The reporters tested 30 stores at each of seven leading chains as well as numerous independent pharmacies. Most stores were in the Chicago area; some were in Indiana, Wisconsin and Michigan.

Reporters presented the prescriptions together or a couple of days apart, then waited to see if the orders would be filled.

In Illinois, pharmacists who detect a serious interaction must contact the prescribing doctor to see if the order is correct or if an alternative therapy is available, according to the Illinois Department of Financial and Professional Regulation. Pharmacists are then supposed to alert the patient.

Carmen Catizone, executive director of the National Association of Boards of Pharmacy, said the professional standard is clear. “Anytime there’s a serious inter-
action, there’s no excuse for the pharmacist not warning the patient about that interaction,” he said.

In the Tribune study, a test was considered a pass if the pharmacist attempted to contact Fox about the interaction or warned the reporter.

Drug information leaflets placed inside the bag or stapled to the outside were not considered sufficient to warrant a pass. Illinois regulators said these materials typically are not adequate replacements for verbal warnings; some of the materials don't warn about specific interactions, and experts say patients frequently throw out the leaflets without reading them.

After the tests, reporters called many of the pharmacists to inform them of the results and to discuss the findings.

Why were so many pharmacies missing dangerous drug combinations?

**Speed vs. safety**

Mayuri Patel, a pharmacist at a Wal-Mart in west suburban Northlake, said she typically fills 200 prescriptions in a nine-hour shift, or one every 2.7 minutes.

At another Wal-Mart where she was trained, it was even busier, she said: “We were doing 600 a day with two pharmacists with 10-hour shifts.” That works out to one prescription every two minutes.

In the Tribune tests, she caught a potentially deadly drug pair, warning the reporter at the counter: “This is a common interaction.”

It is difficult to say why so many pharmacists failed the same test, but interviews and studies point to a possible explanation: the emphasis on speed.

Several stores dispensed risky drug pairs with no warning in less than 15 minutes. At a Kmart in Valparaiso, Ind., it was 12 minutes. At an independent pharmacy on the North Side, it was five.

The Tribune found that pharmacists frequently race through legally required drug safety reviews — or skip them altogether. According to Illinois law, pharmacies are required to conduct several safety checks, including whether the dose is reasonable and whether the medication might interact with other drugs the patient is taking.
But in the Tribune tests, pharmacies rarely asked what other medications testers were using.

“They’re cutting corners where they think they can cut,” said Bob Stout, president of the New Hampshire Board of Pharmacy, which sampled data from two retail chains in the state and found that pharmacists spent an average of 80 seconds on safety checks for each prescription filled.

“What happens, I found on the board, is people stop doing (safety) reviews,” Stout said. “They’re not going in looking at patient records.”

Most pharmacies use computer software designed to flag drug interactions. But experts say computer alerts are so common that pharmacists can get “alert fatigue” and ignore many of the warnings.

At the same time, chain pharmacies are increasingly promoting quick service. Drive-through windows are now common, and services like CVS’ walk-in Minute Clinics appeal to consumers’ preference for speed.

These efforts may send a message to patients that speed is more important than quality health care. Patients have internalized that message and feel entitled to short wait times, pharmacists said.

“The patient will get mad if you call the doctor and take time,” said Sadia Shuja, a pharmacist at Skypoint Pharmacy in Schaumburg who caught a dangerous drug pair in the Tribune tests. “Sometimes they think it is fast food.”

To ease workload, most pharmacies employ technicians to manage tasks that require less medical expertise.

Arsen Mysllinj, a Kmart pharmacist in Rockford who passed the Tribune test, said technicians at his store and others often screen for drug interactions after entering patients’ drug orders into a computer. If interactions appear, he said, the technicians are trained to print out the warning on the screen and hand it to a pharmacist.

It would be better, he said, for pharmacists to do the screening.

Kmart said that in light of the test results, it would review its relevant policies, computer systems and training programs.

Unionized pharmacists, including those in Illinois, have periodically pushed for minimum staffing rules, but those efforts have not gone far. Some pharmacists say
time spent pitching company promotions could be better spent on patient safety.

In the Tribune tests, the majority of Kmart pharmacists dispensed risky drug combinations without warning testers. But several did take time to try to enroll the reporters in the company’s savings program.

‘Scorecard’ pressures

At CVS, prompt service isn’t just a vague goal. It is a carefully measured metric that the chain uses, along with other assessments, to grade its pharmacies and rank them against one another, records and interviews show.

Several current or former CVS pharmacists criticized the practice, saying it pressures them to focus more on corporate criteria than on drug interactions and other safety checks.

“You get stressed, and it takes your mind away from the actual prescriptions,” said Chuck Zuraitis, head pharmacist at a CVS in south suburban Park Forest and a union steward for Teamsters Local 727, which represents 130 CVS pharmacists in the Chicago area. His pharmacy was not among those tested.

Performance and business metrics are common at big chain pharmacies and in other industries. Supporters say they make companies more efficient and responsive to customers.

In 2012, the nonprofit Institute for Safe Medication Practices conducted a national survey of 673 pharmacists and found that nearly two-thirds worked at stores that track the time it takes to fill prescriptions. About 25 percent worked at companies that guaranteed short wait times.

Of the pharmacists at stores that advertised quick service, 4 in 10 said they had made a medication error as a result of hurrying to fill a prescription within a set time.

In 2013, the National Association of Boards of Pharmacy called on states to prohibit, restrict or regulate company policies that measure the speed of pharmacists’ work. But, the association says, little has changed in state law.

Internal CVS records obtained by the Tribune show that the company tracks numerous pharmacist tasks, including whether prescriptions are filled in the time promised to customers and whether voicemails are retrieved in a timely fashion.

“Every prescription is timed,” said Deepak Chande, a former head pharmacist at a CVS in southwest suburban Worth, “and this is the worst of the pharmacist’s nightmares.”

If pharmacists fall behind, the backlog pops up in color on their computer screens, said Chande, also a former union steward. “It’s an unreal pressure,” he said. “Your mind is kind of frantically trying to obey it.”

CVS officials declined to be interviewed about metrics but issued a statement and answered questions in writing. The company said prescriptions do not have to be filled quickly, but it expects pharmacists to have medications ready by the time promised to the customer.

Records show that head pharmacists receive a monthly “WeCARE Scorecard” that tracks the percentage of prescriptions filled by the times promised. The pharmacies are ranked by district, by region and nationwide.

CVS’ computer system prioritizes prescriptions based on patients’ requested pickup times, with preference given to customers with urgent needs — for instance, someone on his way home from the hospital after surgery. Pharmacists can reset a promised pickup time if they think it cannot be met, the company wrote.

The color indicators on computer screens are meant to help pharmacists with prioritizing their work, CVS said. The company also wrote that several years ago it removed a red indicator for prescriptions that had gone beyond the promised
pickup time because pharmacists “felt the color red denoted something negative or alarming.”

“We switched to an ‘orange’ indicator to inform a pharmacy team which prescriptions may not be ready before a customer’s expected arrival time,” CVS wrote.

Another CVS metric, documents show, tracks how many patients sign up for automatic refills. Zuraitis said posters on pharmacy walls record how many flu shots have been administered. “You feel like you’re trying to sell people something,” he said.

CVS said automatic refills help patients stay on schedule with the drugs they need to treat chronic conditions. The company said it measures the number of flu vaccinations offered to customers to help support the recommendation by the federal Centers for Disease Control and Prevention that people receive a flu shot annually.

At Walgreens, officials said the company collects business metrics as a way to monitor staffing levels and service. The firm said it does not use them in a manner that emphasizes productivity over patient safety.

Alethea Little, a Walgreens pharmacist in west suburban Forest Park who properly warned a tester, said metrics are no excuse for missing drug interactions.

“Our flu shot goal is 10 a day, 12 a day, 50 a day,” she said. “And the phone rings off the hook. You just got to do what you got to do, essentially.”

Squeezed by chains

Independent pharmacies face a different kind of pressure: intense competition from the big chains.

B.M. Patel, a pharmacist for 40 years who owns Riteway Pharmacy on Chicago’s Northwest Side, missed the test interaction but didn’t make excuses. “It was a mistake,” he said. “Maybe I should be paying more attention.”

But he also said small pharmacies know that if they don’t fill a prescription, the customer might simply go to a nearby chain store. Business at his store, he said, “is
not good. I can still survive, but not too long. We don’t really know how long it’s going to last.”

The number of independent stores has been shrinking nationwide. In Illinois, the number dropped about 9 percent from 689 in 2013 to 624 last year, according to the National Community Pharmacists Association.

Several independents tested by the Tribune looked like classic drugstores, offering medications alongside greeting cards, stuffed animals and candy bars. Others were less inviting. One dispensed drugs behind a thick window; at another, a reporter had to knock several times to gain entry.

In Chicago’s Pilsen neighborhood, independent pharmacist Audrey Galal passed her test while working at a Mexicare Pharmacy, a small storefront on a block of brick buildings. The store is in the process of closing, she said, in part because of competition from chains.

Galal said she doubts that small drugstores would knowingly sell harmful medications but thinks they might be reluctant to turn away business.

“These pharmacists are acting like businesspeople, just trying to keep their pharmacies afloat instead of being clinicians,” said Galal, who now works at a Mexicare in Little Village.

Andy Politis, a pharmacist and part owner of Oakmill Pharmacy in north suburban Niles who passed the test, said he was surprised how many independents failed. “The independent guys should be better because they don’t have the same pressure as the big stores with so many prescriptions,” he said.

B. Douglas Hoey, chief executive of the national community pharmacists group, said the results were alarming. “It’s something that shouldn’t happen — both for chains and independents,” he said. “Even one is too many.”

Several independents said the findings prompted them to make changes. After failing its test, Summit Medical Pharmacy in the southwest suburbs beefed up internal checks and worked with a software company to ensure that even minor drug interactions are detected.

Since then, the new system has flagged several interactions that led to consultations with doctors and patients, head pharmacist Pankaj Bhalakia said.

“We changed the whole system,” he said. “I don’t think there could be a problem in the future.”

CONTRIBUTORS: Tribune staffers who conducted the tests or who lent their names for the prescription orders were Chuck Burke, Angela Caputo, Alexia Elejalde-Ruiz, Ted Gregory, Vikki Ortiz Healy, Jared S. Hopkins, Karisa King, Colleen Kujawa, William Lee, Ray Long, Jennifer Smith Richards, Sam Roe, Nara Schoenberg, Nancy Stone, Kaarin Tisue, E. Jason Wambsgans, Lindsey Woods and Lauren Zumbach.
Major U.S. pharmacy chains promise safety improvements

At companies in the Tri-state area, some of the nation's largest pharmacy chains said they would take significant steps to improve patient safety.

CVS

CVS said it will change its policies and computer systems to require pharmacists to call the prescribing doctor or nurse when a patient asks for a drug that appears to conflict with other medications.

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Walgreens

Walgreens said it will require all its pharmacists to check the Comprehensive Medication Review database when a patient asks for a medication that appears to conflict with other medications.

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Kmart

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Squeezed by chains

Pharmacy chains have squeezed independent pharmacists into a difficult kind of pressure competition from the chains.

R.M. Ford, a pharmacist for 66 years who owns UW Pharmacy in Chicago's North Side, said he has recently seen a decline in the number of independent pharmacists, as well as a decline in the number of customers. Ford said he believes the decline is due to the chains.

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Both the chains and the independent pharmacists are squeezed by the chains.

The chains have squeezed independent pharmacists into a difficult kind of pressure competition from the chains.

Independent pharmacists have complained about pressure from the chains, and some have decided to join the chains.

The chains also have squeezed independent pharmacists into a difficult kind of pressure competition from the chains.

Ford said he believes the decline is due to the chains.

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CONTRIBUTORS

"These pharmacists are affected by the same pressures," said Ford. "They are squeezed by the chains, just as independent pharmacists are."
Major U.S. pharmacy chains promise safety improvements

In response to the Tribune tests, some of the nation’s largest pharmacy chains said they would take significant steps to improve patient safety.

**CVS**

CVS said it will change its policies and computer system to require pharmacists to call the prescribing doctor or warn the patient when a serious drug interaction is flagged. Those changes will apply to the chain’s 30,000 pharmacists at its 9,600 drugstores.

Currently, CVS allows pharmacists to override computer alerts if they review the warning and accompanying medical literature and conclude the prescription is appropriate. In the future, the system will not allow pharmacies to dispense certain flagged medications unless the pharmacists document in the computer that they have called the doctor or counseled the patient.

CVS said its pharmacists will undergo a comprehensive training and certification program on the new rule, to be implemented early next year. The rule will apply to other safety issues, such as drug-allergy interactions, duplicative therapies and orders involving unusually high or low doses, later in the year.

To reduce “alert fatigue,” CVS said it will work with its database providers to streamline alerts to help ensure that pharmacists are presented the most important warnings.

In addition, CVS said it will change its approach to the “offer to counsel.” Throughout the industry, pharmacists often address a legal requirement that pharmacies must offer to counsel patients by having staff ask customers at checkout, “Do you have any questions for the pharmacist today?” or sometimes simply, “Any questions?” CVS said it will require a more robust and explanatory communication.

CVS said the new wording has not been finalized but that the company’s 50,000 technicians will be trained in the new policy.

**Walgreens**

Walgreens said it will provide additional training on drug interactions for its 27,000 pharmacists at its 8,175 U.S. drugstores, including the 222 pharmacies in the New York metropolitan area under the Duane Reade banner. A pharmacy staff meeting on drug interactions will be held chainwide.

To give pharmacists more time to help patients, Walgreens said it is accelerating efforts to move administrative tasks out of stores and to a centralized office.

Walgreens also said it has notified staffers of relevant policies and procedures, including that pharmacists should always counsel patients on new prescriptions.

**Wal-Mart**

Wal-Mart said it will update and improve its pharmacy alert system. Once that process is completed, the company’s pharmacy operating manual will be amended accordingly, and Wal-Mart’s 16,000 pharmacists at 4,500 stores will be required to undergo computer-based training on the changes.

The company also said it will send a notification to all of its pharmacists reminding them of best practices in terms of identifying drug interactions and warning patients. Wal-Mart said it will reinforce that pharmacists should counsel all patients filling new prescriptions.

**Kmart**

Kmart said it is reviewing its policies, computer systems and training programs relevant to its 528 pharmacies.

The company said it is also studying whether to bolster the way it approaches the “offer to counsel” and whether to require new customers to fill out medication forms to help staff detect drug interactions.
The tests and the results

To determine how often any pharmacies would dispense potentially dangerous drug pairs without warning, the Tribune examined the computerized drugselling system at 1,500 Chicago-area pharmacies. In all, 412 tests were conducted, most of them in Chicago or in nearby suburbs. Two were conducted at large chains in the Chicago area: one tested CVA, Walgreens, 6902 S. MacArthur and Centro — as well as similar chains Jewel-Osco and Mariano’s — to determine if they are routinely and completely alerting individual patrons of combination drug prescriptions. The drug pairs used in the tests were chosen in consultation with experts in drug interactions. Overall, 42 percent of pharmacies failed to issue a warning.

Selecting the drug combinations

In choosing the five test pairs, the goal was to combine pairs of drugs that had been identified as frequent interactors in the literature. The Tribune selected the drug pairs used in the tests in consultation with pharmacists and experts who are leading drug-interaction research. Daniel Molinari of the University of Arizona and John Hamers of the University of Washington, according to Molinari and Hamers, said the five pairs chosen for the study are among the most common of contraindicated drug interactions, with the exception of one pair that is included in an Outpatient National Surveillance System database but is not considered a significant concern.

The Tribune selected pairs such as those for the names of the Tribune—Journal, 13 of often-conducted tests in the field. These experts provided the prescriptions written in their names or in similar fashion, called the computerized drug-selling system in the pharmacies and observed for two weeks to see whether interactions were identified and, if necessary, what actions were taken.

The prescriptions

Drugs tested to date include the classes of antibacterial agents, antihistamines, and antipsychotic drugs, which are the most hazardous to patients, and anti-inflamatory drugs, which are the most hazardous to patients.

The results

A pharmacy was considered to have had a failed test if it did not alert the customer about drug interactions or at least supply the information before filling the bag or if a drug that had failed the study was not completed to fill in order. Drug orders were sent through pharmacy

HOW THE PHARMACIES PERFORMED

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<thead>
<tr>
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<tr>
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Successful testing at Target after its pharmacies were acquired by CVS.

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INTERACTIONS

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The tests and the results

To determine how often area pharmacies would dispense potentially dangerous drug pairs without warning, customers, the Tribune launched what would become the most extensive testing project of its kind. In all, 285 tests were conducted, most of them in Chicago or its suburbs. Five national chain pharmacies with a large presence in the Chicago area were tested — CVS, Walgreens, Wal-Mart, Kmart and Costco — as well as local chains Jewel-Osco and Mariano’s. Reporters also tested a randomly selected group of independent pharmacies. The five drug pairs used in the tests were chosen in consultation with national experts on drug interactions. Overall, 52 percent of pharmacies failed to issue a warning.

1 Selecting the drug combinations

In choosing the five test pairs, the goal was to find combinations in which each drug had been on the market for many years, the drugs could cause serious harm when taken together, and the interactions should have been well known to pharmacists.

The Tribune selected the drug pairs used in the tests with the help of two pharmacy professors who are leading experts in drug interactions: Daniel Malone of the University of Arizona and John Horn of the University of Washington.

According to Malone and Horn, drug safety databases used by pharmacies rate each of the pairs chosen as a major, severe or extremeusted interaction, with the exception of a pair that includes an oral contraceptive. That interaction is classified as moderate by Micromedex but major by Medspan and severe by First Databank.

2 The prescriptions

Writing the prescriptions was Dr. Steven C. Fox, a Chicago physician licensed by the state of Illinois. He wrote the orders in the names of 28 Tribune journalists, 15 of whom conducted tests in the field. Those reporters presented the prescriptions written in their names or, in some instances, their colleagues’ names. All prescriptions were for first-time medications as opposed to refills.

3 The test locations

The 285 tests were conducted from October 2015 to June 2016. Seven chains were tested 30 times each to limit chance results. No single location was tested more than once.

Because fewer than 30 Kmart and Costco stores are in the Chicago area, reporters tested some of those stores in downstate Illinois, Indiana, Wisconsin and Michigan. The newspaper also sought to test 30 Target stores but stopped after CVS acquired Target pharmacies during the study. Thirteen tests at Target were completed, and the results are included in the study’s statistics.

The Tribune chose 32 independent pharmacies for testing at random from a list of locations obtained from the state. All were in Chicago or suburban Cook County.

Individual chain stores were not picked randomly, as stores within a large chain generally share the same computer systems and policies. Still, reporters attempted to select chain stores that represented a diverse cross-section of the area.

4 Doing the tests

The reporters presented each pharmacy with prescriptions for one of the five drug pairs. Each pair was tested the same number of times at each chain.

Most prescriptions were dropped off at the same time; some were presented a couple of days apart. In some cases, the prescribing physician called in an order. Drug orders were not run through insurance.

Reporters did not identify themselves as Tribune staffers but used their own names and answered all questions truthfully.

The reporters typically waited at the pharmacy for the order to be filled, taking notes about what transpired from the time they dropped off the prescriptions to when they picked up the medications. In many tests, conversation was extremely limited. Reporters’ notes were then entered into standardized data collection forms.

5 How the pharmacies performed

<table>
<thead>
<tr>
<th>Pharmacy</th>
<th>Failure rate</th>
<th>Falls/tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Independent pharmacies</td>
<td>72%</td>
<td>(23/32)</td>
</tr>
<tr>
<td>CVS</td>
<td>63%</td>
<td>(16/30)</td>
</tr>
<tr>
<td>Target*</td>
<td>62%</td>
<td>(8/13)</td>
</tr>
<tr>
<td>Walmart</td>
<td>60%</td>
<td>(18/30)</td>
</tr>
<tr>
<td>Mariano’s</td>
<td>43%</td>
<td>(13/30)</td>
</tr>
<tr>
<td>Walgreens</td>
<td>43%</td>
<td>(9/30)</td>
</tr>
<tr>
<td>Jewel-Osco</td>
<td>37%</td>
<td>(7/30)</td>
</tr>
<tr>
<td>All chains combined</td>
<td>30%</td>
<td>(9/30)</td>
</tr>
</tbody>
</table>

*Reporters stopped testing at Target after its pharmacies were acquired by CVS.

6 The results

A pharmacy was considered to have failed the test if its staff did not either attempt to contact the doctor about a drug interaction or orally warn the tester. Information leaflets placed inside the bag or attached to the outside were not considered sufficient to warrant a pass.

All purchased medications were cataloged and stored in a secure location. After the tests, the Tribune called many of the pharmacists to inform them of the results and discuss the findings. Some of their comments are included in the story. The Tribune is not identifying all of the individual stores in its article because each location was tested only once, a sample size too small to draw conclusions about a particular store.

SOURCE: Tribune reporting. Daniel Malone, University of Arizona; John Horn, University of Washington

CHICAGO TRIBUNE PHOTOS BY JASON WAMBMSANS CHICAGO TRIBUNE
The hunt for dangerous doses

The experiment began with thousands of patient files, millions of prescription orders, millions of clinical measurements and a single question. Could big data be used to discover deadly drug combinations?

For decades, scientists have wrestled with the problem that trusted prescription medications can combine in dangerous ways, often placing Americans at risk when they take more than one drug. Sometimes the dangers are well-documented. In other cases, they remain hidden from everyday doctors, pharmacists, drugmakers and patients.

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To find the potentially risky combinations, the Tribune enlisted the help of scientists at Columbia, who used sophisticated algorithms to analyze a massive government database of drug complaints for signs of the heart condition. The team then used 300,000 electronic hospital patient files to confirm which drug pairs were indeed associated with an increased risk.

The team turned next to Columbia cellular researchers, who tested one of the drug combinations on individual cells.

The tests found that the combination — clofibric acid, a popular anti-inflammatory, and lamotrigine, a former blockbuster heartburn medication best known by the brand name Procardia — blocked an

By Sam Rose and Karin King | Chicago Tribune
The hunt for dangerous doses

In a unique collaboration, the Tribune and top scientists uncovered drug combinations linked to an increased risk of a serious heart condition. By mining the universe of big data, then testing in a lab, the team created a new model to protect people from hidden drug interactions.

By Sam Roe and Karisa King

The experiment began with thousands of patient files, millions of prescription orders, billions of clinical measurements and a single question: Could big data be used to discover deadly drug combinations?

For decades, scientists have wrestled with the problem that trusted prescription medications can combine in dangerous ways, often placing Americans at risk when they take more than one drug. Sometimes the dangers are well-documented. In other cases, they remain hidden from everyone: doctors, pharmacists, drugmakers and patients.

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To find the potentially risky combinations, the Tribune enlisted the help of scientists at Columbia, who used sophisticated algorithms to analyze a massive government database of drug complaints for signs of the heart condition. The team then used 380,000 electronic hospital patient files to confirm which drug pairs were indeed associated with an increased risk.

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The tests found that the combination — ceftriaxone, a popular antibiotic, and lansoprazole, a former blockbuster heartburn medication best known by the brand name Prevacid — blocked an electrical channel crucial to the heart, providing a biological explanation for why these drugs might be interacting.
The investigation is believed to be the first time anyone has discovered a potential drug interaction by searching for signals in the Food and Drug Administration’s complaint archive, then confirming the findings through patient records and cellular testing.

The project is also noteworthy for how it mined the data: The team intentionally looked for evidence where none was visible.

Typically, researchers trying to spot drug interactions analyze the FDA archive and scientific literature for signs that a pair of medications is causing harm. If no patient has reported a particular interaction, there won’t be any obvious clues. But that doesn’t mean the problem isn’t occurring, or that it can’t be found.

To identify hidden interactions, the scientists working with the Tribune analyzed indirect evidence: side effects associated with the dangerous heart condition. The researchers could use the side effects to lead them to drug pairs that might be risky.

It’s similar to the way astronomers infer the presence of black holes by observing their side effects, such as the gravitational pull on neighboring stars.

The Columbia scientists cautioned that the study, published Wednesday in the journal Drug Safety, does not prove cause and effect and that the results are preliminary. They said further research and, potentially, a clinical trial are needed.

But the project has demonstrated the potential of an innovative scientific model that offers a new way to protect patients and save lives.

The FDA, which is charged with protecting consumers from drug interactions, said it welcomed the new data mining effort and would look at the findings.

Drugmakers contacted by the Tribune because the study flagged their medications stressed their commitment to safety. Citing medical literature or their own research, several companies said they had seen no evidence that their drugs caused such interactions.

It’s unclear how many people in the U.S. die each year of drug interactions, but researchers estimate tens of thousands are hospitalized annually. And the risks are escalating. One in 5 Americans take three or more drugs. One in 10 people take five or more — twice the percentage as in 1994.

Yet the issue has few advocates, there is little public awareness and the amount
of research is startlingly thin.

At the same time, doctors and hospitals are collecting and storing an enormous amount of data every day: prescription drug orders, lab measurements, diagnoses and patient complaints — digital information with the potential to transform the way we identify health hazards.

Joining the Tribune in the quest to make use of this new information were a creative data scientist who was determined to prove his skeptics wrong; a former medical school dean who spent years raising awareness about drug interactions but was often left frustrated; and a noted Columbia scientist who opened up his cellular research lab to see if the signals detected deep in the data were indeed real.

**Something to prove**

Five years ago, Nick Tatonetti fed 40 mice nothing but butter and Sprite. Every Friday he used a tiny needle to inject each mouse with insulin and then carefully nicked its tail with a razor blade to draw samples of blood.

It was a curious sight: a data scientist logging long hours in the animal lab. But Tatonetti had something to prove. Critics were skeptical about his novel approach to identifying risky drug combinations.

At the time, Tatonetti was a 27-year-old doctoral student at Stanford University, working in the growing field of biomedical informatics, or the use of data science to study medicine. Drug interactions intrigued him, and he began exploring the most complete database on the problem: an FDA archive of millions of reports from physicians, drugmakers and consumers about bad reactions to medications.

But Tatonetti thought the database had a weakness: If a bad reaction to a drug was rare, or rarely reported, researchers couldn't determine whether there was a problem. There simply wouldn't be enough complaints to analyze.

Tatonetti wondered if the concept of signal detection could be used to reveal hidden drug interactions.

Signal detection theory had been in use for years and has its roots in radar. When early radar operators looked at a screen, they had to determine whether they were seeing a real signal — an enemy plane, ship or missile — or insignificant noise.

Likewise, when scientists analyze big data, they try to distinguish between a real event — say, a health risk caused by a new drug — or random complaints one would expect by chance.

But Tatonetti wanted to take this concept one step further, using a technique he called latent signal detection.

Instead of looking for a direct signal in the FDA database, could he search for indirect evidence — the black hole approach? Could he find hidden interactions that way?

Using nothing more than his MacBook Pro, Tatonetti identified all side effects linked to drugs known to cause diabetes-related complications, such as high blood sugar. This created a side effect profile for such medications. He then scanned the FDA database for which drug pairs, when taken together, had side effects that closely matched this profile.

He made a surprising discovery. Two of the world's most prescribed drugs, the antidepressant paroxetine and the cholesterol-lowering medication pravastatin, were associated with high blood-glucose levels when administered together — a finding important to people with diabetes.

Tatonetti published his work in peer-reviewed scientific journals and was invited to speak at conferences. But invariably somebody would ask: How do you know for sure these drug combinations are harmful? Isn't this all speculative?

Tatonetti hit the animal lab to see if his findings would hold up to traditional
scientific testing. He fed his mice a high-fat, high-sugar diet until they teetered on
the edge of being diabetic—a condition that would help reveal any changes in their
health once Tatonetti treated them with drugs. The results: Mice given both parox-
etine and pravastatin had higher blood sugar than the control groups.

He emailed his findings to the FDA, but agency officials were unimpressed. Ac-
cording to Tatonetti, the officials looked in their database and saw few complaints
of paroxetine and pravastatin causing high blood sugar.

“That was the entire point of my work,” Tatonetti said. “They didn’t get it.”

The FDA declined to comment.

Soon after, Columbia’s medical school in New York hired Tatonetti to be an as-
sistant professor of biomedical informatics and to run his own data lab.

The Tribune, which was investigating drug interactions, met Tatonetti the fol-
lowing fall, in September 2013. His office was a small, windowless room in an aging
building near 168th Street and Broadway.

Tatonetti had a trim black beard and wore jeans and a sweater. A tattoo of an ana-
tomically correct Sacred Heart was visible on his left forearm. “My mom is super
Catholic,” he said. “It’s a little bit of my mom in it, a little bit me.”

Picking up a red marker, he drew a diagram directly on the office wall—a wall he
had coated with washable, whiteboard paint—and explained his work on interac-
tions.

But he remained frustrated by the FDA and seemed ready to move on to other
projects.

The Tribune made a proposal: Instead of looking at drug combinations that
might raise blood sugar, what if he searched for drug combinations that might cause
sudden death? The FDA might pay attention to those findings.

Tatonetti said he was not an expert on sudden death. The Tribune said it knew
somebody who was and believed he would be willing to help.

A baffling condition

Drive north on Oracle Road out of Tucson, Ariz., and you come to the foothills
of the Catalina Mountains, red granite peaks harboring rattlesnakes, bobcats and
hummingbirds. There, in a gated community, lives Dr. Ray Woosley, one of the nation’s leading experts at uncovering dangerous drug combinations.

Back in the 1990s, when he was chairman of pharmacology at Georgetown University Medical Center, Woosley and his colleagues helped show that the popular antihistamine Seldane, when taken with certain antibiotics and antifungal drugs, could cause abnormal heart rhythms and sudden death. Unlike Tatonetti, Woosley’s work got the FDA’s attention; Seldane was eventually pulled from the market.

Woosley went on to become the dean of the University of Arizona’s medical school but never lost interest in drug interactions. “It’s a huge public health problem,” he said, “but it is enormously frustrating. People are dying and the problem is ignored.”

Now retired as dean, he still researches the same side effect that doomed Seldane: a baffling abnormality of the heart’s electrical activity known as QT prolongation.

The “Q” and the “T” refer to the electrical waves on a patient’s electrocardiogram. To demonstrate, Woosley makes a fist, squeezes it, relaxes it and squeezes it again, simulating a heart pumping. The time between when the heart starts squeezing to when it finishes relaxing and prepares to beat again is the QT interval.

If this interval lengthens markedly, the condition is called QT prolongation. And an increase of 50 milliseconds — faster than the blink of an eye — can trigger a potentially fatal arrhythmia. The heart starts beating so fast that it is essentially quivering and not pumping any blood. The heart’s waves on the electrocardiogram resemble twisted spikes — hence, the name of this form of arrhythmia: torsades de pointes, French for “twisting of the points.”

Not enough blood reaches the brain, and victims black out. “And it happens very quickly,” Woosley said, “within seconds.”

Some people are born with a long QT interval and are at risk of the dangerous arrhythmia, but more than 50 medications have been shown to cause both conditions. No one knows how many people have died, because unless a person is connected to an ECG monitor at the time of death, it is difficult to prove that an abnormal heart rhythm was the culprit.

Woosley and other scientists think many unexplained deaths, such as young peo-
ple suffering heart attacks or good swimmers who drown, are actually cases of arrhythmia triggered by QT prolongation, perhaps brought on by prescription drugs.

The Tribune told Woosley about Tatonetti’s data mining algorithms and how the news organization wanted to use them to try to find drug combinations that might be silently causing QT prolongation. Woosley agreed to help, supplying a list of drugs already known to cause the heart condition as well as related side effects. Back in New York, Tatonetti used the lists to start writing computer code to drill down on the FDA database.

Cognizant that an early coding error could sabotage the entire effort, Tatonetti carefully crafted 10 to 20 lines at a time. Computers catch most typographical mistakes, but an error in logic — typing a plus sign when a minus symbol is needed — could go undetected for weeks, if it is caught at all.

One afternoon, furious typing was followed by long stretches of silence in which Tatonetti stared at the screen and stroked his beard. At one point, he muttered, “It’s still not working. Not sure why.” Eventually, he found the coding bug and began to rewrite the script. Emphatically banging out the last few keystrokes, he swiveled in his chair and announced: “Awright! So! That’s running!”

After weeks of tweaking his algorithm, Tatonetti had results: hundreds of drug combinations with statistically significant signals for QT prolongation. In other words, these pairs were more closely associated with the disorder’s profile than one would expect by chance.

But were they truly affecting patients?

**Verifying signals**

Now was the time to tap into Columbia’s rich patient archive — one of the largest of its kind. It contained clinical data on 4 million patients at New York-Presbyterian Hospital/Columbia University Medical Center going back to 1989; 20 million prescription orders; and more than 300 million lab results.

Most important, the archive had patients’ QT measurements.

Using “de-identified” data that did not include patient names, Tatonetti wrote a computer script that searched for all patients who had ever been prescribed the
suspected drug combinations.

For many pairs, few patients popped up. For others, hundreds did. In those cases, Tatonetti compared the patients’ QT levels in the 36 days after they were prescribed the drug combinations to levels for patients prescribed only one of the medications.

As the results slowly appeared on his computer, Tatonetti’s eyes lit up. “Whoa! This is a great hit,” he said. “An increase of 15 milliseconds in females and 14 in males.”

In the end, the patient records validated Tatonetti’s algorithm. Dozens of drug pairs were associated with increases in the QT interval in real people.

The team eventually narrowed the list to eight combinations, based largely on which pairs showed the greatest QT increases. In addition, more patients prescribed these pairs had at least one QT value over 500 milliseconds — the threshold for clinical concern — compared with those prescribed just one of the drugs.

But Tatonetti remained concerned. Would skeptics say the findings were largely speculative?

He couldn’t test mice, because the hearts of mice and humans are too different. Then Woosley had an idea. One of his old friends worked at Columbia’s medical center, in a building attached to Tatonetti’s. His name was Robert Kass, but people called him Rocky.

Kass had the perfect background for the project. He had experience researching arrhythmia, was interested in drug interactions and — more important — ran a lab where scientists conducted cellular research.

Woosley wondered: Would Kass be willing to apply the suspected drug pairs to individual cells to see if they affected a crucial electrical channel in a way that could trigger QT prolongation? If so, it would offer a biological explanation for why these drug combinations might be causing the condition.

Tatonetti and Kass soon met in Kass’ office. Kass was impressed by Tatonetti and his big data approach. Tatonetti was impressed by Kass and his spacious lab: “It’s like its own wing. It has its own doors.”

Kass offered more than Tatonetti expected. He agreed to have his lab conduct cellular testing on multiple drug pairs, and work could begin immediately.

Tatonetti walked away ecstatic, but he wondered if this influential figure — at the time vice dean for research at the medical center — was merely humoring him. “I think he might think it’s a little crazy,” Tatonetti said.

A tricky test

At Kass’ lab, electrophysiology scientist Kevin Sampson opened an incubator the size of a mini-fridge and pulled out a flask where cells are grown for testing. They were Chinese hamster ovary cells — commonly used in medical research, he said, but tricky to handle.

The cells must be fed a nutrient-rich solution or they will not multiply. Once enough are grown for testing, the cells are washed in a chemical to peel them apart. Not enough chemical and the cells stick together; too much and they burst.

And individual cells must be spherical. For the test to work, a single, perfectly shaped cell must roll into a tiny well for analysis.

Of the eight suspected drug pairs, four were determined to be the best candidates for cell testing, and the combination of ceftriaxone and lansoprazole was selected to be tested first. Both are immensely popular medications.

Ceftriaxone, an antibiotic also known by the brand name Rocephin, is sold in 110 countries and is on the World Health Organization’s list of essential medicines. Lansoprazole, commonly sold as Prevacid, is a proton pump inhibitor that reduces stomach acid. The drug once generated annual sales of more than $3 billion; it’s
now also available over the counter.

The test would determine whether the drugs affected an electrical pathway in the cell called the hERG channel, which helps coordinate the beating of a heart. When drugs cause QT prolongation, it is almost always because this channel becomes blocked.

The first phase of testing went as expected. When ceftriaxone and lansoprazole by themselves were applied to the cells, the channel was not affected.

But what would happen when the drugs were added together? Several weeks later, after new cells were grown, the team gathered to find out.

Lab manager Jenny Rao handed a tube containing 2 million cells to Sampson. She said the cells appeared healthy, round and mobile. Sampson carefully poured the cells into a receptacle atop the lab’s Patchliner, a $313,000 testing machine no bigger than a suitcase.

He said they had an hour to do the experiment; after that, the cells would begin to die. Tatonetti was anxious.

“There are so many ways that this can go wrong and only one way that it can go right,” he said.

Sampson clicked the play button on an adjacent computer screen, and the testing machine made a high-pitched whirring sound. A pencil-thin robotic arm glided back and forth, pipetting the cell solution into tiny chambers filled with fluid. Sampson checked the computer screen and reported that seven cells had rolled into wells for testing.

The machine then applied suction to break holes in each cell. To establish a current, electrical pulses were applied to the cells every 20 seconds. Then the drugs were added, slowly flowing across the exterior of the cell membranes.

Sampson pointed to a flat line on the computer screen representing the current going through the cells. If the drugs did not affect the cells, the line would remain flat. “If something happens,” he said, “you’ll see a dip in that line.”

At first, the line didn’t budge, but Sampson said the concentration of the drugs was still extremely low. A few minutes later, when the machine added higher concentrations, the line began to stir.
Four potentially risky drug pairs flagged through data mining

Columbia scientists, in collaboration with the Tribune, identified drug pairs associated with an increased risk of QT prolongation, a heart condition that can lead to a potentially fatal arrhythmia. The results are based on public FDA records as well as patient archives at a New York hospital. The researchers stress the results are preliminary and do not show cause and effect. The team agreed that four pairs were worthy of study via cellular testing. The Tribune contacted firms that developed the drugs or are current sales leaders. They emphasized their commitment to safety: several said their own research had shown no evidence that their drugs caused such interactions.

<table>
<thead>
<tr>
<th>Drug pairs</th>
<th>Treatments</th>
<th>Patients with at least one QT value above 500 milliseconds</th>
<th>Patients with at least one QT value above 500 ms for both drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metoprolol</td>
<td>Blood pressure, chest pain</td>
<td>Sedures</td>
<td><strong>+18ms</strong></td>
</tr>
<tr>
<td>Cefazolin</td>
<td>Bacterial Infections</td>
<td>Meperidine</td>
<td><strong>+12ms</strong></td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>Bacterial Infections</td>
<td>Lansoprazole</td>
<td><strong>+12ms</strong></td>
</tr>
<tr>
<td>Meperidine</td>
<td>Pain</td>
<td>Vancomycin</td>
<td><strong>+7ms</strong></td>
</tr>
</tbody>
</table>

* Difference in average highest QT value in 36-day period for patients prescribed both drugs vs. one drug. QT is QT interval duration corrected for heart rate.

Tatonetti leaned in. Bit by bit, the line fell as more of the drugs were added — suggesting the drug combination was indeed blocking the cell's electrical current.

But the test wasn’t over. “It might not be stable,” Sampson said. Minutes later, he announced: “Ah! It’s holding up.”

“Holding up!” Tatonetti said triumphantly.

The test had supported the hypothesis. The drug combination blocked the current — by up to 58 percent, later analysis found.

Tatonetti, who cautioned that the results were preliminary, said testing is planned in coming months for other suspected drug pairs. He said he will also apply for a grant to find and test dozens more.

“The most exciting thing about this project,” Woosley said, “is that it’s right on the cutting edge of science. It’s using all of the science out there in novel ways.”

Drug companies for the two medications that were injected into the cells said they had no prior evidence that the combination was potentially risky.

Swiss drugmaker Roche, which discovered ceftriaxone, said the firm would not comment further until the study was published. Japanese drugmaker Takeda, which helped develop lansoprazole, said it would analyze the results but no evidence has emerged since the drug hit the market to indicate it would adversely affect the heart.

Among the other drug combinations flagged in the data mining effort that Tatonetti now wants to test in the cell lab: the blood pressure medication metoprolol, which had nearly $1 billion in sales in 2014, and the anticonvulsant fosphenytoin.

AstraZeneca, the 2014 sales leader for metoprolol, said its own research found no sign of QT prolongation attributed to taking metoprolol and fosphenytoin together. Pfizer, the sales leader for fosphenytoin, said it was unaware of any data for the drug that signals concerns regarding the heart condition.

To meet growing demands for data science, Columbia moved the biomedical informatics department into the renovated top floor in an adjacent building. There are two terraces with skyline views. Tatonetti’s office has a sliding glass door and a large window overlooking the Hudson River.

It’s an exciting time for data scientists, he said. He predicted that he and others will discover hundreds of dangerous drug interactions, one after another, and by doing so will create new knowledge in many fields — molecular biology, pharmacology, genetics.

“That’s the dream,” Tatonetti said. “I think we will.”
From big data to cell testing

To search for hidden drug interactions, the Tribune collaborated with data scientist Nick Tatonetti of Columbia University Medical Center, who had pioneered a new method of data mining called latent signal detection. The team also included a top pharmacology expert and cellular researchers.

The team went looking for drug pairs that could raise the risk of a cardiac condition called QT prolongation, an abnormality of the electrical activity in the heart that can lead to a potentially fatal arrhythmia. If the team succeeded, the project would demonstrate the potential of a method that ultimately could help protect patients and save lives.

The research had three steps:

**Step 1: Data mining**

Some medications are known to cause QT prolongation. The team compiled all the side effects associated with these drugs, plus a list of side effects that were definitely not associated. Tatonetti then searched through a federal health database, looking for drug pairs that seemed to fit this specific profile.

**Step 2: Patient records**

The data mining yielded a long list of suspected drug pairs. The next step was to check the pairs against patient records at Columbia University Medical Center to see if the association with QT prolongation could be confirmed. For eight pairs, a significant number of patients prescribed those drugs had longer QT intervals. The team chose four combinations as the best candidates for cellular testing.

**Step 3: Cellular tests**

The membranes of cells have thousands of hERG channels that are conduits for electricity and help coordinate the beating of a heart. If a drug pair blocked these channels, it would provide a biological explanation for why this combination might increase QT intervals. The first pair tested was ceftriaxone, an antibiotic, and lansoprazole, a heartburn medication.

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**Diagram:**

- **Associated side effects:**
  - Rhabdomyolysis
  - Sudden cardiac death
  - Vomiting
  - Abdominal discomfort
  - Hemorrhage
  - Myocardial infarction

- **Not associated side effects:**
  - Increased body temperature

**When ceftriaxone** alone was applied to the cells, the electrical current was unaffected. Same thing with lansoprazole. The drugs alone did not disrupt the hERG channels.

But when the two drugs were combined, the electrical current was blocked by up to 58 percent.

**Sources:** Columbia University Medical Center; Centers for Disease Control and Prevention; FDA; Dr. Ray Wesley; Tribune reporting.
Conservative icon on court

With biting wit and piercing legal mind, associate justice wrote many fiery dissents

By Denver R. Korson

Washington, D.C. — Supreme Court Justice Antonin Scalia, the vocal conservative and popular icon of the Court's right wing, died early Friday. The 79-year-old judge died while on a hunting trip in West Texas, according to a statement issued Saturday by Press Secretary supreme court clerk Eileen Johnson, a spokesperson for the U.S. Supreme Court in Washington. The statement noted that Scalia had been seen earlier in the previous evening and was found dead in his tent shortly after he did not respond to phone calls.

"He was an extraordinary individual and a wise, talented and measured lawyer and judge," Chief Justice John Roberts said in a statement. "He brought his wide-ranging knowledge of history to the Court and the country he served with pride.

In a statement Saturday night, President Barack Obama said he was "shocked and saddened" by the news, describing Scalia as a "relisher of simple things, a true originalist who will be remembered as one of the greatest jurists ever to serve on this Court".

"We are all indebted to his steadfast commitment to our Constitution and the rule of law," Obama said. "And the American people are all the richer for his lifetime of service to our country and our Court."

"We must respect his wishes and the law, that the Senate confirm a successor nominated by the President."
Prescription for harm

Becki Conway went to a doctor for help. He put her on two medications. Soon she was fighting for her life.

By Karisa King and Sam Roe

The first symptoms mimicked the flu. Becki Conway had a sore throat, a dry cough and irritated sinuses.

But the next signs were more puzzling.

A sharp pain radiated through her chest. Her eyes turned red and itchy. It seemed like she was fighting off some strange bug, or maybe it was just the normal exhaustion of keeping up with twin toddlers.

Then the scalding rash began.

Red spots popped up on Conway’s face and neck. The next day, painful sores appeared in her mouth and then her throat.

Within hours Conway was in a hospital bed, watching with alarm as the rash spread across her torso, arms and face. The red dots turned into blisters that welted so quickly it looked like her skin was burning from the inside out.
No treatment could stop it. Within a day or two she wasn’t recognizable. Eventually, the rash covered her eyelids with blisters and attacked the lining of her lungs. Her skin peeled off in sheets.

Only after it was too late to stop the rash did anyone figure out that Conway had taken a potentially dangerous mix of medications that can trigger the immune system to attack the body’s own cells.

Drug interactions in which one drug alters the effect of another are a hidden epidemic in America, a decadeslong threat to public health that has been barely acknowledged, let alone addressed.

Many interactions involve relatively safe drugs that become dangerous only when taken at the same time. Hundreds of risky combinations involve common antibiotics, blood thinners, antidepressants, cholesterol drugs and medicine to treat migraines, heart problems and high blood pressure.

The tragedy is that much of the harm is preventable. The particular drug interaction that hospitalized Conway was identified years ago. But experts estimate that thousands of patients still become sick every year from drug interactions because of errors and neglect by front-line providers of medical care.

The result in such cases: Victims and their families are left with few answers, and the underlying safety failures go uncorrected.

The doctor who prescribed Conway’s medications did not heed a black box warning about a fatal rash that could result from the drug pairing, according to medical and legal records and interviews. The pharmacy that dispensed the medicine did not call her attention to the danger. And as her symptoms rapidly worsened, a string of doctors and nurses missed the connection to the drug combination.

Most patients rely on their doctors to protect them, but studies show that prescribers often are unaware of harmful drug combinations or trust that pharmacists have more expertise. Pharmacists, in turn, tend to respect the discretion of doctors.

For pharmacists, warning patients about the risky mixing of drugs is one of the major responsibilities of the profession, according to the National Association of Boards of Pharmacy. Yet when injured patients sue, pharmacies often take the legal position that they have no duty to do so.

Pharmacies and hospitals use computer programs to screen for unsafe drug pairs. But those systems trigger so many alerts about potential drug interactions — including many that pose little risk to patients — that doctors and pharmacists frequently ignore them. Research has found that some pharmacists are more likely to approve dangerous mixes of prescriptions while working busy shifts.

When drug interactions hurt patients, the Food and Drug Administration along with most state medical and pharmacy boards do not require doctors and pharmacists to report cases. Pharmacists and doctors rarely face sanctions unless patients take the initiative to complain, according to the national pharmacy group.

“When you look at it from every conceivable aspect, the system is badly broken,” said Philip Hansten, a professor of pharmacy at the University of Washington who has studied drug interactions for nearly 50 years. “It’s really disheartening to see people are still dying from interactions we’ve known about for decades.”

Dozens of legal complaints reviewed by the Tribune described how patients be-

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**Risks rising for drug interactions**

The percentage of U.S. residents who report taking multiple prescription drugs in the past 30 days has been increasing.

<table>
<thead>
<tr>
<th>Year</th>
<th>3 or more drugs</th>
<th>3 or more, age 65+</th>
<th>5 or more drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1988-1994</td>
<td>12%</td>
<td>35%</td>
<td>4%</td>
</tr>
<tr>
<td>1999-2002</td>
<td>18%</td>
<td>52%</td>
<td>8%</td>
</tr>
<tr>
<td>2009-2012</td>
<td>21%</td>
<td>65%</td>
<td>10%</td>
</tr>
</tbody>
</table>

*Sources: Centers for Disease Control and Prevention, National Center for Health Statistics*
came sick or died from a toxic mix of drugs that was mishandled in nearly every health care setting, from family practice offices and corner pharmacies to specialty clinics, hospitals, emergency rooms and nursing homes.

One physician prescribed the cholesterol drug simvastatin to a patient in north suburban Niles who was already taking ketoconazole and cyclosporine because of a kidney transplant years earlier. The potentially lethal mix led to a toxic buildup of the heart medication and left the man too sick to walk and requiring hospital care, according to a lawsuit that was later settled.

In North Carolina, the state pharmacy board found that a CVS pharmacist had ignored computer safety warnings about combining allopurinol for gout and the kidney transplant drug azathioprine. The 49-year-old woman who took the medications together for weeks grew increasingly ill as her bone marrow failed to produce enough blood cells, leaving her hospitalized, according to pharmacy board and medical records.

The interactions don’t always set off a toxic reaction. In many cases, one drug makes the other drug ineffective, leaving patients vulnerable to the effects of HIV, cancer and other serious ailments.

When Becki Conway sought help, trusted health care providers failed her at nearly every turn, leaving her in a fight for her life.

A case of anxiety

At 37, Conway was a high-energy mother of five children ranging in age from 2-year-old twin boys to a 17-year-old son.

The summer of 2009 was one of the most hectic periods in her life. She and her husband were working full time, installing a new roof on their two-story brick home in central Michigan and preparing to open a pizzeria in a month. Their twins were not yet potty-trained.

Making matters worse, Conway was battling an ex-boyfriend in a child custody dispute and had been feeling extremely anxious. She found herself lashing out at her husband and shouting at the kids.

Conway worked at Sparrow Urgent Care in the town of Mason, registering pa-
tients as they arrived at the clinic. She decided to seek help from a doctor she was friendly with, Thomas Bellinger. The two met for 15 minutes in a break room where employees often chatted, drank coffee and ate lunch, according to interviews and documents in a later court case.

Conway mostly talked about her family history, childhood abuse and previous medications. She told Bellinger she had taken medicine for depression years earlier but hadn’t taken anything since. He told her he empathized with her and promised to bring her a book on bipolar disorder.

Bellinger had practiced family and emergency medicine since receiving his medical degree in 1985 from Michigan State University. He worked at several hospitals and urgent care clinics in Michigan before taking a job at the Sparrow clinic.

Minutes after their consultation, Bellinger approached Conway at her desk and handed her two prescriptions: one for Lamictal, the other for Depakote, according to medical records and her legal deposition. Both drugs are used to treat epilepsy and bipolar disorder. Lamictal carries the FDA's strongest label, a “black box” warning, which highlights the potential danger of combining Lamictal and Depakote.

Research on the ability of doctors to identify harmful drug pairs shows that although many physicians consider the issue when they write prescriptions, their specific knowledge about drug interactions is generally poor.

In one 2008 study, researchers asked 950 prescribers to classify various drug combinations by severity of risk. More than a third of the prescribers answered “not sure” for half of those pairs. For three of the four highest-risk combinations, less than 25 percent of the prescribers correctly recognized that the drugs should not be taken together.

Training on specific drug interactions in medical schools is lacking because of time constraints and the vast number of hazardous combinations, said Dr. Alfred George, chair of the pharmacology department at Northwestern University's Feinberg School of Medicine. Doctors also are not required to demonstrate knowledge of drug interactions to state licensing boards or when seeking hospital credentials, he said.

"New drugs are hitting the market every day, and clinicians rarely have time to read all the literature on the drugs they prescribe," George said.

Adding to the problem, no list of medications automatically follows patients from one medical provider to another. One physician may not know what another doctor has prescribed.

The label for Lamictal warns that the drug’s concentration level in the body more than doubles when taken with Depakote. To lower the risk of a deadly reaction, the label advises doctors to decrease the normal starting dose of Lamictal by half when it is combined with Depakote.

Physicians may read such warnings but make prescribing decisions at their own discretion. Bellinger gave Conway a prescription for the full initial dose of Lamictal.

In depositions, Bellinger said his diagnosis of bipolar disorder was based on multiple conversations with Conway over a period of months and that his prescriptions were in line with successful treatment plans for other patients. He said he was familiar with the black box warning but assessing the combined risk of the two drugs was difficult because Lamictal also can cause a dangerous skin rash when taken alone.

Citing language on the drug label, Bellinger said the extent to which Depakote potentially increases the risk is unclear. He believed the possible risk posed by giving Conway the full dose of Lamictal was outweighed by the danger of giving her a dose that was too low to relieve her symptoms.

In her deposition, Conway said Bellinger made a prediction as he handed over the prescriptions. She would feel better by the next day.
No warnings

Conway faxed the prescriptions to her usual pharmacy at Sparrow Hospital in nearby Lansing, part of the same health system as the urgent care clinic. Her husband, Tim Conway, worked there transporting patients and picked up her prescriptions the next day.

No one at the pharmacy called his attention to the potentially lethal drug pair, he said in an interview. No one mentioned that the dose of Lamictal exceeded the guidelines for taking it with Depakote. And no one talked to him about a rash.

“There were no special warnings — nothing,” he said.

Pharmacists serve as the last line of defense against bad drug combinations. Those who see a potentially unsafe pairing can ask questions of the patient, consult with the physician and ultimately withhold the medications.

“If a patient has a significant drug interaction that the pharmacist should’ve been aware of and didn’t catch, then their license could be affected,” said Carmen Catizone, executive director of the pharmacy group.

Yet pharmacists who are busy, distracted or inundated with alerts may fail to intercept potential drug interactions.

Sophisticated software systems automatically screen prescriptions for risky drug combinations and alert pharmacists about the danger. But more than a decade of research shows those systems fail to fully protect patients.

The safety checks produce a flood of alerts about a range of potential dangers, including drug interactions that cause only minor side effects. Pharmacists must contend with so many alerts that they can become desensitized to even the most serious warnings and dismiss them. One study found that pharmacists overrode more than 90 percent of alerts, including warnings about some risky drug interactions.

Heavy workloads for pharmacists also pose a threat. A 2007 study by University of Arizona researchers found that the risk of dispensing two drugs that could interact rose about 3 percent for each additional prescription filled by a pharmacist in an average hour.

The pharmacist who filled Conway’s prescriptions, Ryan Hamelin, later testified
in a deposition that he handled as many as 80 orders on a busy shift. He signed off on her medications at 6:51 a.m., nine minutes before his overnight shift ended.

When a technician entered the two prescriptions into a pharmacy computer, a red screen appeared with a warning that required a pharmacist’s review, Hamelin said. The alert noted a potential overlap between the medications, which are both used to treat the same illnesses, but it did not call attention to the drug interaction, he said.

Hamelin, who had received his doctor of pharmacy degree a year earlier, said he had seen such drugs paired together previously. He also said he was aware of the drug interaction and the black box warning on Lamictal.

But it seemed to him that the doctor had used some discretion when writing the prescriptions, as Bellinger had prescribed initial doses that increased over time. Hamelin trusted the prescriber’s judgment, he said.

Hamelin said he did not see a need to warn Conway personally about the drug pair. Package inserts that advise patients about drug risks typically satisfy a pharmacist’s obligation to warn about such dangers, he said.

Hamelin approved the scripts and left work.

‘This is not right’

That day, Conway began taking the two drugs. She felt better almost immediately.

But two weeks later, she felt a tickle in her throat and pain inside her ears. She had a cough and bloodshot eyes. Then she woke up with her eyes matted shut with thick gunk. Conway went to work early to get medication for what she assumed was pinkeye.

At the urgent care clinic, Conway told the medical staff about taking Lamictal and Depakote, according to her deposition. She described her symptoms, including chest pains she suffered for a day or so before the episodes stopped.

No one realized that the seemingly unconnected symptoms foretold an agonizing condition called Stevens-Johnson syndrome in which the immune system attacks the patient’s skin and mucous membranes.

The cells in the lining of Conway’s eyes, mouth and lungs were self-destructing. It was as if some switch in her body had been flipped and nothing could shut it off.

Exactly how the disease develops is not fully understood, but it is most often triggered by medications. Numerous drugs including Lamictal have been linked to the condition when taken on their own. There is no cure; the best treatment is to stop taking the drugs that caused it.

Had Conway’s condition been diagnosed, she would ideally have been sent to a hospital burn unit, which is best suited to treat the massive loss of skin as the disease progresses, said Jean McCawley, director of the Stevens Johnson Syndrome Foundation, a patient advocacy group.

Instead, Conway’s chest pains became the main concern. A doctor at the clinic ordered X-rays and an electrocardiogram to test for possible heart problems. Both showed normal results. To be cautious, Conway was sent by ambulance to nearby Sparrow Hospital for more comprehensive heart tests, medical records show.

Conway told the hospital intake nurse that she was taking Lamictal and Depakote. Because Conway’s eyes were too inflamed for her to see, the nurse pulled the pill bottles from Conway’s purse and noted the medications in a hospital record.

The second round of heart tests showed no abnormalities, and Conway was released from the hospital with a suspected strained chest muscle, records show. Her husband came to the emergency room to take her home.

After receiving her discharge papers, Conway went to a bathroom to change out
of her hospital gown. She glanced at herself in the mirror before getting dressed. On her way out, she caught another glimpse and stopped to stare. Bright red spots had popped up on her face and neck. It looked like someone had thrown red pepper on her.

Conway flagged down a nurse and pointed to her face. “This is not right,” Conway said, according to her deposition.

“Wow,” the nurse said.

The nurse retrieved a doctor, who examined Conway. But no one connected the outbreak to the two new medications she had reported to nurses and doctors twice that day.

The nurse gave Conway a shot of Benadryl and sent her home.

Deadly diagnosis

Spotting the signs of a dangerous mix of medications can be critical to saving a patient’s life. But because the interactions often cause common symptoms, such as low blood pressure or confusion, health care providers can easily miss the clues.

“Drug interactions hurt and kill like nobody has any idea,” said David Juurlink, head of clinical pharmacology and toxicology at Sunnybrook Health Sciences Centre in Toronto.

Juurlink has treated patients who arrived at the emergency room after taking an antibiotic with certain types of blood pressure medication, which can cause a deadly spike in the level of potassium in the blood. Such a death likely would be attributed to heart disease and old age instead of a drug interaction, he said.

After Conway got the Benadryl shot she went home and went to sleep. She woke up at 4 a.m. with painful blisters in her mouth. Her skin rash was turning into red welts. Conway drove herself to the clinic where she worked and was examined by Dr. Kellie Donahue.

The doctor asked Conway about her symptoms and any medication she had been taking. When Conway told her about the Lamictal and Depakote, Donahue stopped taking notes and looked up at her.

“I think you have Stevens-Johnson syn-

Avoiding risky drug interactions

Experts say there are important steps patients can take to help protect themselves from a harmful mix of medications.

■ With every new prescription, ask your doctor and pharmacist about what other medications you should avoid, including over-the-counter drugs, foods and dietary supplements.

■ Carry a list of all current medications and bring it to any medical appointments. The list should include drugs taken only occasionally, over-the-counter medications, patches, tablets, inhalers, drops, liquids, ointments and injections, as well as herbal, vitamin and dietary supplements.

■ Read the complete package insert for all medications you’re taking.

■ Use one pharmacy for all your prescriptions.

■ Educate yourself about potential drug interactions for any medications you are taking.

■ If a doctor provides you with a new drug sample, ask if it interacts with the medications you’re currently taking. Routine computer safety checks may have been skipped.

■ Take as few medications as possible.

■ Do not take medications prescribed to someone else.

— Karisa King
drome,” she said, according to Conway’s deposition.

Donahue, the first medical professional to notice the dangerous drug mix, explained to Conway that she was suffering from a serious skin rash caused by medications.

But even Donahue didn’t realize how severe the rash would become.

After telling Conway to stop taking the drugs, which Conway had done when the chest pains began, Donahue gave her a steroid shot and sent her home.

Conway took a short nap and woke up with blisters spreading into her throat. She called Donahue, who instructed her to go to the hospital immediately.

Her first night in the hospital, Conway sat up in bed until dawn researching Stevens-Johnson syndrome on her laptop computer. She’d never heard of the disease. The more she learned, the more alarmed she became. She discovered that, in its most extreme form, many victims die. The biggest risks stem from infections.

In the next days, Conway’s blisters spread and erupted. Swallowing food was too painful. She couldn’t stop coughing and complained that she was struggling to breathe.

Her skin began to peel off in sheets, leaving angry patches of exposed flesh that turned black and bloody.

Worried about infection, her husband laid down a trail of towels so she didn’t have to walk to the bathroom on the hospital floor. He spent the nights at her bedside in a chair. He didn’t know what to tell the kids, especially the three youngest. He didn’t want them to visit their mother — her wounds looked too gruesome. He did not disclose his biggest fear, that she might not come home.

Conway sporadically roused herself from a stupor of morphine, but mostly she was in too much pain to speak or open her eyes.

On Conway’s 10th day at the hospital, nurse Kathy Sandoval was assigned to treat her. The nurse had treated one other Stevens-Johnson victim years earlier, but when she walked into the room, she had never seen anything that compared to how Conway looked that day, Sandoval recalled in an interview.

From head to toe, only patches of skin could be seen. “It was red, open, exposed.”
Sandoval said. “She wasn’t gushing blood, but there was blood everywhere.”
Sandoval was afraid to touch Conway.
“She looked like she’d been in a fire,” Sandoval said.
She knew how lethal the condition could be and worried that the sloughing tissue in Conway’s lungs and throat might block her airway. Sandoval hovered over Conway’s bed watching for signs of distress.
That night, at Sandoval’s insistence, Conway was transferred in unstable condition from Sparrow to an intensive care burn unit at the University of Michigan Medical Center, records show.
At that point, about 70 percent of Conway’s skin had blistered or peeled off. She could barely communicate.
The next day, an ophthalmologist tried to examine the damage in her eyes, but Conway was in too much pain to cooperate. In the doctor’s notes from that day, he wrote that Conway told him she didn’t expect to survive.

**Fighting to live**

Medical records document the flurry of activity that surrounded Conway at the Ann Arbor hospital. Nurses checked her vital signs at regular intervals. Doctors inserted a feeding tube. The wound care was constant. Every hour, nurses pried open her eyelids to apply drops of medicine.
“They’re just trying to keep the patient alive at that point,” said McCawley of the Stevens-Johnson advocacy group. “Patients are usually monitored 24/7 with the most intensive care they can give them. ... The reaction has to run its course.”

On Conway’s third day at the hospital, her condition improved slightly. She was able to sit up on her own and was taken off contact isolation, which meant that staff no longer had to wear gowns and gloves to enter her room.
Over the next few days, the rash stopped spreading and parts of her skin began to grow back.

In an attempt to save her eyesight, doctors grafted amniotic membrane onto her eyes to help them heal. She continued to gain strength and looked better.

Medication was more effective in easing her extreme pain. The lesions on her face were clearing. Doctors removed her feeding tube and she was able to swallow soft food.

After nearly three weeks, Conway returned home with her eyes stitched shut so they could heal from surgery. Wounds were still red and visible on her face and neck. Her twins were too scared of her appearance to sit on her lap, so her husband turned off the lights in the living room and they sat with her on the couch.

She held their hands in the dark, tracing the outlines of their small fingers. Unable to see, she learned to distinguish the boys by the shape of their fingernails.

Conway spent the next two months unable to open her eyes and later received training on how to walk with the help of a long white cane. In the years since, she has slowly regained her strength, taking long walks and working on home repair projects with her husband.

But the trauma left Conway legally blind. In her left eye she can see only shadows and light. By holding a computer tablet close to her right eye and magnifying the text, she can read in limited amounts.
She can’t drive a car or watch the kids at sports events or read a paperback book.
She also suffers stabbing pains in her eyes from nerve damage, leaving her unable to get out of bed on her worst days. She must frequently apply medicated eyedrops because her tear ducts were destroyed. She fights a constant cough caused by her lung injuries. The family now lives in Florida where the high humidity provides some relief for her eyes.
Conway said her approach to taking medication has changed.
“The general public trusts that what their doctors give them is OK,” she said. “They don’t question it, but they should question it — every time.”

In 2012, Conway filed a lawsuit against Bellinger and Sparrow Health System that was settled in 2014 under confidential terms. She and her husband talked about her ordeal in several interviews but declined to disclose the names of the defendants, whom the Tribune identified through court records.

Her attorney, Andrea Dalton, said she has handled more than a dozen lawsuits for other patients, many of them children, who suffered from Stevens-Johnson syndrome after taking the same drug combination as Conway. The cases fit a pattern of errors, Dalton said.

“It starts with a hospital or physician error, then there’s a pharmacy error and diagnostic errors, and that becomes the perfect storm,” she said. “At the end of this is someone who has to live with it for the rest of their life.”

Citing a confidentiality agreement, Bellinger’s attorney declined to comment on the case. An attorney for Sparrow Health System said Hamelin, the pharmacist, turned down requests for interviews. The health system released a brief statement saying: “Sparrow cannot discuss specifics of this case due to the nature of the settlement agreement. But the safety and security of patients is always our top priority.”

Bellinger stopped prescribing the two drugs together after Conway became ill, he said in a deposition. It wasn’t worth the risk, he decided.

The case did not appear to change anything for Hamelin, the pharmacist who handled the prescriptions. He testified he would not have a problem filling the same order again.