The European Institute for the PCB Community

EIPC SPEeDNEWS

The Weekly On-Line Newsletter from the European Institute of Printed Circuits.
Issue 25 - August 2021

NEWS FROM GERMANY

Invitation to SCHWEIZER Earnings Call: 1. Half Year 2021

On Friday, August 6, 2021 Schweizer Electronic AG (ISIN DE0005156236) will publish its report for the 1st half year 2021.

The company cordially invites you to the **Earnings Call with Mr Nicolas Schweizer (CEO) and Mr Peter Bosenius (Director Finance & Controlling) on Friday, August 6, 2021, at 10:30 hours.**

We are looking forward to an exciting exchange and your registration via the online platform CONNECT:

Montega CONNECT: Schweizer Electronic AG - Earnings Call H1 2021

If you have any question, please do not hesitate to contact us.

Best regards
Schweizer Electronic AG

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ELECTRONIC INDUSTRY NEWS

Component Prices Rise 10% to 40%

Global Electronics Industry Faces Continuing Supply Disruptions

Summary

- The latest IHS Markit Global Electronics Purchasing Managers' Index (PMI) for June was strongly expansionary, boosted by buoyant demand in key markets.
- The strong rebound in world consumer markets, notably in the US, China and Western Europe, is continuing to drive growth in demand for electronics.
- The impact of the pandemic has accelerated the pace of digital transformation due to the global shift to working remotely.
-

The latest IHS Markit Global Electronics Purchasing Managers' Index (PMI) for June was strongly expansionary, boosted by buoyant demand in key markets. Rebounding consumer spending and industrial production in key economies, notably the US, China, EU and UK, are helping to drive demand for a wide range of electronics products.

However, the strength of global electronics demand is continuing to exacerbate semiconductors shortages for some manufacturing industries, notably the global

automotive sector. Supply chain disruptions to semiconductors production have also impacted on the situation. The new COVID-19 waves in East Asian electronics manufacturing hubs such as South Korea, Taiwan, Malaysia and Vietnam have further increased risks of potential supply chain disruptions at electronics plants due to escalating domestic pandemics. Meanwhile, the latest IHS Markit Global Electronics PMI survey shows evidence of sharp increases in electronics industry input prices as well as output prices, mainly due to shortages of essential raw materials.

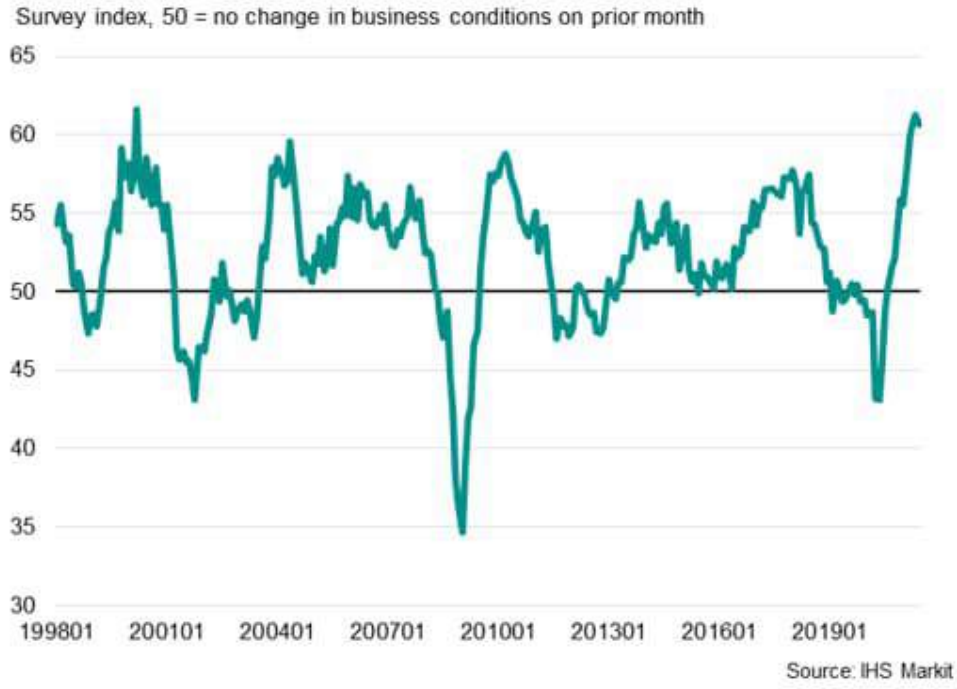
Global electronics industry continues to strengthen

The strong rebound in world consumer markets, notably in the US, China and Western Europe, is continuing to drive growth in demand for electronics. This is resulting in buoyant growth in household spending on electronics products as well as products that are intensive users of electronics, notably autos.

The headline seasonally adjusted IHS Markit Global Electronics PMI registered 60.7 in June, continuing to show strong operating conditions, albeit edging down from 61.2 in May. Sharp growth was once again seen across output and new orders, driving another strong rise in employment.

The IHS Markit Global Electronics PMI new orders index meanwhile rose from a low of 35.0 in May 2020 to a level of 61.5 in June 2021. The rate at which demand improved during June was strong, despite easing slightly from the 17-year high recorded in the previous month.

IHS Markit Global Electronics PMI



IHS Markit Global Electronics PMI new orders

The electronics sector rebound is making an important contribution to the recovery of manufacturing exports and industrial production in many East Asian industrial economies. The electronics manufacturing industry is an important part of the manufacturing export sector for many Asian economies, including South Korea, China, Japan, Malaysia, Singapore, Philippines, Taiwan, Thailand and Vietnam.

Furthermore, the electronics supply chain is highly integrated across different economies in East Asia.

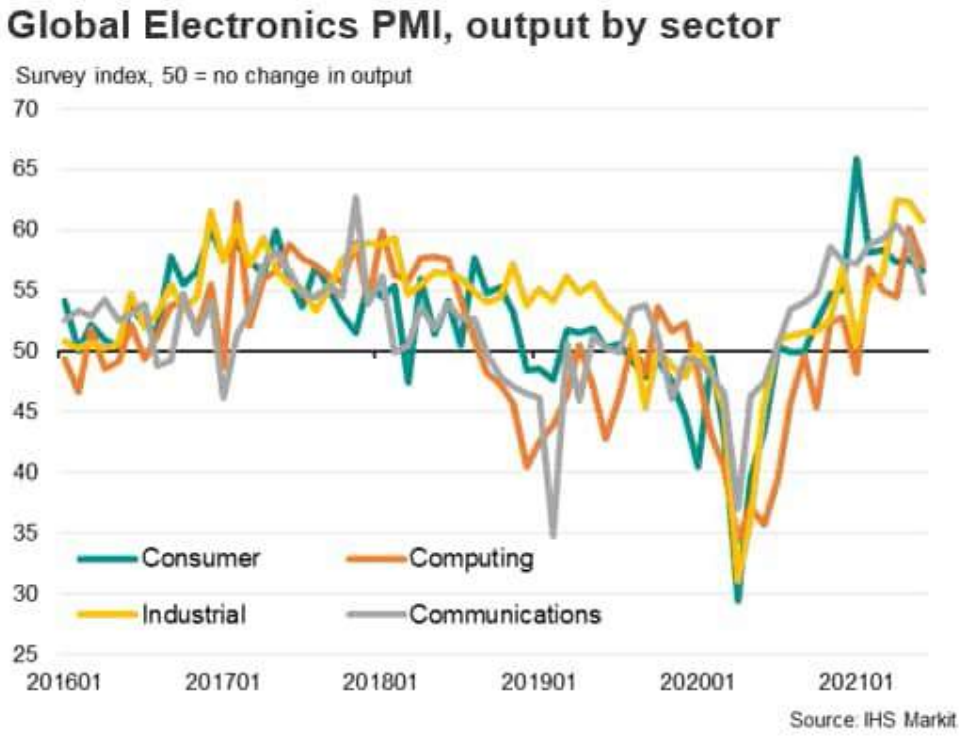
Global electronics demand has risen strongly due to the global shift to remote working and online shopping. This has resulted in surging demand for consumer electronics products such as laptops, mobile phones and wearables.

China's exports for June 2021 continued to show strong growth, rising by 32.2% y/y according to trade data from China's General Administration of Customs. This reflected continued strong global demand for electronics and PPE equipment as well as the impact of base year effects due to global lockdowns a year earlier. China's exports of LCD panels in value terms were up 56% y/y in the first six months of 2021, while exports of integrated circuits were up 32% y/y. Exports of mobile phones rose by 33.5% y/y in the same period.

South Korea's exports of information and communications technology (ICT) goods have also shown strong growth in the first half of 2021 and increased by 29% y/y in June. South Korean semiconductor exports rose by 34% y/y, with exports of memory chips up 31%, while exports of system chips rose by 47% y/y. Exports of displays rose by 30% y/y. Electronics exports to key markets showed large increases, with exports to the US up 32% y/y, while exports to the EU were up 51% y/y. Exports to Vietnam, which is a key manufacturing hub for South Korean electronics firms, also showed rapid growth of 25% y/y.

Japanese exports of electronics have also performed strongly, with semiconductors exports up 25% y/y in June, while exports of integrated circuits rose by 14% y/y.

All four monitored sub-sectors of the global electronics industry continued to show robust expansion in June, according to the IHS Markit Global Electronics survey, with very strong growth in the industrial and computing segments.



Sharply rising electronics input pricing pressures

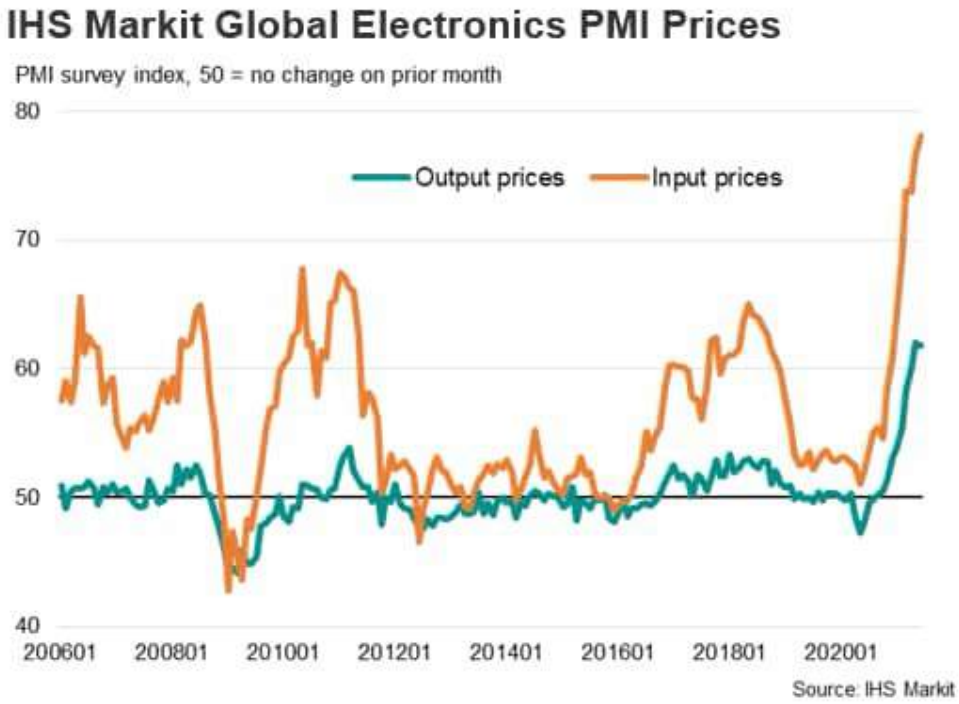
The rapid rise in electronics production has also triggered a sharp upturn in raw materials input prices for electronics firms during the first half of 2021. The IHS Markit Global Electronics PMI Input Prices Index has continued to rise rapidly during the second quarter of 2021, increasing from 72.8 in April to 77.8 in May and 78.1 in June. Notably, the rate of input price inflation is the quickest since the PMI series began in January 1998. Companies that were surveyed overwhelmingly linked raw material shortages to rising prices.

Reflecting the sharp increases in input prices, the IHS Markit Global Electronics PMI Output Price Index continued to signal strong pricing pressures, at 61.8 in June.

The near-term pricing outlook for the remainder of 2021 according to IHS Markit Pricing & Purchasing analysis for semiconductors and components generally is that supply shortages are likely to continue to translate into price escalation. Printed circuit board assemblies are the most severely affected, but semiconductors, bare printed circuit boards, resistors, capacitors, and connectors are all expected to see price pressures. Escalation generally over the second half of the year will be greater than 10%. (See "Prices: Pricing Analysis - Semiconductors", by IHS Markit Pricing & Purchasing, 1st July 2021.)

In 2022 and 2023, capacity expansion will bring supply and demand closer to balance and lead to stabilizing prices. According to IHS Markit Pricing & Purchasing, moderating demand for electronic components and improving semiconductors production is expected to bring supply and demand closer to balance and lead to

some price relief. Specific categories will show some resilience in pricing, given the changing demand landscape. For example, the expansion of electronics in light vehicles will keep pressure on certain commodity electronic components.

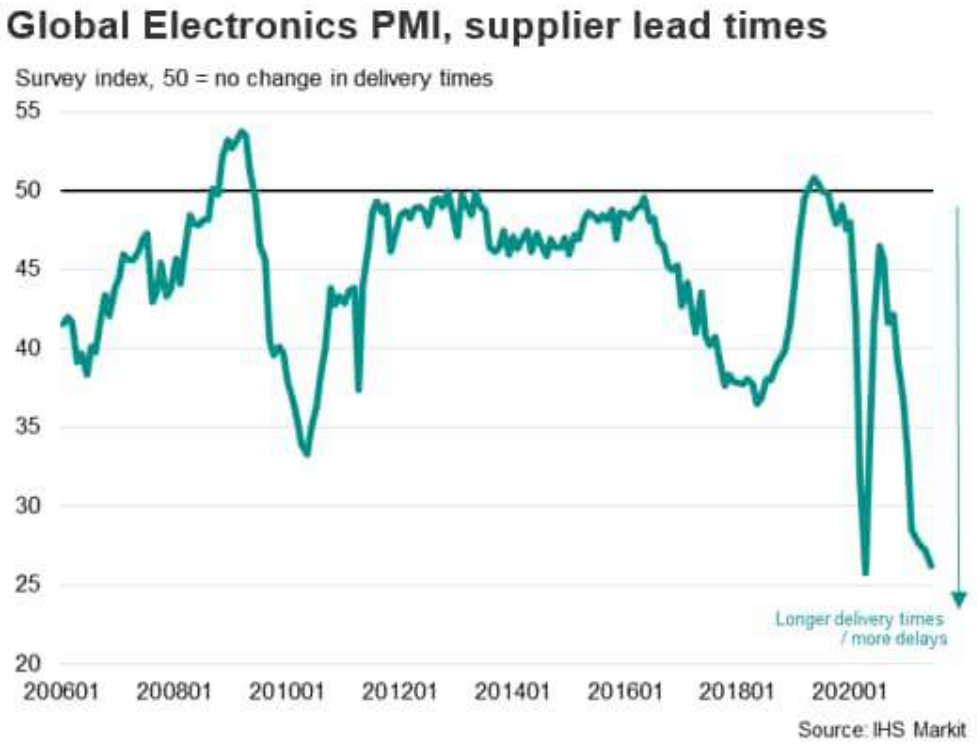


With significant shortages of semiconductors having become evident globally during the first half of 2021, this is expected to further boost South Korean semiconductors exports during 2021.

Electronics supply chain disruptions

In the electronics industry, the strength of global electronics demand is continuing to exacerbate semiconductors shortages for some manufacturing industries, notably the global automotive sector. Supply chain disruptions to semiconductors production have also impacted on the situation. Semiconductors and electronic components are in very short supply. According to analysis by IHS Markit Pricing & Purchasing, sporadic electronics production outages because of COVID-19 continue, and while many or most facilities are operating at or near full capacity, the supply chain for electronic components is highly sensitive to disruptions.

Meanwhile, the latest IHS Markit Global Electronics PMI survey shows evidence of sharp increases in electronics industry input prices as well as output prices, mainly due to shortages of essential raw materials.



Global auto manufacturers as well as smartphone producers are among the industry segments that have been impacted by semiconductors shortages. According to IHS Markit Automotive research, vehicle manufacturers have faced increased disruption to the supply of systems using semiconductors in the first half of 2021. Many automakers worldwide have reported disruptions to production due to shortages of semiconductors, including Ford (NYSE:F), VW Group (OTCPK:VWAGY), GM (GM), Honda (NYSE:HMC) and Mazda (OTCPK:MZDAY).

According to IHS Markit Automotive research, reports of disruption within the supply chain of semiconductors to the automotive sector began in late 2020 and have continued in the first half of 2021, with further disruption expected during the third quarter of 2021. These disruptions of supply of important electronic components have resulted in significant disruption of global auto production during the first half of 2021, amounting to auto production being reduced by around 4 million units during that period. (See IHS Markit Automotive, 20th July 2021, "Semiconductor Supply Issue: Light Vehicle Production Tracker").

The extent of the shortages of critical electronics components became so severe that high level consultations were held involving key industry bodies as well as government officials from major industrial economies including the US and Germany. Technology companies including semiconductors manufacturing firms participated in the White House Summit on 12th April on semiconductors shortages and supply chain vulnerabilities.

Global semiconductors shortages have also been impacted by temporary supply disruptions to semiconductors production in Texas due to power outages in February

as a result of severe weather, as well as production disruptions in Japan due to a fire in a Renesas Electronics (OTCPK:RNECF) semiconductors plant in mid-March.

Chip stockpiling during 2020 due to US government sanctions on certain Chinese technology companies have also contributed to the shortages. Global auto manufacturers as well as smartphone producers are among the industry segments that have been impacted by these shortages. The US Department of Commerce added seven Chinese supercomputing firms to its entity list in early April 2021.

Risks from new Covid waves in East Asia

Since April, a number of East Asian economies with large electronics manufacturing industries have been hit by escalating COVID-19 Delta waves.

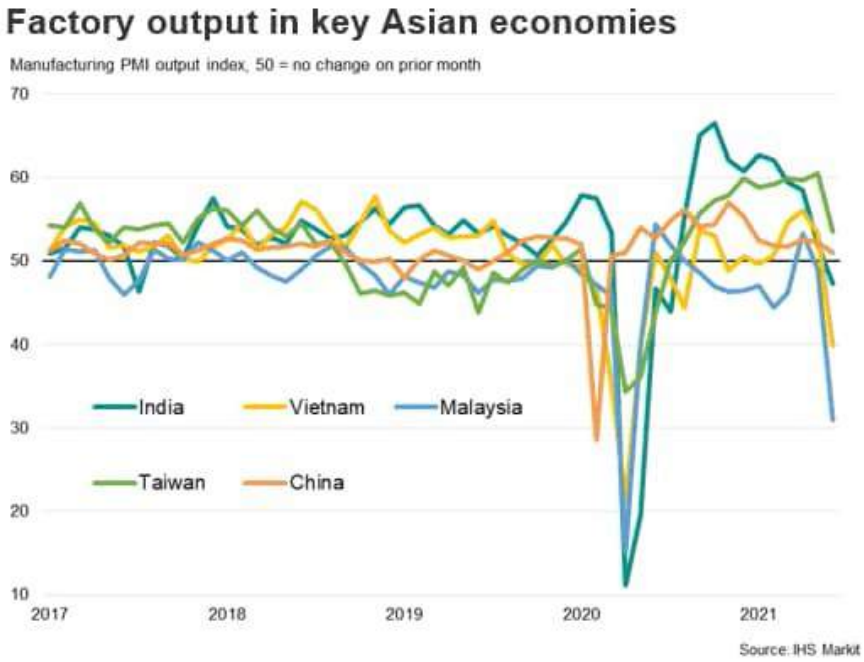
Due to the new COVID-19 outbreak that has occurred in Taiwan during May and June, electronics production has faced some impact effects. The King Yuan Electronics Co. (KYEC) chip-testing plant shut down temporarily in early June due to a Covid cluster among workers on its factory floor, although operations resumed within days, using other staff. Another chip-testing firm, Greatek Electronics, has also been impacted by a Covid cluster in its facility. However, with daily new COVID-19 cases having fallen sharply in recent weeks, the situation has been gradually improving.

In Southeast Asia, Malaysia, Thailand, and Vietnam, which are significant electronics manufacturing hubs, are all currently experiencing significant Covid waves that have triggered lockdowns and are creating significant disruption to economic activity.

The latest IHS Markit Manufacturing PMI surveys for Southeast Asia have reflected the impact of these new lockdown measures, which have disrupted industrial production and consumption spending.

In Malaysia, the headline IHS Markit Malaysia Manufacturing Purchasing Managers' Index (PMI) fell sharply in June, to 39.9 compared with 51.3 in May. This pointed to a severe decline in business conditions in the Malaysian manufacturing sector.

Vietnam's economy has also been hit by the impact of the latest Covid wave, after its economy showed considerable resilience during 2020 as the domestic pandemic was successfully contained. The latest wave of COVID-19 cases in Vietnam led to a sharp decline in business conditions for manufacturers during June. The IHS Markit Vietnam PMI dropped sharply to 44.1 in June from 53.1 in May, pointing to the most rapid deterioration in business conditions for over a year and ending a six-month period of growth.



With reported daily new cases having risen sharply in recent weeks in many Southeast Asian nations, there is still significant uncertainty about how protracted and severe the current Covid waves will be, posing continuing risks to electronics supply chains in the region.

APAC electronics sector outlook

During the first half of 2021, global electronics demand has shown a strong rebound from the lows of the first half of 2020, when lockdowns disrupted production and consumer spending. With improving economic recovery underway in the US and EU as COVID-19 vaccines are progressively rolled out, demand for electronics products is expected to remain strong during the remainder of 2021.

The impact of the pandemic has accelerated the pace of digital transformation due to the global shift to working remotely, which has boosted demand for electronic devices such as computers, printers and mobile phones. The easing of lockdowns in many countries has also triggered a rebound in consumer spending, helping to boost demand for a wide range of consumer electronics. Spending on consumer electronics has also been boosted by fiscal stimulus measures in many OECD countries that have provided significant pandemic relief payments to support households in many large economies, including the US, UK, Japan, and Australia. Meanwhile global auto demand has also shown a rebound after slumping during the first half of 2020, which is boosting demand for auto electronics, albeit contributing to intensifying supply-side problems related to semiconductors shortages.

The medium-term economic outlook is also supportive for the electronics industry, with sustained strong world economic growth forecast over 2022-2024.

With shortages of semiconductors disrupting manufacturing supply chains in early 2021, the importance of having domestic electronics production capacity for critical electronics components has become a national priority for major industrial nations, including the US, EU and China. For the US and EU, reducing reliance on Asian semiconductors production has become a key strategic priority over the next decade.

A key risk is excessive global vulnerability to semiconductors supply from South Korea and Taiwan, which are major electronics production hubs but also potential geopolitical flashpoints in the Asia-Pacific region. Military tensions in the Taiwan Strait and South China Sea have escalated during the first half of 2021, highlighting these vulnerabilities.

The outlook for electronics demand is also supported by major technological developments, including 5G roll-out over the next five years, which will drive demand for 5G mobile phones. Demand for industrial electronics is also expected to grow rapidly over the medium term, helped by Industry 4.0, as industrial automation and the Internet of Things boost rapidly growth in demand for industrial electronics.

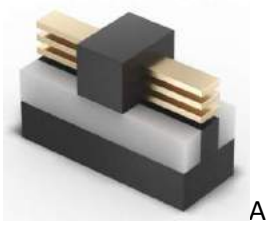
Competition amongst leading technology nations in strategic electronics production has also intensified. Consequently, strategic global competition amongst the world's leading high-technology nations is also likely to play a greater role in reshaping the global electronics industry landscape over the next decade.

Intel Charts Manufacturing Course to 2025

The company's roadmap includes a new transistor architecture, and new interconnect

By Brian Santo

Intel CEO Pat Gelsinger has had enough. 10 nanometers will continue to be 10 nanometers — Intel is stuck with that. But as of today, the next version of 10 nm, aka SuperFin, will instead be Intel 7, and 7 nm will henceforth be Intel 4 (no "nanometers"). There will then be an Intel 3, after which Intel will then cease even *thinking* in nanometers; after 3, Intel will be alluding to angstroms, starting with nodes it will call 20A and 18A.


A graphic representation of the ribbonFET, Intel's version of the gate all-around (GAA) transistor.

That'll be five nodes taking Intel into 2025. The roadmap the company just announced includes a new transistor architecture — a gate all-around variant Intel calls the ribbonFET; a new interconnect technology called PowerVia that uses the back of the wafer; and the announcement that Intel is contributing to an evolution of EUV technology with lithography specialist ASML.

The renaming of nodes seems like it might be specious flapdoodlery from a company trying to get everyone to forget that it stumbled and lost the technology lead it once had, but the node designations used by its competitors to make Intel sound like it's lagging are already almost meaningless marketing blah-blah.

So why shouldn't Intel reset its nomenclature? Intel has always argued that the performance it can deliver at any given node is better than the performance enabled by the like-numbered nodes of its competitors, anyway. The company has made a good case, for example, that it's 10nm process is equivalent to TSMC's 7nm process.

The key issues for IC designers are performance, performance improvement from node to node, and the pace of the progression from node to node. Intel famously missed its own deadline for delivering the 10nm process node (now in full production swing).

Losing the technology lead (or being perceived as having lost the lead) was bad enough, but stumbling on the node progression was just as bad, if not worse. An IC manufacturer's customers have their own roadmaps, and if their key chip supplier can't get them where they need to go, then it's time to consider finding a new key supplier.

Which explains why Gelsinger since taking the reins of Intel has repeatedly vowed that Intel would start progressing from one node to the next on a regular cadence, each coming with substantial performance gains. Delivering is essential. If Intel were to experience another failure to progress from one node to the next in a timely manner, that would not just jeopardize existing relationships, it would be fatal to Intel's brand new foundry business, Intel Foundry Services (IFS).

Today Intel announced a fairly detailed roadmap for node progression:

- Intel 7 will be introduced this year and will be in production in 2022
- Intel 4 will be introduced late in 2022 and will be in production in 2023
- Intel 3 will be introduced later in 2023, implying production in 2024
- Intel 20A will be introduced early in 2024
- Intel 18A is scheduled to be introduced in early 2025

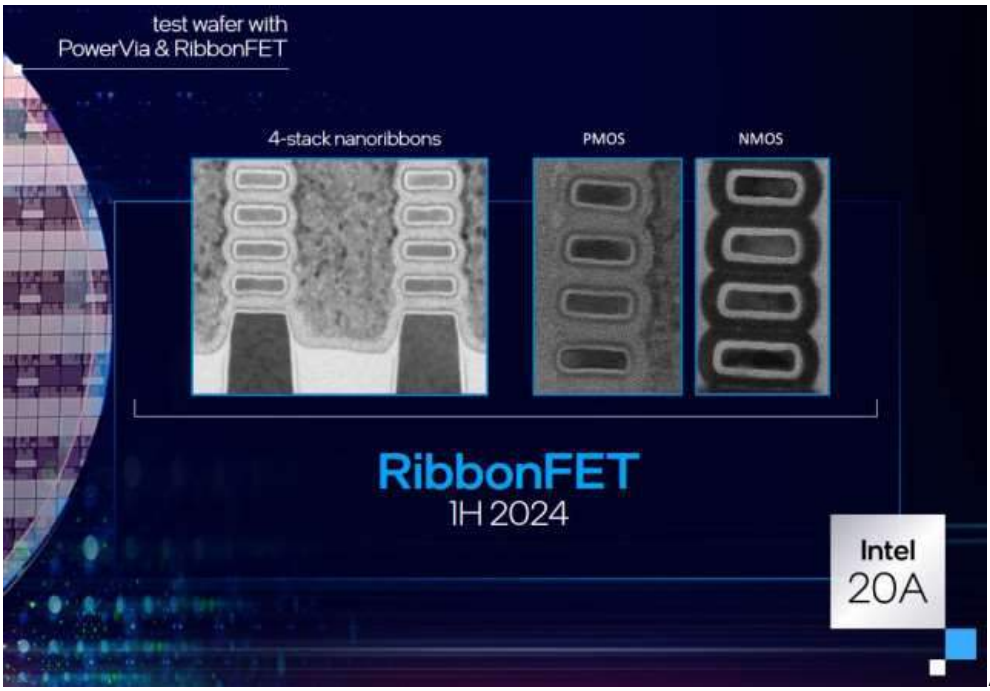
Intel also mapped processors on its product roadmap to some of its upcoming process nodes.

For example, Intel 7 will be featured in products such as Alder Lake for client in 2021 and Sapphire Rapids for the data center, which Intel said is expected to be in

production in the first quarter of 2022. Intel 4 will be used to create Meteor Lake ICs for client and Granite Rapids for the data center.

Nodes and manufacturing processes

Intel said it will “fully embrace” EUV lithography with Intel 4. The company will continue refining finFET technology through Intel 3; after that, starting with 20A, it will shift to a gate all-around (GAA) structure. Everyone working on advanced process nodes is anticipating moving from finFET to GAA. Intel has its own approach to GAA, however, that it’s calling the ribbonFET.



An image of the ribbonFET from Intel’s presentation.

Intel also talked about a new interconnect technology called PowerVia. Traditionally, interconnect is positioned on top of transistors. Historically that’s worked fine, but at smaller dimensions with new architectures, Intel said inefficiencies arise. PowerVia describes a process of putting interconnect on the underside of the chip. The company plans to experiment with it for Intel 3, so that it will be ready to commercialize fully in Intel 20A.

Intel said it is partnering with Qualcomm to develop a major smartphone platform at the 20A node. If the relationship holds, Qualcomm’s endorsement would be significant. Intel has been trying to achieve a foothold in the smartphone market for some time, with minimal success.

To hammer home its commitment to manufacturing, Intel said it is working with ASML to help define, build, and deploy a refinement on EUV technology, called high numerical aperture EUV. Intel said it will have the first production high-NA EUV

system in the industry. Intel said high-NA EUV would contribute to ribbonFET improvements in the 18A process node.

For years Intel has been boasting that it leads in new packaging technologies, which will be critical for improving semiconductor performance moving forward. The company said IFS has signed up AWS as its first customer for packaging solutions.

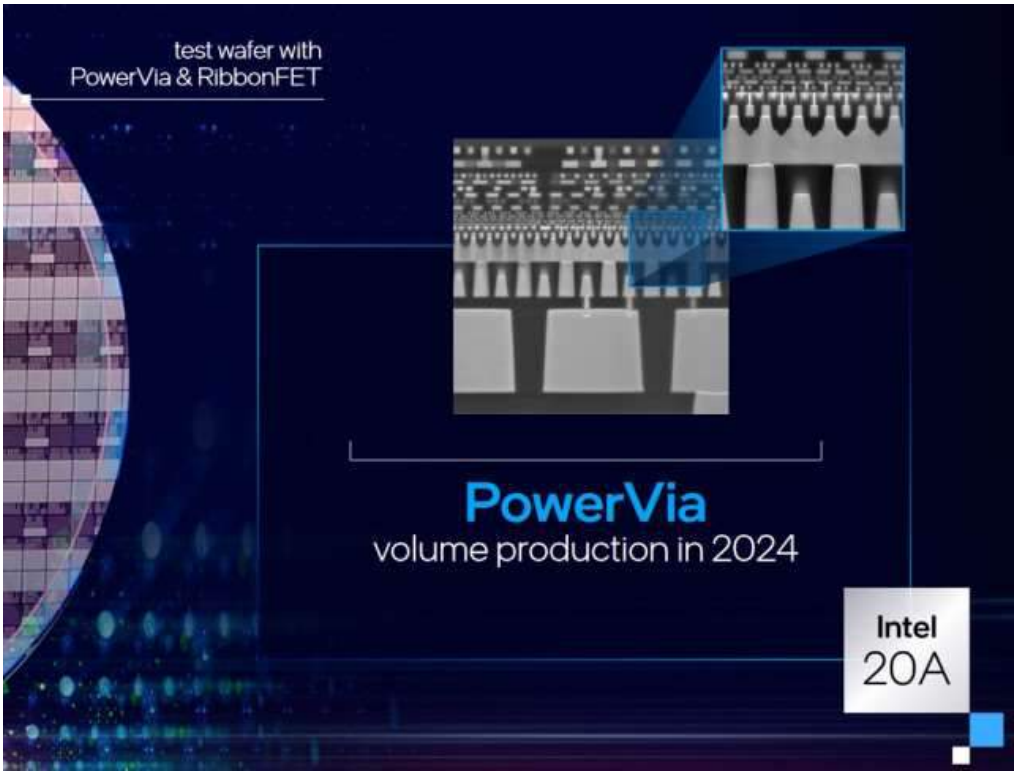


Image of the PowerVia from Intel's presentation.

Node designations

Historically, there used to be some relationship between the minimum size of a transistor gate and node designations. It's arguable when that relationship fully broke down. Some say it was at the 32 nm node, which arrived around 2010. Intel today said it was back in 1997, which would have been right about the time the industry was shrinking down to 0.18 micron. Whenever the disconnect started, there's no relationship now.

That's why, according to Tirias Research analyst Keven Krewell, "The number reset was overdue. Intel had been doing 14nm+++ stuff that was meaningless to anyone outside of Intel. TSMC meanwhile would create intermediate nodes like 8nm. That said, it's really hard to make a detailed transistor to transistor comparison," he wrote.

Asked about Intel's plan for the next five nodes, Krewell wrote, "The roadmap is extremely aggressive, but Intel feels it's ready for this leap forward. Each new node is tied to a specific product, so it will be transparent how Intel is performing. The Qualcomm win for 20A is years in the future, but impressive that Qualcomm is willing to publicly commit to it.

"Packaging is important part of the story, with Intel getting AWS as a customer," Krewell added.

Intel made its announcements in a conference call Monday afternoon. During the question-and-answer session following the company's presentations, Gelsinger was asked about other customers beyond AWS and Qualcomm. He stopped to note that the work with Qualcomm demonstrates that IFS customers will get access to the most advanced manufacturing technology concurrent with Intel getting it to use for internal purposes.

Gelsinger said Intel was talking with other customers beyond Qualcomm, but begged off on naming any. He did say that some are in the industrial segment, some in automotive, and some are semiconductor companies — including some traditional rivals — who need foundry. "IFS is off to the races," he enthused.

Brian Santo

Brian Santo is Editor-in-Chief of EE Times. He has been writing about technology for over 30 years, for a number of publications including Electronic News, IEEE Spectrum, and CED; this is his second stint with EE Times (the first was 1989-1997). A former holder of a Radio Telephone Third Class Operator license, he once worked as an engineer at WWWG-AM. He is based in Portland, OR.

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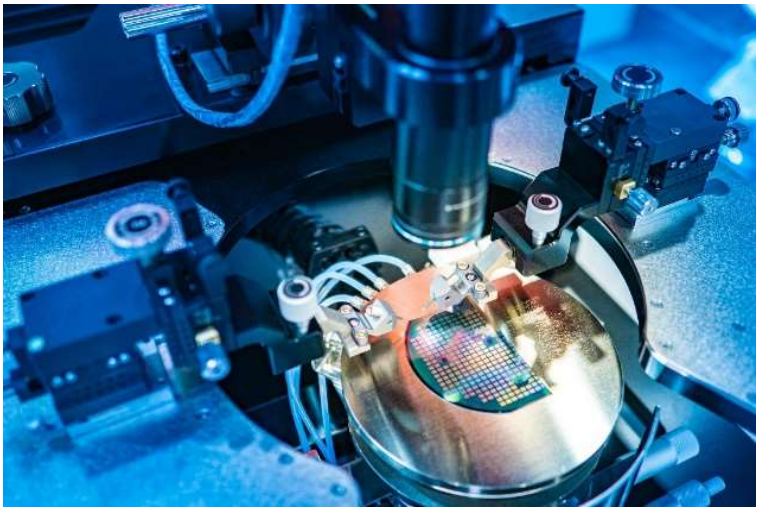
NEWS FROM ITALY

Seica

Full Probe Card Test

The latest fixtureless technology available for production and validation testing the most challenging Probe Cards

Wafer fabrication is a sequential or “front end” process that starts to create the electronic circuit. The manufacturing process of silicon wafers simplifies the process and allows many integrated circuits to be placed onto a semiconductor wafer. This wafer is then diced and packaged. Before the dicing is performed, the circuits need to be tested. This electrical test is carried out with the help of a probe card.



What is a Probe Card?

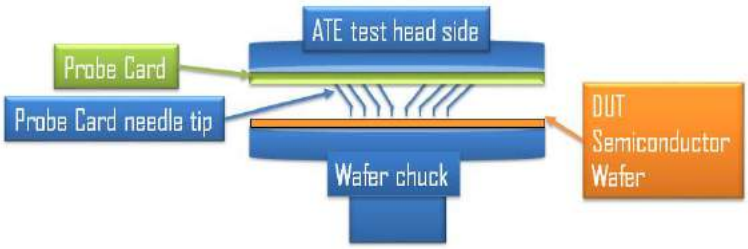
A Probe Card is basically an interface that provides electrical and mechanical contact between the device under test [DUT], which is the semiconductor wafer, and the test system electronics.

A Probe Card consists of the following elements:

- The Multilayer Organic substrate (MLO™)
- The Printed Circuit Board (PCB)

The wafer test system is composed of different parts:

- The wafer under test [DUT] is presented to the Wafer chuck
- The Probe Card is docked onto the wafer and it serves as a connector between the bonding pads of the DIEs and the test system.



How probe cards are tested?

We have seen that the Probe Card is a critical part of the wafer test system, and it is mandatory to test it before integrating it into the wafer test system. When the device I/O bandwidth and the power demands increase, it is necessary to meet the requirement for high performance power and signal delivery during the electrical test. These requirements drive the challenges for the testing of the probe cards.

Thanks to many years of experience in testing probe cards, Seica has designed the **PilotV8XL HR Next> series,** which is the ONLY flying Probe that can offer a full turnkey solution for the Probe Card test.

The **PilotV8XL HR Next> series** brings together in a unique system three different tools and solutions to perform a complete test, they are:

- **Bare Board Test** for single MLO™ & PCB Test
- **ICT & Functional Test** for assembled PCB Test
- **Probe Card Test** for PCB+MLO™

Along with the three test strategies above the PilotV8XL HR Next> series ensures ICCT (Integrity Connection Certification Testing). This ICCT is a requirement for certification for the integrity of the connections between the MLO™ and PCB.

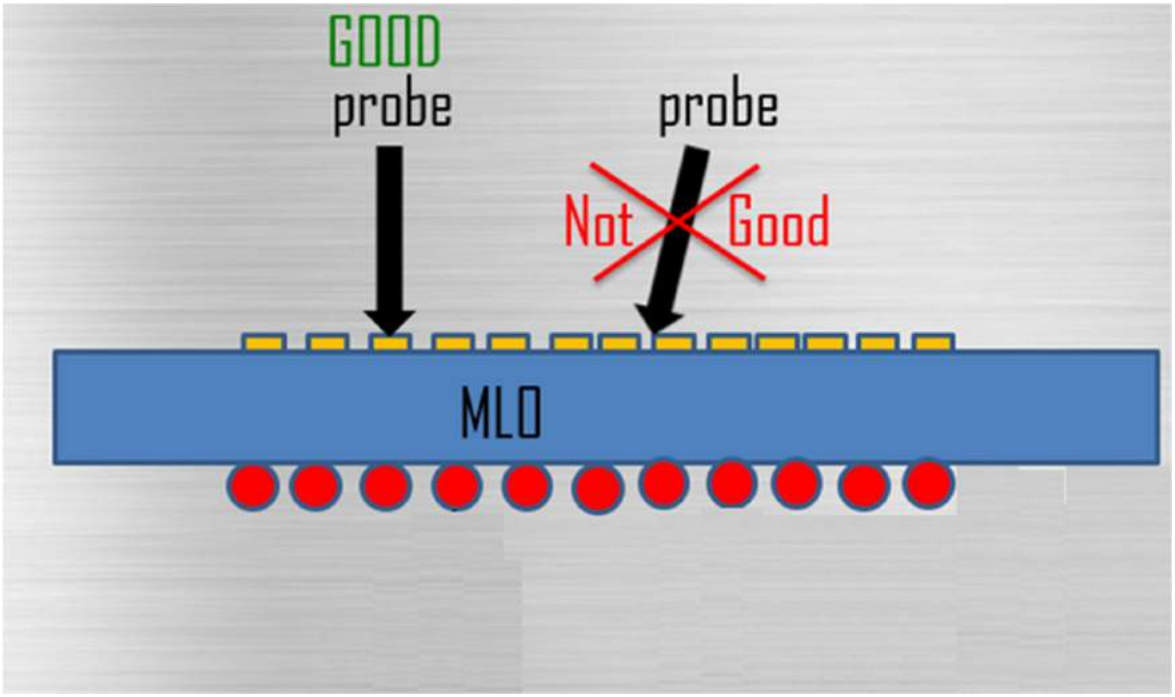
Pilot V8 XL HR Next> series Hardware Features

The main hardware characteristics of the **Pilot V8 XL HR Next> series** are**:**

- Vertical Platform (easy to load and unload all board types including round boards)
- 8 Full independent axes
- Front side: 2 standard probes + 2 HR (high resolution) probes
- Rear side: 4 standard probes
- Large test area: 800 x 650 mm
- Laser sensor(s) for full warpage control

PilotV8 XL HR Next> series "takes care" of MLO™ pads

With any sensitive product to test it is mandatory to balance the probe contact force in order to not leave witness or scrub marks on the pads or wafers to be probed.
The best approach to not have any visible mark on the Die pads are to have a Z movement perpendicular to the MLO™. With this approach, the prober can guarantee the best touch possible without leaving any witness/scrub marks.
Any other different angle in the movement of the Z axis will increase heavily the chance to leave a scratch on the Die pads.
When the probe card is fully assembled and the MLO™ is mounted on the PCB interface, the final ICCT test must be performed in order to test the integrity of each single connection between MLO™ and PCB interface itself.
The **PilotV8 XL HR Next> series** will generate automatically the specific tests taking into account the resistance of each single path that can be different from one to another.



More about Seica:

About Seica

Founded in 1986, Seica S.p.A. is a global supplier of automatic test equipment and selective soldering systems, with an installed base of more than 1800 systems on 4 different continents. Seica offers a complete line of test solutions, including bed of nails and flying probe testers able to perform MDA, in-circuit and full functional tests of assembled electronic boards and modules and printed circuit boards, as well as LASER-based selective soldering systems for electronic board manufacturing and a full range of test application services. Company headquarters are located in Strambino, Italy, with direct offices in USA, Germany, China, Mexico and France, supported by a vast distribution network covering the rest of the world. Since 2014, Seica S.p.A. is supported by a sister company Seica Automation, located in Milan, and producing board handling systems and other automation equipments for the electronic manufacturing industry

Please see www.seica.com

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NEWS FROM Switzerland

DYCONEX is celebrating 30 years of leading-edge printed circuit board (PCB) manufacturing

Driven by demanding customers over the past 30 years, DYCONEX has continuously been at the forefront of developments in printed circuit board (PCB) manufacturing, and has repeatedly set important technological milestones, beginning with the introduction of high-reliability rigid-flex multilayer boards (DYCOflex®).

Today, DYCONEX is the world's leading manufacturer of highly reliable, high quality and flexible PCBs for the medical industry, especially for medical implants. Biocompatible interconnect solutions are also one of the company's strengths. In addition, DYCONEX also produces rigid and rigid-flex substrates for various other industries. The continuous innovation process is part of the DYCONEX DNA and is both the driver and the guarantee for the ongoing global competitiveness of the company. In addition to all technical developments, we are very proud of our employees who permanently ensure enduring improvements.

Our enormous investment efforts in the latest technologies and the ongoing outstanding commitment of our employees in process and product development allows us to maintain our role as a forerunner in technology which we were over the last three decades and made us what we are right now. We are thankful to our customers for their trust in us and to our outstanding, highly innovative and passionately committed workforce, that we have become the top-selling Swiss printed circuit board manufacturer since 1991 and the global market leader in the field of highly reliable flexible substrates for the MedTech industry.

Visit our dedicated Dyconex 30th Anniversary page to find an interactive timeline of milestones from the company's history, an inspiring celebration video, and lots of other exciting content.

DYCONEX AG, Grindelstrasse 40, 8303 Bassersdorf, Switzerland

www.mst.com/dyconex

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PANDEMIC NEWS

"We never created a supervirus." Ralph Baric explains gain-of-function research.

The work has helped in the development of mRNA coronavirus vaccines and the first approved Covid drug.

By Rowan Jacobsen
M.I.T.

Ralph Baric of the University of North Carolina has engineered coronaviruses to study their threat to humans.

In May, the long-time coronavirus researcher Ralph Baric found himself at the center of the swirling debate over gain-of-function research, in which scientists engineer new properties into existing viruses. And during a congressional hearing, Senator Rand Paul of Kentucky implied that the National Institutes of Health had been funding such research at both the Wuhan Institute of Virology and Baric's University of North Carolina lab, and that the two labs had been collaborating to make "superviruses."

Baric released a statement clarifying that according to the NIH, the research in question did not qualify as gain-of-function, none of the SARS-like coronaviruses he'd used in the experiments were closely related to SARS-CoV-2 (the original virus behind the Covid pandemic), and his collaboration with the Wuhan Institute of Virology had been minimal.

Yet that did little to quell questions about the role Baric's research may have played in furthering scientists' ability to modify coronaviruses in potentially dangerous ways. Such questions have dogged Baric since 2014, when he became the reluctant spokesperson for gain-of-function research after the NIH declared a moratorium on such experiments until their safety could be assessed, temporarily halting his work.

Baric believes such research is essential to the development of vaccines and other countermeasures against emerging viruses, a project he has been engaged in for

more than 20 years. That work has made him the country's foremost expert on coronaviruses, and his high-security UNC lab has been a centre of the US response to the pandemic, testing numerous drug candidates for other labs that lack the biosafety clearance or the expertise.

His research laid the groundwork for the first approved anti-Covid drug and helped speed the development of the mRNA vaccines that have proved so pivotal. Recently, his lab announced the creation of the world's first pan-coronavirus mRNA vaccine.

Yet Baric also pioneered the reverse-genetics techniques that have allowed other researchers, including those at the Wuhan Institute of Virology, to engineer viruses with altered functions. Some scientists fear that the technique, which allow coronaviruses to be recreated from their genetic code, could engender a future pandemic, and other critics, like Senator Paul, imply they might have led to the creation or release of SARS-CoV-2.

MIT Technology Review recently asked Baric to explain what constitutes a gain-of-function experiment, why such research exists, and whether it could have played any role in the pandemic. The interview has been edited and shortened for clarity.

Q: Now that Rand Paul has announced on the floor of the Senate that you're creating superviruses and performing gain-of-function experiments, this seems like a good time to talk about your work.

Ralph Baric: Well, let me start off by saying that we've never created a supervirus. That's a figment of his imagination and obviously being used for political advancement. Unfortunately, the way social media works today, this fabrication will be repeated many times.

How do you define gain-of-function research?

Human beings have practiced gain-of-function for the last 2,000 years, mostly in plants, where farmers would always save the largest seeds from the healthiest plants to replant the following year. The reason we can manage to have 7 billion people here on the planet is basically through direct or indirect genetic engineering through gain-of-function research. The simple definition of gain-of-function research is the introduction of a mutation than enhances a gene's function or property—a process used commonly in genetic, biologic, and microbiologic research.

In virology, historically, attenuated vaccines were generated by gain-of-function studies, which took human virus pathogens and adapted them for improved growth in cell culture, which reduced virus virulence in the natural human host.

So gain-of-function has been used in virology and microbiology for decades as a part of the scientific method. But that classic definition and purpose changed in 2011 and 2012, when researchers in Wisconsin and the Netherlands were funded to do gain-of-function research on avian flu transmissibility.

Those were the experiments that took H5N1, which had a high mortality rate in humans but low transmissibility, and made it highly transmissible through respiratory avenues.

The NIH, the FDA, the CDC, and the WHO all held meetings to identify the critical topics in influenza research that were least understood. What information and insight would better prepare us for flu pandemics that emerge from animal reservoirs in the future? The number-one conclusion was that we needed to understand the genetics and biology of flu emergence and transmission.

In response, the NIH called for proposals. Two researchers responded and were funded, and they discovered genetic changes that regulated H5N1 transmissibility in ferrets.

After that, they were labelled as rogue scientists, and gain-of-function was defined in negative terms. But in fact, they were working within the confines of the global health community's interests.

Then again, the other side argues that regardless of how safe your BSL-3 or BSL-4 research infrastructure is, human beings are not infallible. [Pathogen labs are assigned a biosafety level rating of 1 to 4, with 4 being the highest.] They make mistakes, even in high-containment facilities. Consequently, the risks may outweigh the benefits of the experiment. Both sides of the argument have justified concerns and points of view.

In addition to concerns over a lab escape, there were also concerns about whether the knowledge of how to do such experiments might fall into the wrong hands.

That's certainly part of the issue. And there was a fair amount of debate about whether that information [about genetic changes associated with flu transmission] should be made public. There are two or three instances in the virology literature of papers that are a potential concern.

Some consider my 2015 paper in this light, although after consultation with the NIH and the journal, we purposely did not provide the genetic sequence of the chimera in the original publication. Thus, our exact method remained obscure.

However, the sequence was repeatedly requested after the covid-19 pandemic emerged, and so after discussion with the NIH and the journal, it was provided to the community. Those who analyzed these sequences stated that it was very different from SARS-CoV-2.

How did that chimeric work on coronaviruses begin?

Around 2012 or 2013, I heard Dr. Shi present at a meeting. [Shi's team had recently discovered two new coronaviruses in a bat cave, which they named SHC014 and WIV1.] We talked after the meeting. I asked her whether she'd be willing to make the sequences to either the SHC014 or the WIV1 spike available after she published.

And she was gracious enough to send us those sequences almost immediately—in fact, *before* she'd published. That was her major contribution to the paper. And when a colleague gives you sequences beforehand, co authorship on the paper is appropriate.

That was the basis of that collaboration. We never provided the chimeric virus sequence, clones, or viruses to researchers at the WIV; and Dr. Shi, or members of her research team, never worked in our laboratory at UNC. No one from my group has worked in WIV laboratories.

And you had developed a reverse-genetics technique that allowed you to synthesize those viruses from the genetic sequence alone?

Yes, but at the time, DNA synthesis costs were expensive—around a dollar per base [one letter of DNA]. So synthesizing a coronavirus genome could cost $30,000. And we only had the spike sequence. Synthesizing just the 4,000-nucleotide spike gene cost $4,000. So we introduced the authentic SHC014 spike into a replication-competent backbone: a mouse-adapted strain of SARS. The virus was viable, and we discovered that it could replicate in human cells.

So is that gain-of-function research? Well, the SARS coronavirus parental strain could replicate quite efficiently in primary human cells. The chimera could also program infection of human cells, but not better than the parental virus. So we didn't gain any function—rather, we *retained* function. Moreover, the chimera was attenuated in mice as compared to the parental mouse-adapted virus, so this would be considered a loss of function.

One of the knocks against gain-of-function research—including this research—is that the work has little practical value. Would you agree?

Well, by 2016, using chimeras and reverse genetics, we had identified enough high-risk SARS-like coronaviruses to be able to test and identify drugs that have broad-based activity against coronaviruses. We identified remdesivir as the first broad-based antiviral drug that worked against all known coronaviruses, and published on it in 2017. It immediately was entered into human trials and became the first FDA-approved drug for treating covid-19 infections globally. A second drug, called EIDD-2801, or molnupiravir, was also shown to be effective against all known coronaviruses prior to the 2020 pandemic, and then shown to work against SARS-CoV-2 by March 2020.

Consequently, I disagree. I would ask critics if they had identified any broad-spectrum coronavirus drugs prior to the pandemic. Can they point to papers from their laboratories documenting a strategic approach to develop effective pan-coronavirus drugs that turned out to be effective against an unknown emerging pandemic virus?

Unfortunately, remdesivir could only be delivered by intravenous injection. We were moving toward an oral-based delivery formulation, but the covid-19 pandemic emerged. I really wish we'd had an oral-based drug early on. That's the game-changer that would help people infected in the developing world, as well as citizens in the US.

Molnupiravir is an oral medication, and phase 3 trials demonstrate rapid control of viral infection. It's been considered for emergency-use authorization in India.

Finally, the work also supported federal policy decisions that prioritized basic and applied research on coronaviruses.

What about vaccines?

Around 2018 to 2019, the Vaccine Research Centre at NIH contacted us to begin testing a messenger-RNA-based vaccine against MERS-CoV [a coronavirus that sometimes spreads from camels to humans]. MERS-CoV has been an ongoing problem since 2012, with a 35% mortality rate, so it has real global-health-threat potential.

By early 2020, we had a tremendous amount of data showing that in the mouse model that we had developed, these mRNA spike vaccines were really efficacious in protecting against lethal MERS-CoV infection. If designed against the original 2003 SARS strain, it was also very effective. So I think it was a no-brainer for NIH to consider mRNA-based vaccines as a safe and robust platform against SARS-CoV-2 and to give them a high priority moving forward.

Most recently, we published a paper showing that multiplexed, chimeric spike mRNA vaccines protect against all known SARS-like virus infections in mice. Global efforts to develop pan-sarbecoronavirus vaccines [sarbecoronavirus is the subgenus to which SARS and SARS-CoV-2 belong] will require us to make viruses like those described in the 2015 paper.

So I would argue that anyone saying there was no justification to do the work in 2015 is simply not acknowledging the infrastructure that contributed to therapeutics and vaccines for covid-19 and future coronaviruses.

The work only has value if the benefits outweigh the risks. Are there safety standards that should be applied to minimize those risks?

Certainly. We do everything at BSL-3 plus. The minimum requirements at BSL-3 would be an N95 mask, eye protection, gloves, and a lab coat, but we actually wear impervious Tyvek suits, aprons, and booties and are double-gloved. Our personnel wear hoods with PAPRs [powered air-purifying respirators] that supply HEPA-filtered air to the worker. So not only are we doing all research in a biological safety cabinet, but we also perform the research in a negative-pressure containment facility, which has lots of redundant features and backups, and each worker is encased in their own private personal containment suit.

Another thing we do is to run emergency drills with local first responders. We also work with the local hospital. With many laboratory infections, there's actually no known event that caused that infection to occur. And people get sick, right? You have to have medical surveillance plans in place to rapidly quarantine people at home, to make sure they have masks and communicate regularly with a doctor on campus.

Is all that standard for other facilities in the US and internationally?

No, I don't think so. Different places have different levels of BSL-3 containment operations, standard operating procedures, and protective gear. Some of it is dependent on how deep your pockets are and the pathogens studied in the facility. An N95 is a lot cheaper than a PAPR.

Internationally, the US has no say over what biological safety conditions are used in China or any other sovereign nation to conduct research on viruses, be they coronaviruses or Nipah, Hendra, or Ebola.

The Wuhan Institute of Virology was making chimeric coronaviruses, using techniques similar to yours, right?

Let me make it clear that we never sent any of our molecular clones or any chimeric viruses to China. They developed their own molecular clone, based on WIV1, which is a bat coronavirus. And into that backbone they shuffled in the spike genes of other bat coronaviruses, to learn how well the spike genes of these strains can promote infection in human cells.

Would you call that gain-of-function?

A committee at NIH makes determinations of gain-of-function research. The gain-of-function rules are focused on viruses of pandemic potential and experiments that intend to enhance the transmissibility or pathogenesis of SARS, MERS, and avian flu strains in humans. WIV1 is approximately 10% different from SARS. Some argue that "SARS coronavirus" by definition covers anything in the sarbecoronavirus genus. By this definition, the Chinese might be doing gain-of-function experiments, depending on how the chimera behaves. Others argue that SARS and WIV1 are different, and as such the experiments would be exempt. Certainly, the CDC considers SARS and WIV1 to be different viruses. Only the SARS coronavirus from 2003 is a select agent. Ultimately, a committee at the NIH is the final arbiter and makes the decision about what is or is not a gain-of-function experiment.

Definitions aside, we know they were doing the work in BSL-2 conditions, which is a much lower safety level than your BSL-3 plus.

Historically, the Chinese have done a lot of their bat coronavirus research under BSL-2 conditions. Obviously, the safety standards of BSL-2 are different than BSL-3, and lab-acquired infections occur much more frequently at BSL-2. There is also much less oversight at BSL-2.

This year, a joint commission of the World Health Organization and China said it was extremely unlikely that a lab accident had caused SARS-CoV-2. But you later signed a letter with other scientists calling for a thorough investigation of all possible causes. Why was that?

One of the reasons I signed the letter in Science was that the WHO report didn't really discuss how work was done in the WIV laboratory, or what data the expert panel reviewed to come to the conclusion that it was "very unlikely" that a laboratory escape or infection was the cause of the pandemic.

There must be some recognition that a laboratory infection could have occurred under BSL-2 operating conditions. Some unknown viruses pooled from guano or oral swabs might replicate or recombine with others, so you could get new strains with unique and unpredictable biological features.

And if all this research is being performed at BSL-2, then there are questions that need to be addressed. What are the standard operating procedures in the BSL-2? What are the training records of the staff? What is the history of potential exposure events in the lab, and how were they reviewed and resolved? What are the biosafety procedures designed to prevent potential exposure events?

Should they have been doing such experiments in a BSL-2 lab?

I would not. However, I don't set the standard for the US or any other country. There's definitely some risk associated with these and other SARS-like bat viruses that can enter human cells.

We also know that people who live near bat hibernacula [bat caves] have tested positive for antibodies against SARS-like bat viruses, so some of these viruses clearly can infect humans. While we have no idea whether they could actually cause severe disease or transmit from person to person, you want to err on the side of increased caution when working with these pathogens.

As a sovereign nation, China decides their own biological safety conditions and procedures for research, but they should also be held accountable for those decisions, just like any other nation that conducts high-containment biological research. As other nations develop BSL-3 facilities and begin to conduct high-containment research, each will have to make fundamental decisions about what kind of containment they use for different viruses and bacteria, along with the underlying biosafety procedures.

This is serious stuff. Global standards need to exist, especially for understudied emerging viruses. If you study hundreds of different bat viruses at BSL-2, your luck may eventually run out.

Do you think their luck ran out?

The possibility of accidental escape still remains and cannot be excluded, so further investigation and transparency is critical, but I personally feel that SARS-CoV-2 is a natural pathogen that emerged from wildlife. Its closest relatives are bat strains. Historical precedent argues that all other human coronaviruses emerged from animals. No matter how many bat viruses are at the WIV, nature has many, many more.

At this time, there's really no strong and actionable data that argues that the virus was engineered and escaped containment. As the pathogenesis of SARS-CoV-2 is so complex, the thought that anybody could engineer it is almost ludicrous.

When you think about the diversity of SARS-related strains that exist in nature, it's not hard to imagine a strain that would have the complex and unpredictable biological features of SARS-CoV-2. As scientists, we tend to do experiments, read the literature, and then think we understand how nature works. We make definitive statements regarding how coronaviruses are supposed to emerge from animal reservoirs, based on one or two examples. But nature has many secrets, and our understanding is limited. Or as they said in *Game of Thrones,* "You know nothing, Jon Snow."

In addition to the WIV and you, are other groups doing coronavirus engineering?

Before covid-19, there were probably three to four main groups globally. That's changed dramatically. Now the number of labs doing coronavirus genetics is likely three or four times higher and continuing to increase. That proliferation is unsettling, because it allows many inexperienced groups, globally, to make decisions about building and isolating chimeras or natural zoonotic [viruses].

By "inexperienced," I mean that they are applying previous discoveries and approaches in the coronavirus field, but perhaps with less respect for the inherent risk posed by this group of pathogens.

People are making chimeras right now for the variants of concern, and each of those variants is providing new insights into human transmissibility and pathogenesis.

So the virus itself is contributing to gain-of-function knowledge?

The virus is a master at finding better ways to outcompete its ancestors in humans. And each of these successful SARS-CoV-2 variants out-competes the old variants and reveals the underlying genetics that regulate increased transmissibility and/or pathogenesis. And that information is being learned in a real-time setting and in humans, as compared to the avian-flu-transmission scenario, which was conducted under controlled artificial conditions in ferrets. I would argue that the real-time knowledge is more relevant and perhaps more unsettling than the research conducted in animal models under high containment.

Given our scientific capabilities today, every new emerging virus that causes an outbreak in the future can be studied at this level of granularity. That is unprecedented. Each could provide a classic recipe for potential dual-use applications in other strains. [Dual-use biological research is that which can be used to develop both therapeutics and bioweapons.]

Anything else about this that keeps you up at night?

The number of zoonotic coronaviruses that are poised to jump species is a major concern. That's not going away.

Also, the biology of this virus is such that its virulence will most likely continue to increase rather than decrease, at least in the short term.

Why is that?

The transmission events occur early, while the most severe disease occurs late, after the virus is being cleared from the body. That means transmission and severe disease and death are partially uncoupled, biologically. Consequently, it doesn't hurt the virus to increase its virulence.

If you are one of the people waiting to get the vaccine, your risk is going up with each new variant. These variants are dangerous. They want to reproduce and spread and show increased pathogenesis, even in younger adults. They have little concern for you or your family's health and welfare, so get vaccinated.

That is the saddest thing about the pandemic. For an effective public health response, you need to respond as a national and global community with one voice. You must believe in the power of public health and public health procedures. Politics has no place in a pandemic, but that is what we ended up with—politically inspired mixed messaging.

How did that work out for America? Did we get diagnostics online quickly? No! Did we use the two-to-three-month lead time to stock hospitals with PPE or respirators? No. Rather, Americans received the message that the virus wasn't dangerous, that it would go away or that the summer heat would destroy it. We heard rumours that mask wearing was detrimental, or that unproven drugs were miracle cures.

Some say that the true tragedy is the hundreds of thousands of Americans who didn't need to die [but did] because the greatest nation in the world did not respond to a pandemic in a unified, science-based manner. Taiwan responded with a unified public health response and had only handfuls of cases and few deaths. The US led the world in deaths and numbers of cases. Why are the failures leading to the deaths of hundreds of thousands of Americans not the subject of rigorous investigation?

Artificial intelligence/Machine learning

Hundreds of AI tools have been built to catch Covid. None of them helped.

Some have been used in hospitals, despite not being properly tested. But the pandemic could help make medical AI better.

by Will Douglas Heaven

When covid-19 struck Europe in March 2020, hospitals were plunged into a health crisis that was still badly understood. “Doctors really didn’t have a clue how to manage these patients,” says Laure Wynants, an epidemiologist at Maastricht University in the Netherlands, who studies predictive tools.

But there was data coming out of China, which had a four-month head start in the race to beat the pandemic. If machine-learning algorithms could be trained on that data to help doctors understand what they were seeing and make decisions, it just might save lives. “I thought, ‘If there’s any time that AI could prove its usefulness, it’s now,’” says Wynants. “I had my hopes up.”

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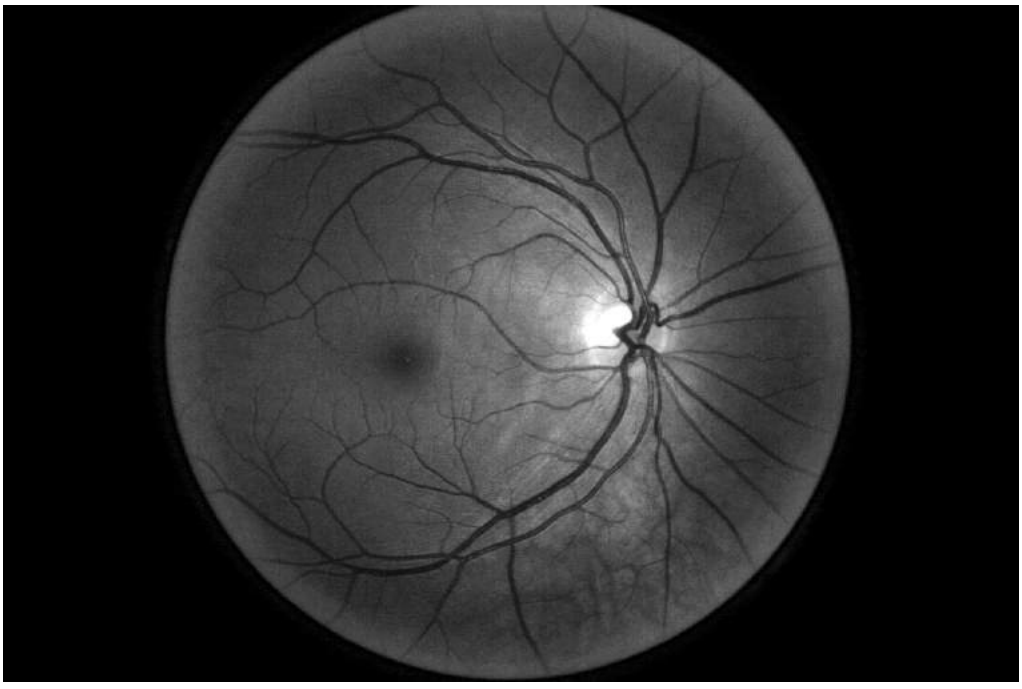

Google’s medical AI was super accurate in a lab. Real life was a different story.

If AI is really going to make a difference to patients we need to know how it works when real humans get their hands on it, in real situations.

It never happened—but not for lack of effort. Research teams around the world stepped up to help. The AI community, in particular, rushed to develop software that many believed would allow hospitals to diagnose or triage patients faster, bringing much-needed support to the front lines—in theory.

In the end, many hundreds of predictive tools were developed. None of them made a real difference, and some were potentially harmful.

That's the damning conclusion of multiple studies published in the last few months. In June, the Turing Institute, the UK's national center for data science and AI, put out a report summing up discussions at a series of workshops it held in late 2020. The clear consensus was that AI tools had made little, if any, impact in the fight against covid.

Not fit for clinical use

This echoes the results of two major studies that assessed hundreds of predictive tools developed last year. Wynants is lead author of one of them, a review in the British Medical Journal that is still being updated as new tools are released and existing ones tested. She and her colleagues have looked at 232 algorithms for diagnosing patients or predicting how sick those with the disease might get. They found that none of them were fit for clinical use. Just two have been singled out as being promising enough for future testing.

"It's shocking," says Wynants. "I went into it with some worries, but this exceeded my fears."

Wynants's study is backed up by another large review carried out by Derek Driggs, a machine-learning researcher at the University of Cambridge, and his colleagues, and published in Nature Machine Intelligence. This team zoomed in on deep-learning models for diagnosing covid and predicting patient risk from medical images, such as chest x-rays and chest computer tomography (CT) scans. They looked at 415 published tools and, like Wynants and her colleagues, concluded that none were fit for clinical use.

Related Story

Doctors are using AI to triage covid-19 patients. The tools may be here to stay

Faced with staff shortages and overwhelming patient loads, a growing number of hospitals are turning to automated tools to help them manage the pandemic.

“This pandemic was a big test for AI and medicine,” says Driggs, who is himself working on a machine-learning tool to help doctors during the pandemic. “It would have gone a long way to getting the public on our side,” he says. “But I don’t think we passed that test.”

Both teams found that researchers repeated the same basic errors in the way they trained or tested their tools. Incorrect assumptions about the data often meant that the trained models did not work as claimed.

Wynants and Driggs still believe AI has the potential to help. But they are concerned that it could be harmful if built in the wrong way because they could miss diagnoses or underestimate risk for vulnerable patients. “There is a lot of hype about machine-learning models and what they can do today,” says Driggs.

Unrealistic expectations encourage the use of these tools before they are ready. Wynants and Driggs both say that a few of the algorithms they looked at have already been used in hospitals, and some are being marketed by private developers. “I fear that they may have harmed patients,” says Wynants.

So what went wrong? And how do we bridge that gap? If there's an upside, it is that the pandemic has made it clear to many researchers that the way AI tools are built needs to change. "The pandemic has put problems in the spotlight that we've been dragging along for some time," says Wynants.

What went wrong

Many of the problems that were uncovered are linked to the poor quality of the data that researchers used to develop their tools. Information about covid patients, including medical scans, was collected and shared in the middle of a global pandemic, often by the doctors struggling to treat those patients. Researchers wanted to help quickly, and these were the only public data sets available. But this meant that many tools were built using mislabeled data or data from unknown sources.

Driggs highlights the problem of what he calls Frankenstein data sets, which are spliced together from multiple sources and can contain duplicates. This means that some tools end up being tested on the same data they were trained on, making them appear more accurate than they are.

It also muddies the origin of certain data sets. This can mean that researchers miss important features that skew the training of their models. Many unwittingly used a data set that contained chest scans of children who did not have covid as their examples of what non-covid cases looked like. But as a result, the AIs learned to identify kids, not covid.

Driggs's group trained its own model using a data set that contained a mix of scans taken when patients were lying down and standing up. Because patients scanned while lying down were more likely to be seriously ill, the AI learned wrongly to predict serious covid risk from a person's position.

In yet other cases, some AIs were found to be picking up on the text font that certain hospitals used to label the scans. As a result, fonts from hospitals with more serious caseloads became predictors of covid risk.

Errors like these seem obvious in hindsight. They can also be fixed by adjusting the models, if researchers are aware of them. It is possible to acknowledge the shortcomings and release a less accurate, but less misleading model. But many tools were developed either by AI researchers who lacked the medical expertise to spot flaws in the data or by medical researchers who lacked the mathematical skills to compensate for those flaws.

A more subtle problem Driggs highlights is incorporation bias, or bias introduced at the point a data set is labeled. For example, many medical scans were labeled according to whether the radiologists who created them said they showed covid. But that embeds, or incorporates, any biases of that particular doctor into the ground truth of a data set. It would be much better to label a medical scan with the result of

a PCR test rather than one doctor's opinion, says Driggs. But there isn't always time for statistical niceties in busy hospitals.

That hasn't stopped some of these tools from being rushed into clinical practice. Wynants says it isn't clear which ones are being used or how. Hospitals will sometimes say that they are using a tool only for research purposes, which makes it hard to assess how much doctors are relying on them. "There's a lot of secrecy," she says.

Wynants asked one company that was marketing deep-learning algorithms to share information about its approach but did not hear back. She later found several published models from researchers tied to this company, all of them with a high risk of bias. "We don't actually know what the company implemented," she says.

According to Wynants, some hospitals are even signing nondisclosure agreements with medical AI vendors. When she asked doctors what algorithms or software they were using, they sometimes told her they weren't allowed to say.

How to fix it

What's the fix? Better data would help, but in times of crisis that's a big ask. It's more important to make the most of the data sets we have. The simplest move would be for AI teams to collaborate more with clinicians, says Driggs. Researchers also need to share their models and disclose how they were trained so that others can test them and build on them. "Those are two things we could do today," he says. "And they would solve maybe 50% of the issues that we identified."

Getting hold of data would also be easier if formats were standardized, says Bilal Mateen, a doctor who leads research into clinical technology at the Wellcome Trust, a global health research charity based in London.

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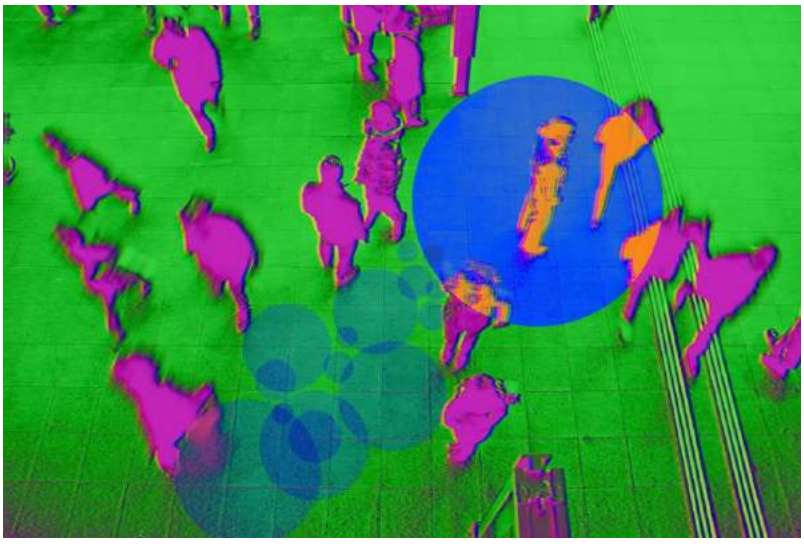

AI could help with the next pandemic—but not with this one

Some things need to change if we want AI to be useful next time, and you might not like them.

Another problem Wynants, Driggs, and Mateen all identify is that most researchers rushed to develop their own models, rather than working together or improving existing ones. The result was that the collective effort of researchers around the world produced hundreds of mediocre tools, rather than a handful of properly trained and tested ones.

“The models are so similar—they almost all use the same techniques with minor tweaks, the same inputs—and they all make the same mistakes,” says Wynants. “If all these people making new models instead tested models that were already available, maybe we’d have something that could really help in the clinic by now.”

In a sense, this is an old problem with research. Academic researchers have few career incentives to share work or validate existing results. There’s no reward for pushing through the last mile that takes tech from “lab bench to bedside,” says Mateen.

To address this issue, the World Health Organization is considering an emergency data-sharing contract that would kick in during international health crises. It would let researchers move data across borders more easily, says Mateen. Before the G7 summit in the UK in June, leading scientific groups from participating nations also called for “data readiness” in preparation for future health emergencies.

Such initiatives sound a little vague, and calls for change always have a whiff of wishful thinking about them. But Mateen has what he calls a “naïvely optimistic” view. Before the pandemic, momentum for such initiatives had stalled. “It felt like it was too high of a mountain to hike and the view wasn’t worth it,” he says. “Covid has put a lot of this back on the agenda.”

“Until we buy into the idea that we need to sort out the unsexy problems before the sexy ones, we’re doomed to repeat the same mistakes,” says Mateen. “It’s unacceptable if it doesn’t happen. To forget the lessons of this pandemic is disrespectful to those who passed away.”

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