Point-of-Care Manufacturing (& Testing)
~~3D Printing~~ During the Pandemic
& Beyond!

Toronto Anesthesia Symposium - April 17, 2021

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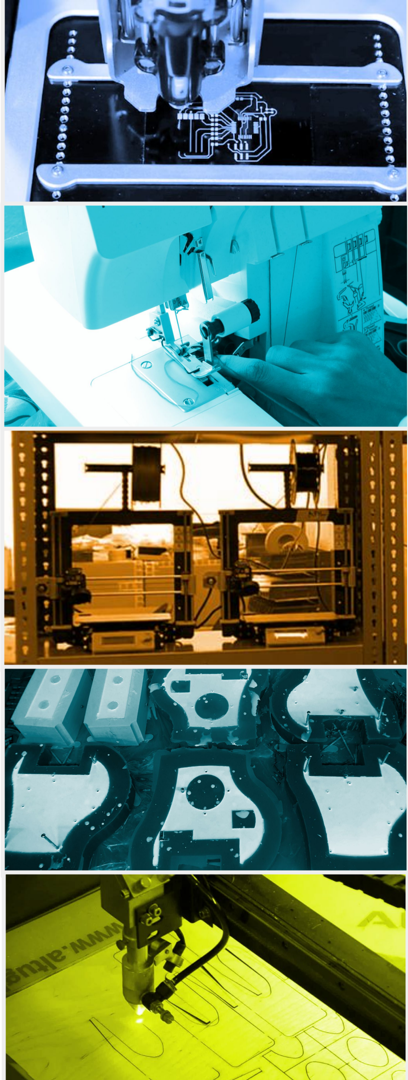


Disclosure - Azad Mashari

Relationships with financial sponsors (APIL research group):

Research & Salary Support:

- UHN Foundation
- UHN-SHS Anesthesia Association
- UHN-SHS Academic Medical Organization
- Ontario Centers of Excellence (with TME Inc)
- NSERC

Speakers Bureau/Honoraria: Nil

Consulting Fees: Nil

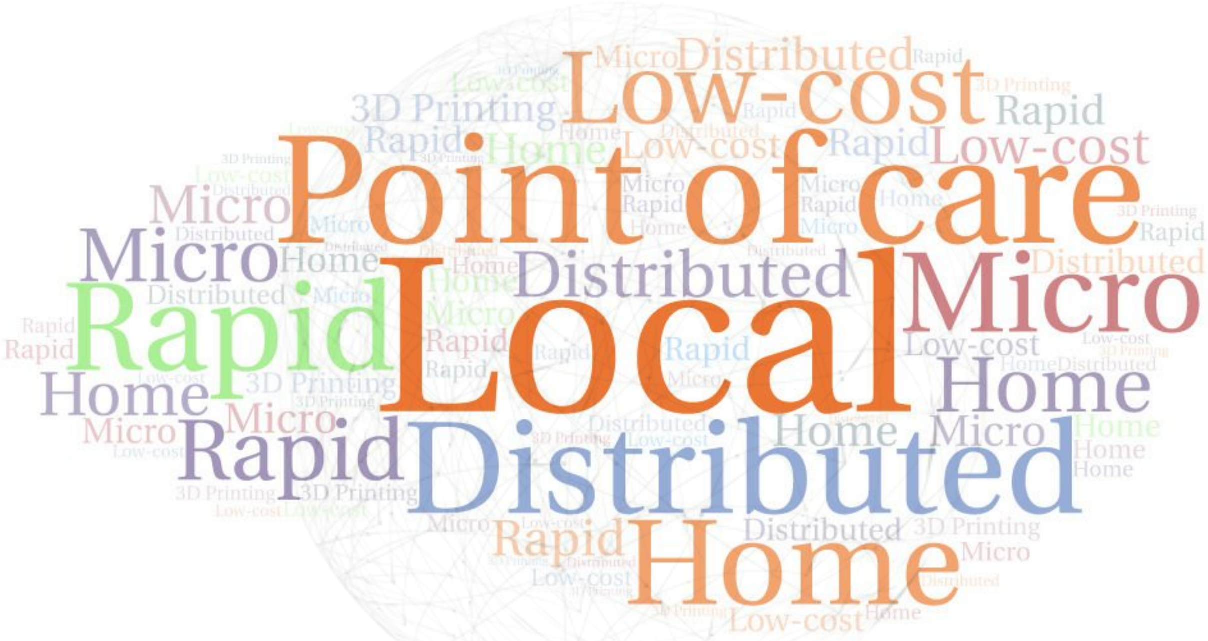
- Glia Inc. (pro bono consulting, research collaboration - COVID and other)
- Promation Engineering (pro bono research collaboration - COVID)
- General Dynamics Land Systems (pro bono research collaboration - COVID)

Patents: Nil

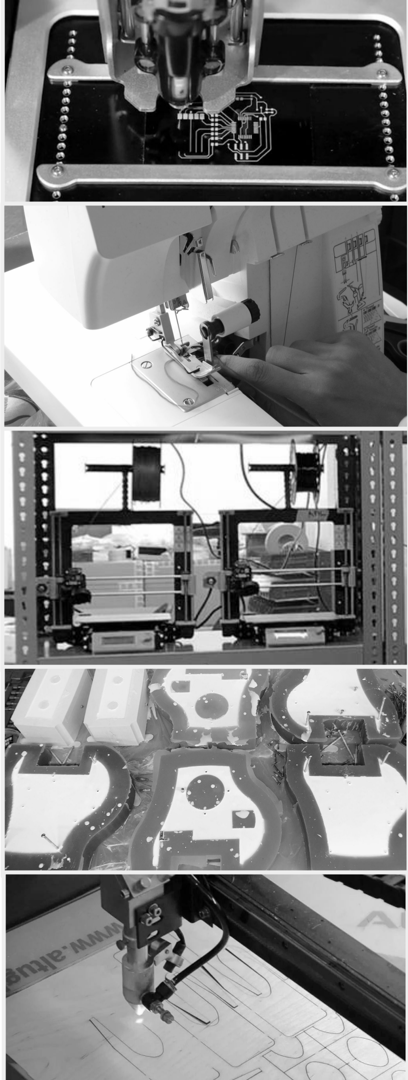
- Project repository (Open-Source): https://github.com/tgh-apil

https://github.com/tgh-apil

A family of Accessible Production Techniques *(e.g. molding)*
& Programmable Machines *(e.g. 3D printers)* for Making Health Care Products



open source



Learning Objectives

After the completion of this session participants will be able to

1. Describe the current capabilities and limitations of local and point-of-care manufacturing systems in addressing shortages of essential health care products
2. Critically discuss the broad contributors to major disruptions in the health care supply chain during the pandemic
3. Critically discuss the potential role of hospital-based manufacturing and device testing laboratories in improving the resilience of large hospital systems in future pandemics.

Outline

1. Who made how much of what?
2. Local efforts
3. What has been achieved?
4. What has not (yet) been achieved? Why?
5. Where to now? How these approaches may contribute to more robust health care infrastructure

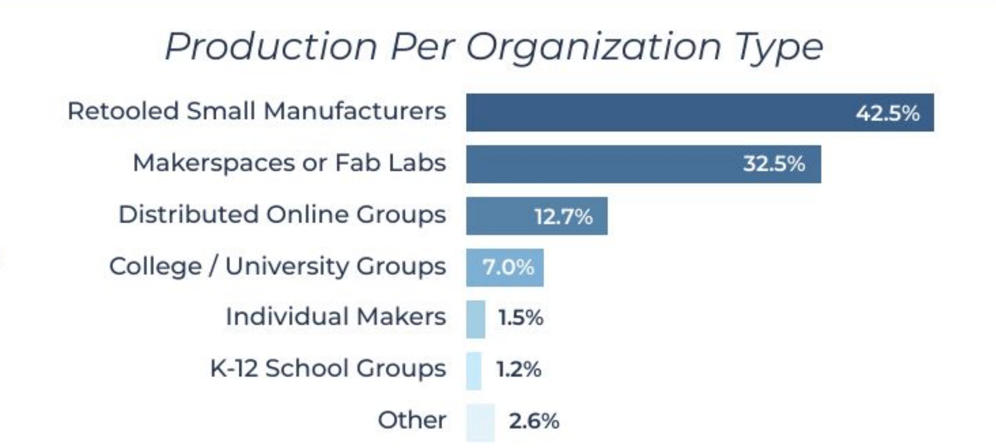
Birds Eye View

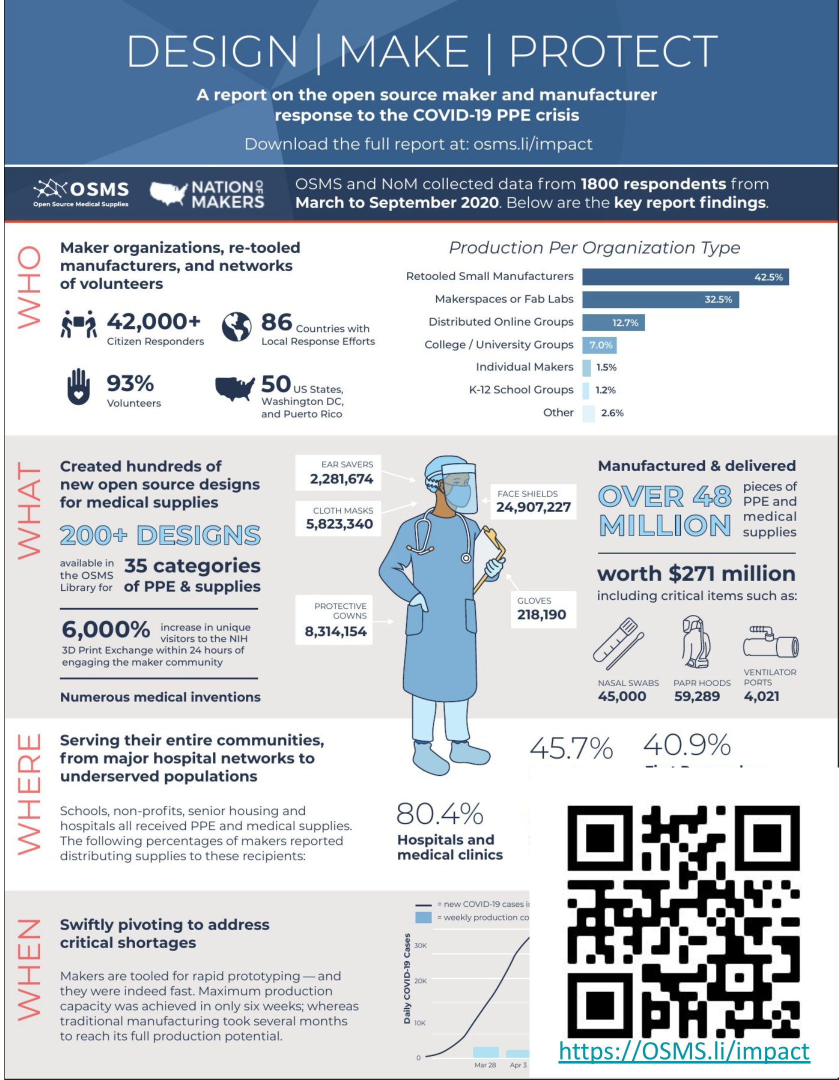
International survey by *Open Source Medical Supplies* & *Nation of Makers*

6 months March - Sept 1 CE (2020)

1800 respondents from 86 countries

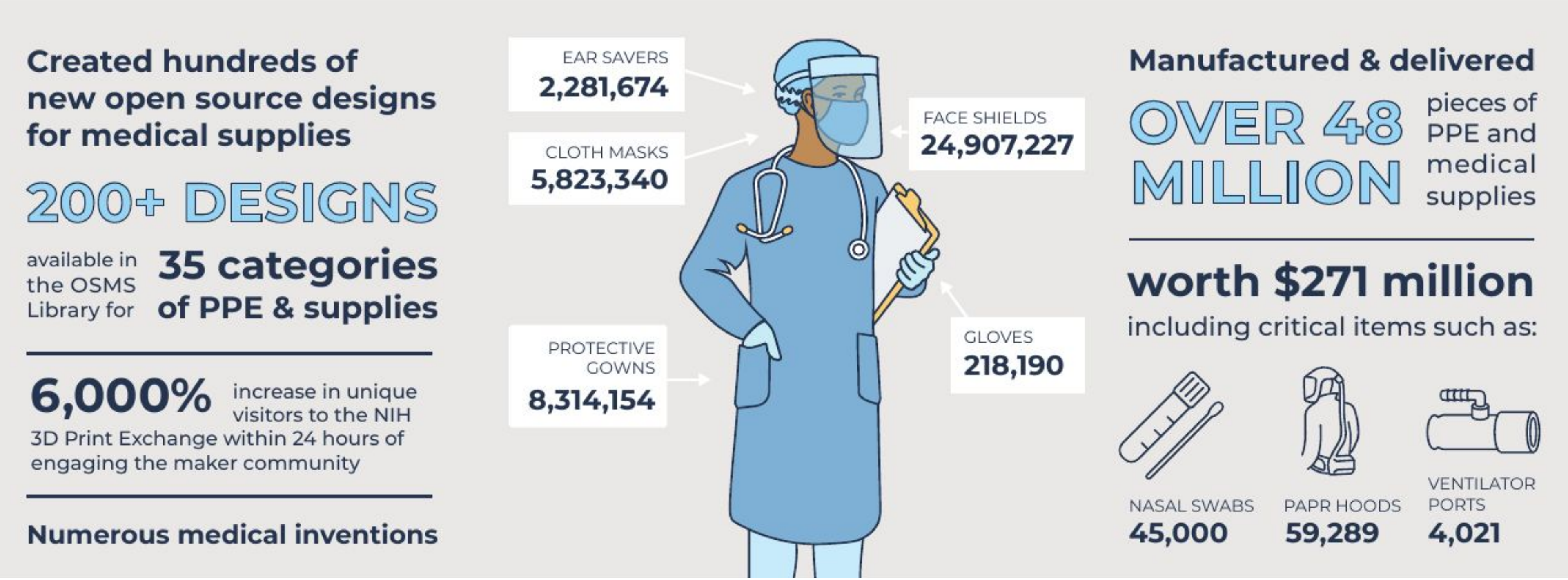
42,000 people involved, 93% volunteers





https://OSMS.li/impact

What was made



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Enabling Network Infrastructure

OPEN SOURCE INFORMATION

"We were able to prepare and organize **weeks before the virus reached our country** due to the experiences, resources, procedures, source files, etc. shared by the maker community as a whole.

Andres Hermes
TecLab, Guatemala

COMMUNITY NETWORKS

71% of respondents depended on networks, community platforms and personal introductions

"It's been fantastic **not only to share but compare and review** what people have been doing.

Sam Haynor
Something Labs,
San Francisco, CA

VETTED DESIGNS

50% of respondents made use of open source design repositories

"Without the **pre-vetted designs** AND **production instructions** we would have spent too much time reinventing the wheel and not enough time producing.

Nathaniel Fairbanks
MakeIt Labs, Nashua, NH

https://OSMS.li/impact

Needs

GOVERNMENT SUPPORT

Less than 3%

received any government financial support through sales or grants.

24%

reported establishing a new relationship with some level of government.

"Now that we know that makerspaces can fill such a vital role [...] **we need lawmakers to invest funds** towards organizing these efforts and making sure they have the materials

COORDINATION OF SUPPLY & DEMAND

"I learned that **distribution is the most expensive and difficult thing to accomplish** — manufacturing is comparatively quite easy!

Sam Neff
Richmond High Robotics Team 841
Richmond, CA

"Most of our sales and distribution were based on **personal contacts**.

Will Holman
Makers Unite, Baltimore, MD

CLARITY ABOUT LIABILITY

"Quite a few people felt they couldn't use their business / shop to make PPE or personally

FUNDING

63% depended on in-kind donations of materials, tools and labor.

13% of respondents listed lack of funding as their primary reason for slowing production.

"We're about to lose our shorts. We've had a good response in fundraising, however, **our costs in production and rent for the space have put us in debt to deferred rent.**

Joey Loman
Synergy Mill Makerspace, Greenville, SC

ACCESS TO TESTING

"**Cost is prohibitive.** Traditional testing of basic mask safety, efficacy, and filtration costs $3-5k per mask

https://OSMS.li/impact

Local Projects

Face shields

Reusable Silicone Stop-Gap Respirator

Reusable Snorkel Mask-Based PAPR

Ventilator Sharing System

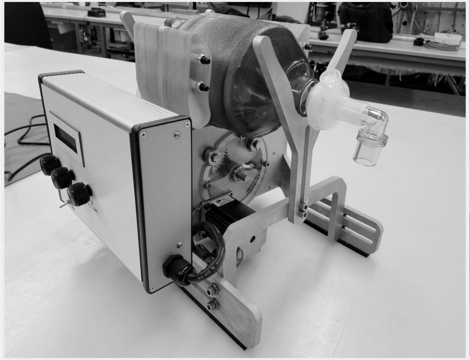
Aerosol Reducing NIV Mask

BVM-Based Emergency Use Ventilator

Evaluation of BVMs for Pre-oxygenation

Open Ventilator Evaluation Framework (NSERC, UT MIE)

Open Ventilator Controller Platform (NSERC, UT MIE)

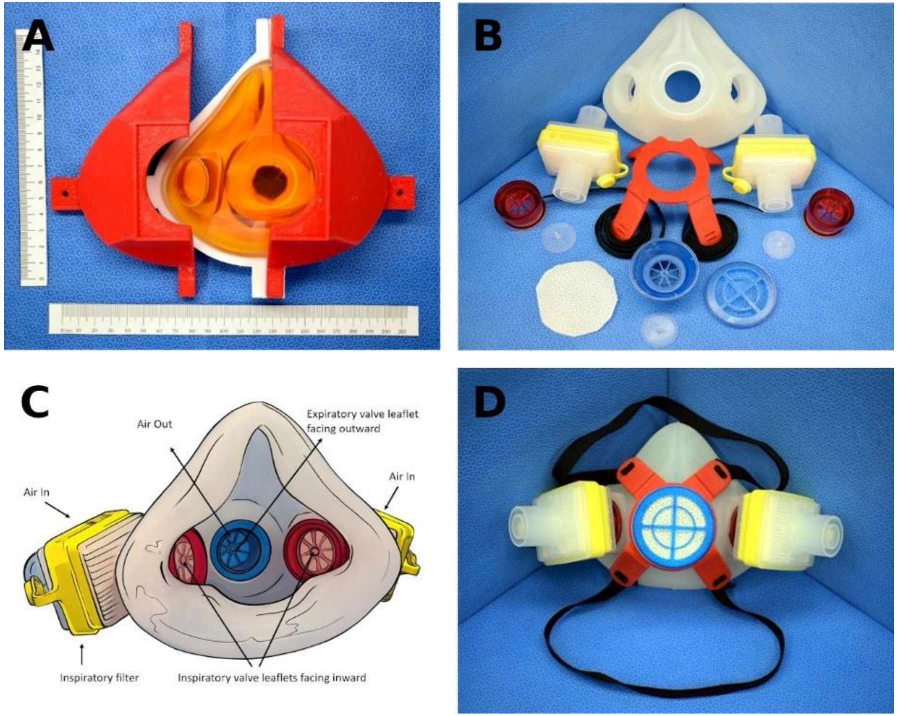


Stop-gap Silicone Respirator Mask (William Ng)

Goal: Develop a locally manufacturable, reusable respirator meeting or exceeding N95 protection

Progress:

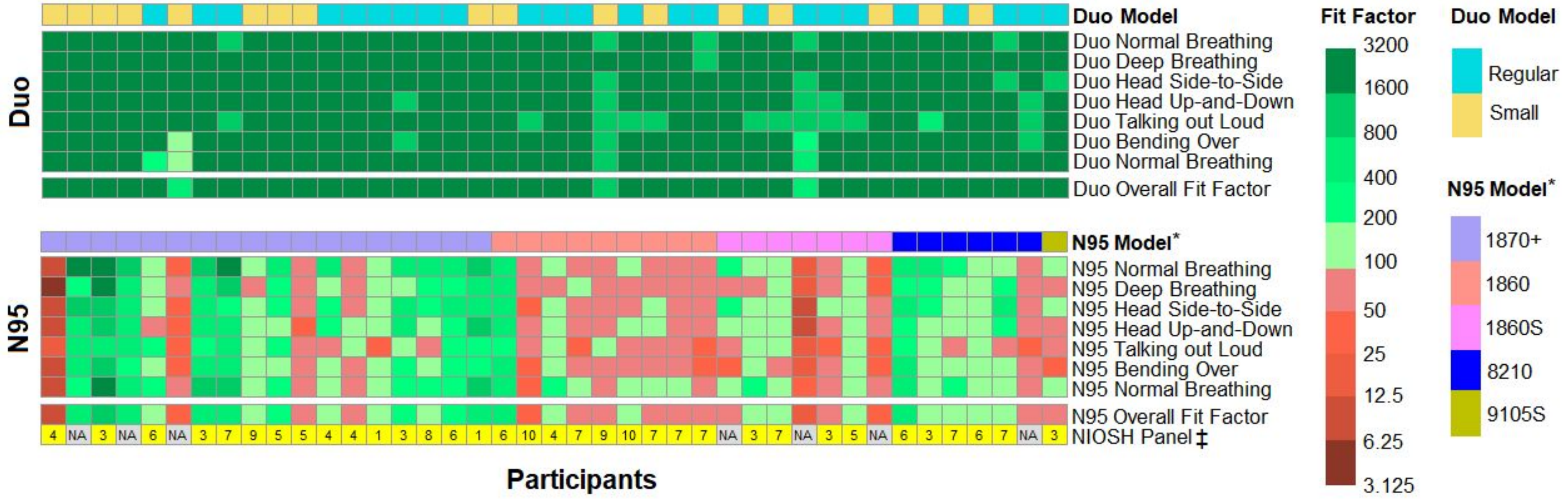
- Second generation design. Exceeds N95 filtration performance. Validated in 40 HCW.
- Undergoing testing and refinement to meet technical standards for resistance and CO_2 retention.
- Planned application for HC.



References:

1. https://github.com/tgh-apil/Reusable-N95-Respirator
2. Ng et al. PLoS ONE. 2020; 15(11):e0242304.
3. Anwari et al. PLoS ONE. 2021;16(3):e0247575.
4. Mbadjeu et al. 2021; In preparation

Stop-Gap Respirator (Duo) vs N95: Quantitative Fit Testing in 40 HCW



Overall **Pass Rate**:

- **N95: 58.5%** (most failures in dynamic maneuvers; difference across models)
- **Reusable SGR: 100%**

Positive-Pressure Air Purifying Respirator (PAPR) - Modified Snorkel Mask (L. Fedorko)

Goal: Develop a locally manufacturable, reusable PAPR

Progress:

- Designed, tested, and validated in 40 HCW.
- 50 units manufactured for UHN. Not deployed.
- Difficulty communicating (like other PAPRs)
- Planned application for HC.

References:

1. https://github.com/tgh-apil/PAPR
2. Clinkard et al. Anaesthesia. 2021;76(5):617–22.

N95 vs. Filtered Snorkel Mask vs. PAPR: Quantitative Fit Testing in 40 HCW

Respirator Feature Summary

	Face Seal	Filtration Performance	Filtered Exhalation	Comfort	Voice
Disposable N95	+/-	+/-	+	+	+/-
3M Elastomeric	++	++	-	+/-	-
Duo Stop-Gap Silicone	++	++	+	+/-	-
Snorkel PAPR	+	++	-	+	-

Ventilation Devices

Emergency Use Device Development

- Aerosol Reducing NIV Mask
- Ventilator Splitter
- BVM Based Emergency Ventilator

Device Evaluation

- Evaluation of BVM Models for Pre-Oxygenation
- Open-Source Ventilator Evaluation Framework
- Use of BVM for Pre-oxygenation

Aerosol-Reducing NIV Mask

glia
equal care

Goal: Develop a locally manufacturable NIV mask that minimized aerosol generation. For use in transport, hospitals and northern health stations

Progress:

- Developed rapidly in collaboration with Glia & General Dynamics Land Systems-Canada
- May 2020 Health Canada granted Interim Order for clinical use in pandemic
- Subsequent evaluation (clinical trial, user feedback, bench testing) suggested significant problems. Device voluntarily held from sale. Second version in development.

References:

1. https://github.com/GliaX/Aerosol-Reducing-Mask
2. Final Report of Device Testing and Clinical Trial Data ARM v1.0

Aerosol-Reducing NIV Mask: Clinical Trial (N=6+8)

Clinical Trial at London Health Sciences Center

Western University HSREB

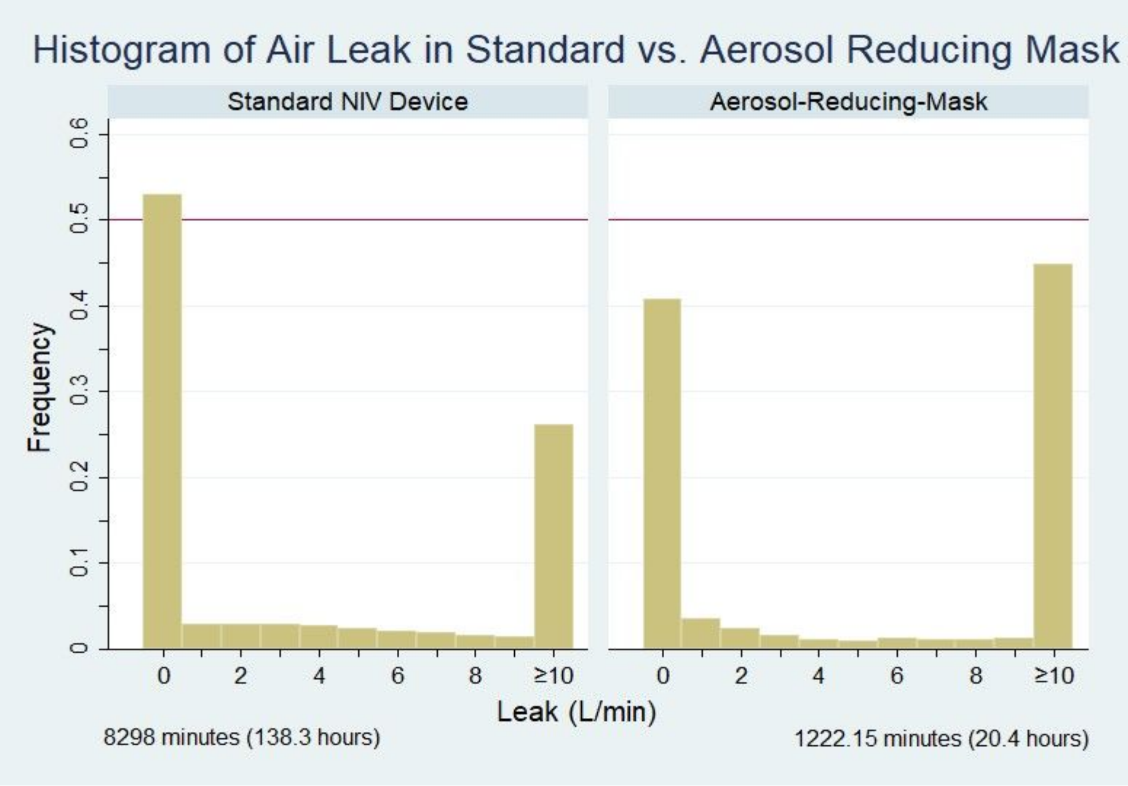
Pts. prescribed NIV in ED randomized to ARM or control mask.

Upto 24 hours.

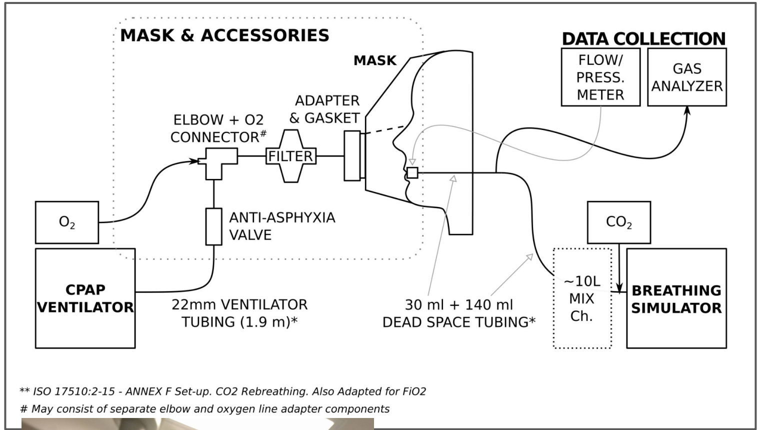
Outcome: Leak L/min.

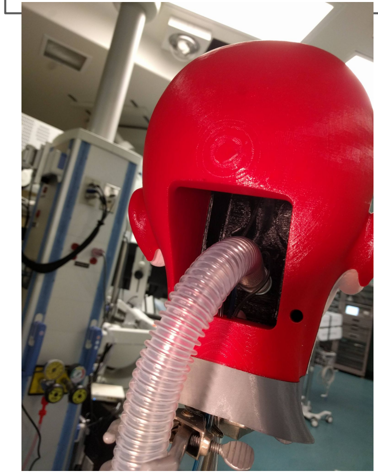
Stopped early after 14 participants
(6 ARM; 8 control) due to loss of equipoise

Device did not reduce leaks



Aerosol Reducing Mask CO_2 Re-breathing Test *(ISO 17150:2)*





Test Condition	End-Tidal CO2 %	End-Tidal CO2 (mmHg)	Increase from baseline (%)	Acceptable Increase (%)
Baseline: No mask/CPAP	5.04	40	-	-
CPAP 5 cm H2O	5.70	46	**13.1**	20
CPAP 10 cm H2O	4.31	35	**-14.4**	20
CPAP 20 cm H2O	2.30	18	**-54.3**	20
Fault: Patient connection port occluded	8.35	67	**65.7**	60
Fault: CPAP connected with no flow	8.36	67	**65.8**	60

- Risk of significant CO_2 rebreathing in event of ventilator failure or disconnection.
- **Only appropriate for supervised use.**
- **Not practical** with current staffing shortages.

Aerosol-Reducing NIV Mask - Quality Control

Health Canada Interim Order Authorization for Clinical Use **May 2020**.

- IO did not require any trial data, bench testing or user/human factors testing

Undertook additional evaluation after IO authorization (no requirement from Health Canada)

- Clinical Trial: **no reduction in mask leak** overall.
- User feedback (RT, RN): several **significant usability limitations**:
  - Opaque face-piece concealing vomiting; No NGT fitting;
  - Heavy;
  - No emergency release;
- CO_2 rebreathing testing showed **failure to meet ISO requirements for rebreathing** in the event of a ventilator failure.

Device sales suspended **Nov 2020**. No units sold. Back to the drawing board. ARM 2.

- At the time device was under consideration by ORNGE & Indigenous Services Canada

Ventilator Splitting System

Society of Critical Care Medicine
The Intensive Care Professionals

STORE

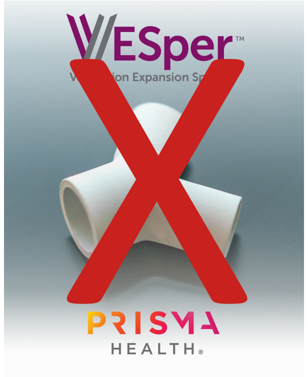
ABOUT SCCM + COMMUNICATIONS + EDUCATION CENTER + FUNDAMENTALS + MEMBER CENTER + PROFESSIONAL DEVELOPMENT +

SCCM > Emergency Resources: COVID-19 > Advocacy

Consensus Statement on Multiple Patients Per Ventilator

Issued: March 26, 2020, 12:00 p.m.

The above-named organizations advise clinicians that sharing mechanical ventilators should not be attempted because it cannot be done safely with current equipment. The physiology of patients with COVID-19-onset acute

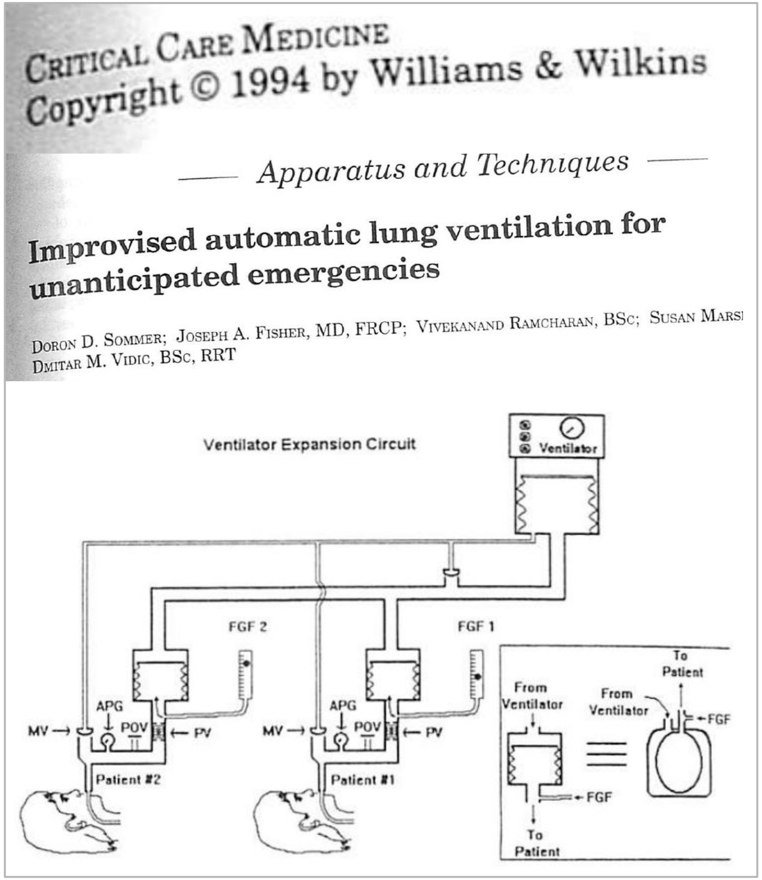


High risk of

- **Barotrauma**: Inability to control distribution of shared tidal volume
- **Hypoventilation** in patient with higher lung compliance
- **Disconnection or blockage** of one circuit affecting both co-ventilated patients
- **Cross Infection**

Ventilator Splitting: Cerberus

Joe Fisher



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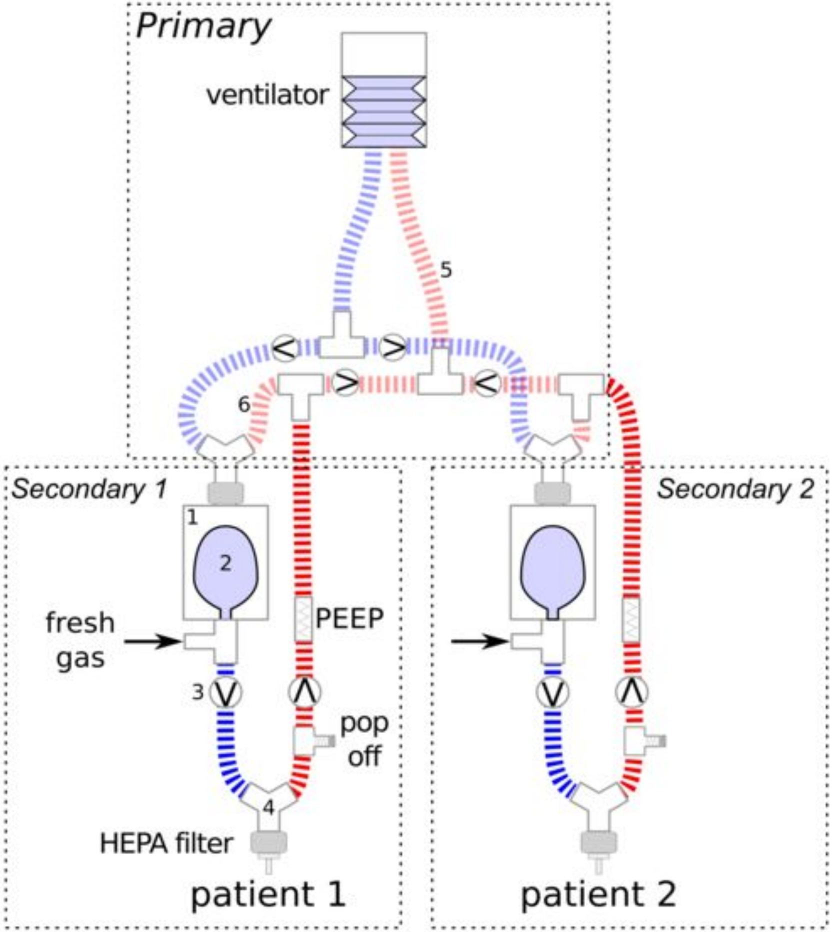
Apparatus and Techniques

Improvised automatic lung ventilation for unanticipated emergencies

DORON D. SOMMER; JOSEPH A. FISHER, MD, FRCP; VIVEKANAND RAMCHARAN, BSc; SUSAN MARS[...] DMITAR M. VIDIC, BSc, RRT



Ventilator Splitting: Cerberus

J. Han, D. Singh, J. Fisher

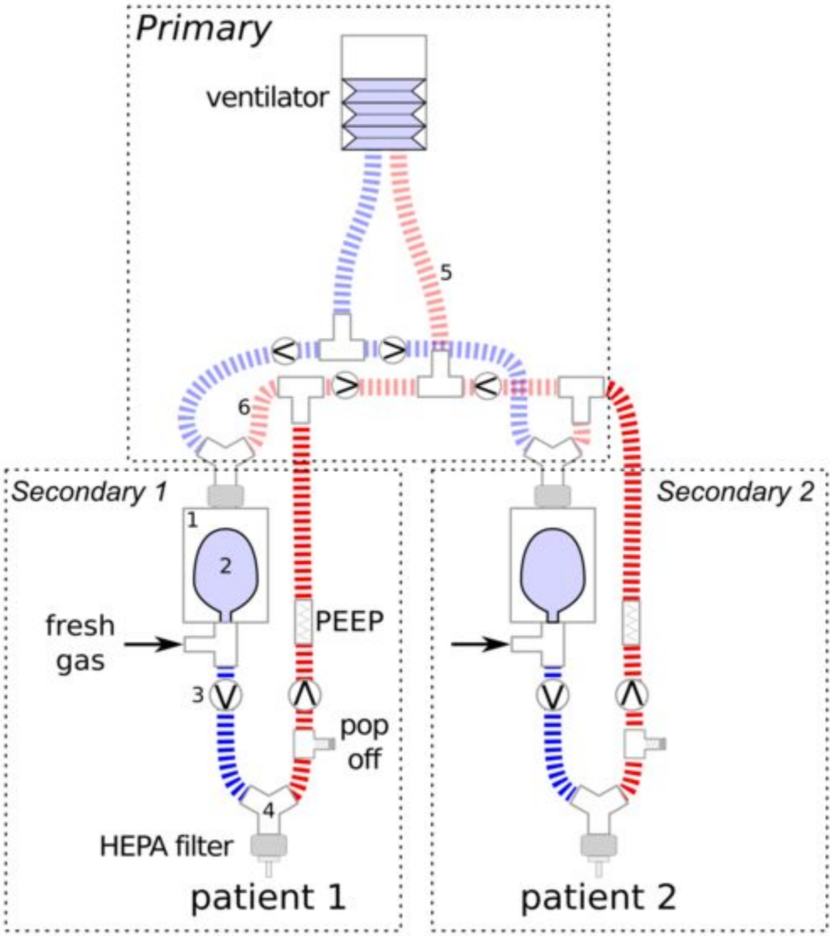
Goal: To build and test an emergency use splitter system that addresses these limitations.

Progress:

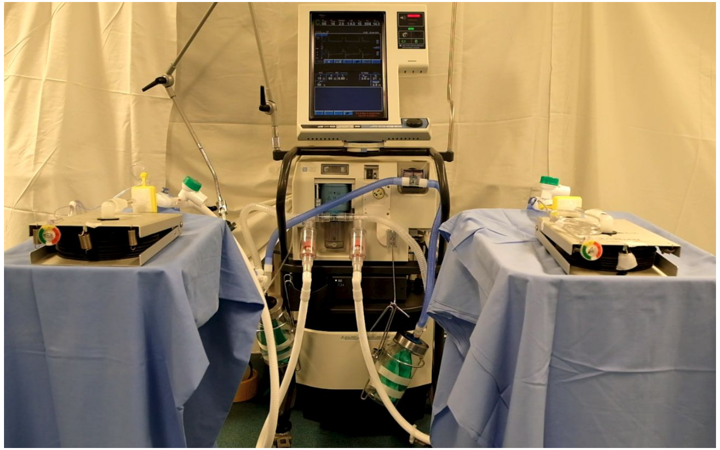
- Massive collaborative effort involving over 100 people across U of T and academic hospitals
- System refined and bench validated
- Validated in two pigs (34 and 80 Kg)
- 40 units (80 patient circuits) ordered for UHN in June 2020
- **Still unable to obtain some "off-the-shelf" parts**

References:

1. https://github.com/tgh-apil/Cerberus-Multivent
2. Han et al. Critical Care Explorations. 2020 May;2(5):e0118.
3. Porcine validation paper in preparation.



Ventilator Splitting: Cerberus



Strengths

- Independent control of tidal volume, FiO_2, PEEP
- Catastrophe on one side (disconnection, obstruction) does not affect other side
- Isolated gas paths to each patient

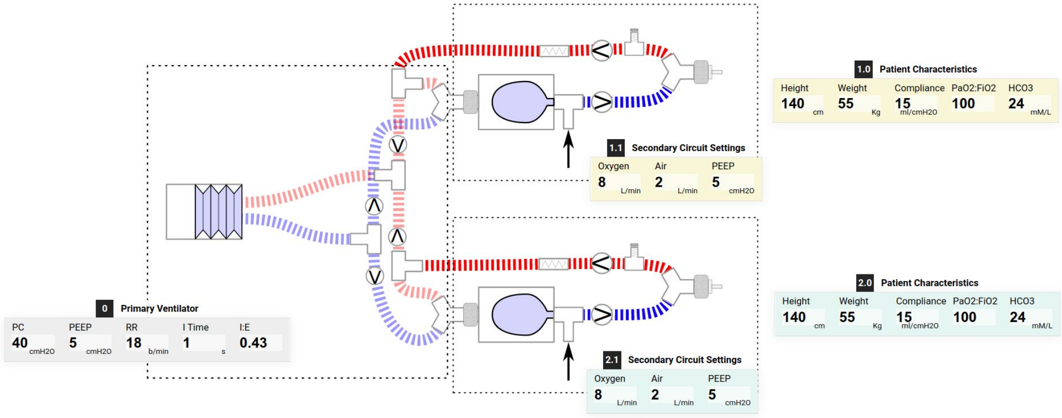
Challenges

- Volume control only
- Deep sedation
- No weaning
- < 48 hours of emergency use
- Close monitoring (1 provider to max 2 patients)
- **Adjustment is not intuitive ...**

Ventilator Splitting: Cerberus Model & Simulator

Eitan Grinspun, Isaac Waller, Bai Li, James Duffin

https://ventilator-simulator.now.sh/



Change the inputs above, then click the "Simulate" button to see results below.

Suggest Settings | Simulate | Reset

Primary Vent					Patient 1										Secondary 1			Patient 2										Secondary 2		
PC	PEEP0	RR	IT	IER	H	W	Cr	PF	VT	FIO2	PaO2	PaCO2	HCO3	pH	FGFtot	PEEP	APEEP	H	W	Cr	PF	VT	FIO2	PaO2	PaCO2	HCO3	pH	FGFtot	PEEP	APEEP
40	5	18	1	0.43	140	55	15	100	555.56	0.84	84.2	25.93	24	7.59	10	5	14.8	140	55	15	100	555.56	0.84	84.2	25.93	24	7.59	10	5	14.8

Click on a row to reset input values to those values. Current values are **bold**

Expert mode (show all variables)

Not All BVM Manual Resuscitators are Safe for Preoxygenation

- Incidental finding of BVM valve incompetence during testing of ARM NIV Mask.
- New model at UHN & CAMH due to shortage of regular model
- Assumed equivalence since HC approved
- Large leak through expiratory port during spontaneous inspiration in new model.
- **Effective delivered FiO_2 35-60% during negative pressure inspiration.**
- Relevant international standard CSA/ISO 10651-4:2002 only requires 35%. Does not require competence of patient valve.
- Models used before voluntarily exceeded the standard.

References:

1. https://github.com/tgh-apil/BVM-Evaluation
2. MS in preparation.

https://github.com/tgh-apil/BVM-Evaluation

Point-of-Care Manufacturing & Testing: What has been achieved

Class I devices - Tens of millions of face shields, stethoscopes, cloth masks made & reached frontlines, many following standard regularly pathways (relatively simple for Class I)

Class II & III - Vast number of collaborations developing open source Class II and III devices N95 Respirators, Swabs, Ventilation Masks, Ventilator components, Ventilators...

- Massive investment of volunteer resources; significant public funding (swabs, ventilators)
- A few devices received emergency use approval (e.g. HC IO, FDA EUA)

Dramatic growth in networks and communities of open source developers, small-medium scale manufacturers, academics, health care providers

Increasing awareness of the potential of local point of care manufacturing

Increasing awareness of the limits of current regulatory processes

What has not (yet) been achieved

Few class II-III devices received accelerated approval

- Very few reached clinical deployment
- Major safety concerns about some device

The open medical device development model is still a work in progress

- Open quality management systems
- Open technical standards

Many effective devices unlikely to translate into practice under current regulatory regiment

Lack of institutional integration of local & POC manufacturing.

- Reuse of disposable preferred to reuse of reusable POC devices

The Medical Device Development Process

1. **Problem Identification**
2. Specifications
3. **Iterative Design, Prototyping, Testing**
4. Formal testing & Validation
5. Manufacturing Process Design
6. Risk Management Process Design
7. Formal Evaluation (bench, clinical, standards conformance)
8. Regulatory Approval
9. **Manufacturing**
10. **Distribution**
11. Post-marketing surveillance

Supply Chain Failure

Spark: Rapid increase in global demand + Closures, worker illness, hoarding, export controls

Tinder:

- **Just-in-time** systems - low stockpiles
- High reliance on **disposable** products and components
- **No advanced emergency planning** in most jurisdictions: e.g. N95s
- **Decentralized supply chain management**: stock information, purchasing; hospitals and LTC fending for themselves on the open market
- **Centralized sourcing**: often single supplier with access to relevant **IP** (drugs, devices, vaccines)
- **Limited local manufacturing capacity**: 90% of health products in NA from China. 73% of Mouth/nose protection devices.
- Inability to **identify appropriate replacement products** - no product coding system: Eg. Bag-Valve-Masks
- Inability **to evaluate** new or alternative products rapidly

SCANH
Supply Chain Advancement Network in Health

Snowdon A. (2021) Key Characteristics of a Fragile Healthcare Supply Chain. CanCOVID Speaker Series https://www.youtube.com/watch?v=hrooLCxsCRY

Safety & Quality Control Failure

Damage control & Fallout:

- Accelerated regulatory approval pathways >>> **Quality control failure**
- Rapid retooling, accelerated manufacturing >>> **Quality control failures**
- Market competition >>> skyrocketing prices (1000% increase N95s, Swabs …) >>> Incentive for **unscrupulous production**

Digital Stockpile?

Separate device design/development from manufacturing

Open-source collections of device designs, test data, manufacturing and QC plans meeting regulatory and technical requirements

Civilian manufacturing corps - small local manufacturers, academic centers, hospitals, community groups etc.

Hospital based manufacturing and testing facilities?

Merlo S. (2020) Building Medical Supply Chain Resilience through a U.S. Manufacturing Reserve and Digital Stockpile. Day One Project; https://www.dayoneproject.org/post/u-s-prototyping-manufacturing-reserve-u-s-digital-stockpile

Acknowledgements

S. Ajami, E. Al-Azazi, K. Behdinan, M. Al-Mandhari, S. Ansari, N. Ayach, V. Anwari, J. Carroll, R. Caragata, D. Clinkard, M. Dinsmore, S. Doshi, J. Duffin, D. Duncan, L. Fedorko, J. Fisher, D. Gucciardo, E. Grinspun, J. Han, J. Qua Hiansen, K. Kazlovich, B. Li, T. Loubani, J. May, A. Mbadjeu Hondjeu, W. Ng, S. Plimmer, S. Russell, D.evin Singh, L. Venkatraghavan, C. Wakem, I. Waller, M. Xiao, T. Yan ...

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