Can Operation Warp Speed Serve as a Model for Accelerating Innovations beyond Covid Vaccines?

Arielle D'Souza
Institute for Progress

Kendall Hoyt
Geisel Medical School

Christopher Snyder
Dartmouth Economics

Alec Stapp
Institute for Progress

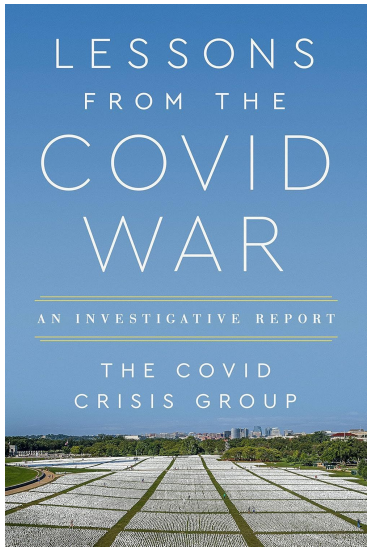
Introduction

- **Operation Warp Speed (OWS)**
  - $18 bil. U.S. program for pharmaceutical response to Covid pandemic
  - Eventually focused on vaccines, spinning off therapeutics, diagnostics

- **Technological marvel**
  - Novel vaccines rolled out to population with unprecedented speed
  - Pfizer and Moderna vaccines new mRNA platform

- **Historical echoes in historical named missions**
  - Manhattan Project, Apollo Mission

- **“OWS for X”**
  - General-purpose tool for other urgently needed innovations?
  - Which program features?
  - Which needs?



- **Interdisciplinary policy paper**
  - You will find: journalistic account, economic concepts, literature references
  - You won’t find: regressions, theorems

OWS Background

- **Launched:** May 2020
- **Leaders:** Dr. Moncef Slaoui and General Gustav Perna

- **Goal:** develop and deliver 300 million doses of Covid vaccines, first doses Jan. 2021
- **Spinoffs:** therapeutics, diagnostics
- **S.O.P. backdrop:** 7% probability of success, 10-year timeline

- **Vaccines developed:** Four of six sponsored candidates received FDA approval
- **Novel technologies:** mRNA (Pfizer and Moderna), viral vector (J&J)

- **Value:** 140,000 lives saved, $2 tril. economic costs avoided in U.S. (Gupta et al. 2021)
- **Return on investment:** One day of avoided harm $26 bil. > $18 bil. OWS price tag
- **Other pandemic spending:** CARES Act $1.8 tril., total outlays $4.4 tril.

- **Whole of government:** combination of DoD, HHS, White House
- **Defense Production Act:** commandeer inputs, prioritize gov't contracts, certain authorities

Innovation Missions

Table 1
Innovation and Infrastructure Missions over U.S. History

Mission	Timeframe	Goal description	Cost (billion 2023 dollars)	Source
(a) Innovation missions				
Manhattan Project	1942–1946	Develop first atom bomb	37	Metcalfe (2023)
Apollo Program	1961–1972	Send humans to Moon and back	177	Dreier (2022)
Space Shuttle program	1972–2011	Develop reusable spacecraft for orbital missions	266	Borenstein (2011)
GPS development	1973–1995	Create global satellite navigation system	10	Page et al. (1995), Appendix B
Strategic Defense Initiative	1984–1993	Develop space-based anti-missile systems	63	Abrahamson and Cooper (1993)
Human Genome Project	1990–2003	Map and sequence human genome	7	National Institutes of Health (2024)
Operation Warp Speed	2020–2021	Accelerate COVID-19 vaccine development and distribution	21	Congressional Research Service (2021)
(b) Infrastructure missions				
Transcontinental Railroad	1863–1869	Connect East and West coasts by rail	2	Klein (2024)
Panama Canal	1904–1914	Create shipping passage between Atlantic and Pacific Oceans	12	McCullough (1978)
Interstate Highway System	1956–1992	Create national highway network	700	Neuharth (2006)
Y2K preparation	1995–2000	Prevent computer failures from year-2000 transition	183	Chandrasekaran (1999)

Innovation Missions: When Called For?

- **National importance**
  - Principle: call for resources and priority
  - Pandemic: $16 trillion in US losses (Cutler & Summers 2020)

- **Time sensitivity**
  - Principle: crisis, now or never
  - Pandemic: disease spread, economic shutdown

- **Uncommon coordination**
  - Principle: multiple agencies, industry, move fast
  - Pandemic: White House, HHS, DoD, Army Corps

Tradeoff

- Yes…strategies accelerate achievement of social goal

- But…expensive
- Reduce checks and balances on waste, fraud

- **Well-defined technological goal**
  - Principle: concentrate attention, evaluate success
  - Pandemic: Covid vaccines

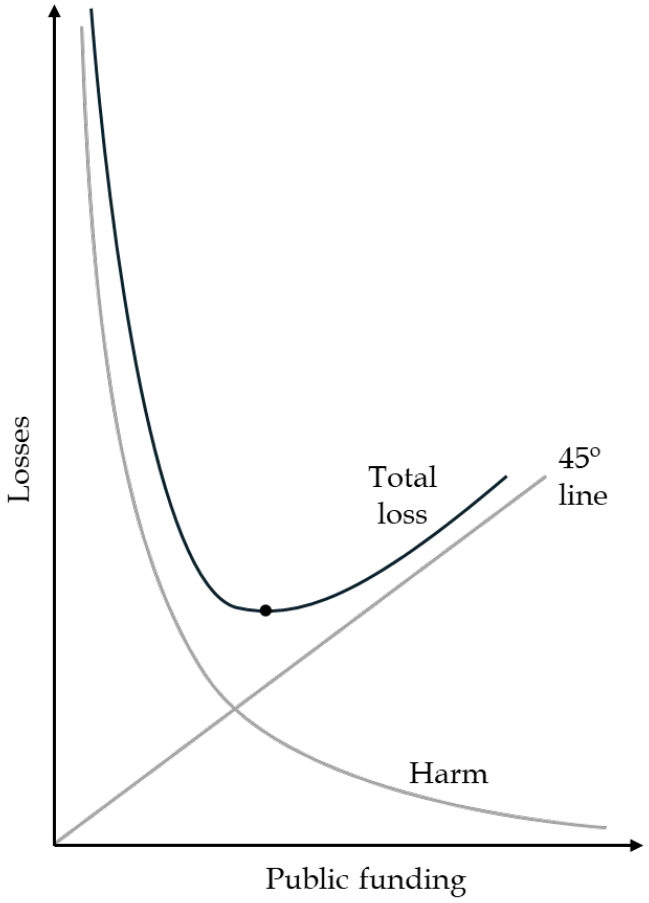
- **Commercial market inadequate**
  - Principle: some socially beneficial innovations not lucrative
  - Pandemic: vaccines $6000 social value vs. $60 price (Castillo et al. 2021)

Key OWS Features

- Prodigious spending
- Multiple shots on goal
- Even long shots
- Push and pull funding
- Leadership and coordination

Prodigious Spending

- **OWS spending**
  - $18 bil. widely cited CRS figure
  - $30 bil. according to Mango (2023)
- **Relatively generous terms**
  - Compare to European procurement deals
  - Compare to COVAX
- **Insights**
  - Precondition enabling all other features
  - Spend billions to save trillions
  - Asymmetric loss function



Multiple Shots on Goal

- **Boost probability of at least one success**
  - High failure rates in pharmaceutical development, notoriously high for vaccines
  - While multiple successes “nice to have”, one success a “must have”
  - Pursue multiple candidates to increase probability at least one succeeds

- **Portfolio approach**
  - Attenuated virus, viral vector, protein subunit, DNA, mRNA technologies
  - Include candidates from different platforms to reduce correlation in failure rates
  - Some cases take candidate with lower standalone probability
  - Hopenhayn and Squintani (2021) congestion in technology pathways

- **Parallel development**
  - Accelerates success relative to sequential

- **Echoes in Manhattan Project**
  - Three approaches to enriching uranium
  - Magnetic field, gaseous diffusion, liquid thermal diffusion

Portfolio Approach

Table 2: Candidates for optimal vaccine portfolio

Clinical platform	Subcategory	Stage	Probability of at least one success in portfolio (%)		Probability of individual vaccine success (%)
			Cumulative	Increment	
Inactivated	Standard	Phase 3	28.8	28.8	28.8
Viral vector	Adenovirus	Phase 3	48.4	19.6	28.8
mRNA	LNP-encapsulated	Phase 3	58.4	10.0	21.6
Inactivated	Standard	Phase 3	65.8	7.4	28.8
Protein subunit	Recombinant	Phase 2	70.8	5.0	18.4
Protein subunit	S protein	Phase 2	74.5	3.7	18.4
Protein subunit	Recombinant	Phase 2	77.0	2.5	18.4
mRNA	LNP-encapsulated	Phase 3	79.0	2.1	21.6
Inactivated	Standard	Phase 3	80.7	1.7	28.8
Viral vector	Adenovirus	Phase 2	82.1	1.4	18.4
Virus-like particle	Standard	Phase 1	83.3	1.2	13.2
Viral vector	Adenovirus	Phase 2	84.1	0.8	18.4
Viral vector	Measles	Phase 1	84.7	0.7	13.2
Protein subunit	S protein	Phase 1	85.3	0.6	13.2
DNA	Electroporation	Phase 2	85.8	0.5	9.2
Protein subunit	S protein	Phase 1	86.2	0.4	13.2
Live attenuated	Standard	Preclinical	86.5	0.3	8.1
DNA	Other DNA	Phase 2	86.8	0.3	9.2
Live attenuated	Standard	Preclinical	87.1	0.3	8.1
Protein subunit	Recombinant	Phase 1	87.3	0.2	13.2

Long Shots

- **Worth funding marginal candidates even in a large portfolio**
  - Exercise of adding seventh candidate to model portfolio of six
  - Athey et al. op-ed call for spending $70 bil. on 15-20 candidates

- **mRNA platform could be viewed as a long shot**
  - Never used in human history for approved vaccine
  - Earlier experience with DNA vaccine disappointing (Hwang 2023)

- **At-risk investing**
  - Massively scale up capacity for candidates before approval
  - If led to three months acceleration of vaccines to U.S. market, worth $360 bil. (Ahuja et al. 2022)

Push and Pull Funding

- **Push funding**
  - Grant funding R&D and capacity investments
  - Except for Pfizer, rest of firms funded by OWS received push
  - Can discipline expenses, control profit margin offered firm

- **Pull funding**
  - Payment for successful product
  - All funded firms received pull funding in form of advance procurement contracts
  - Advance = signed before advent of authorized/approved product
  - Strong incentives to select for entry of serious participants (adverse selection)
  - Strong incentives to push to viable vaccine produced at scale (moral hazard)
  - Incentives can be expensive since payment lucrative enough to induce marginal firm to enter “overpayment” to more efficient inframarginal firms

- **Either or? Both and!**
  - Ensure participation by covering most of cost with push
  - Motivate scale up and supply with pull
  - Double charge?
  - Optimal scheme may involve a partial mix (85% push, rest pull?)

Additional Key OWS Features

- **Leadership**
  - Go outside standard bureaucracy
  - Novel protocols
  - Decision authority
  - Leader skill unusually important

- **Coordination**
  - DoD and HHS
  - Direct line to West Wing
  - Army Corps of Engineers (logistics)

- **Cooperate with industry**
  - FDA iteration with firms
  - VA helped recruit and organize Phase-3 trials
  - Asked producers “what do you need”? Pull for Pfizer, both for Moderna.
  - Government officials in plants to monitor production, coordinate delivery

Evaluating OWS: Comparisons

- **Past vaccines**
  - HPV
- **Rollout of Covid vaccines in other countries**
- **Other products within U.S. during Covid pandemic**
  - Diagnostics
  - Therapeutics

OWS for X

- **X = Alzheimer's disease**
  - Projected leading loss of life in HICs by 2040 (Foreman et al. 2018)
  - Call for global mission (Vradenburg 2015)
  - Receiving public funding through usual channels (NIH $3.8 bil in 2023)
  - Robust commercial incentives
    - Not infectious
    - Few other obvious externalities
    - Value for speed but not "now or never"

- **X = atmospheric carbon removal**
  - IPCC (2023) suggests need 6 bil. tons of carbon removal to meet 1.5^{o}C target
  - Modest programs
    - DoE Carbon Negative Shot ($100 mil.), regional DAC hubs ($3.5 bil.)
    - Frontier $1.2 bil. advance market commitment
  - Case
    - Large-scale, urgent, requiring coordination
    - Well-defined goal ($100 /ton removal)
    - Limited commercial incentives without public funding
  - Repurpose some lessons from OWS in design

THE UNIVERSITY OF CHICAGO
MARKET SHAPING ACCELERATOR

- MSA identifies where pull funding is best suited and tailors mechanisms for these markets
- Ran $2 mil. Innovation Challenge receiving 188 submissions from 16 countries
- Shepherding winners and other market-shaping projects including…

Climate change

- Climate-resilient crops
- Greenhouse gas removal

Pandemics & public health

- Neonatal sepsis diagnostics
- Broad-spectrum antivirals

- Faculty directors helped create successful $1.5 bil. pneumococcal Advance Market Commitment
- Advised int'l agencies on Covid vaccine strategy
- Advisors on Frontier AMC for carbon removal

Rachel Glennerster
CGD President

Michael Kremer
Nobel laureate

Christopher Snyder
Dartmouth College