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Health Solutions

16 September 2021

HEOR Evidence for Emergent Infectious Diseases: Opportunities and Challenges in Generating and Communicating Evidence for COVID-19 Treatments and Vaccines

The power of **knowledge.**
The value of **understanding.**

Objective

To discuss opportunities, challenges, and best practices for developing HEOR materials in the rapidly changing COVID-19 setting

Agenda

1. Background and COVID market overview
2. Value of HEOR/market access deliverables
3. Key challenges
4. Literature reviews
5. GVDs
6. AMCP dossiers
7. Epidemiological and health economic models
8. Best practices
9. Discussion

Our Presenters

Shahnaz Khan, MPH

Executive Director, Market Access and Outcomes Strategy

Anne Heyes, MBA

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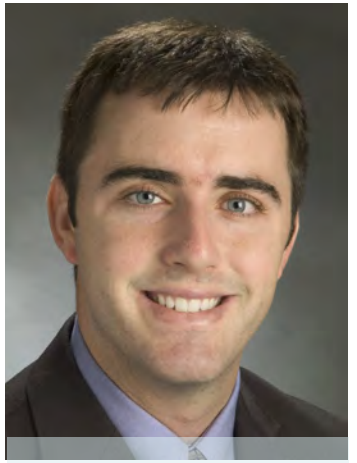
Kati Copley-Merriman, MBA

Vice President, Market Access and Outcomes Strategy



Mickey Wilson, PhD

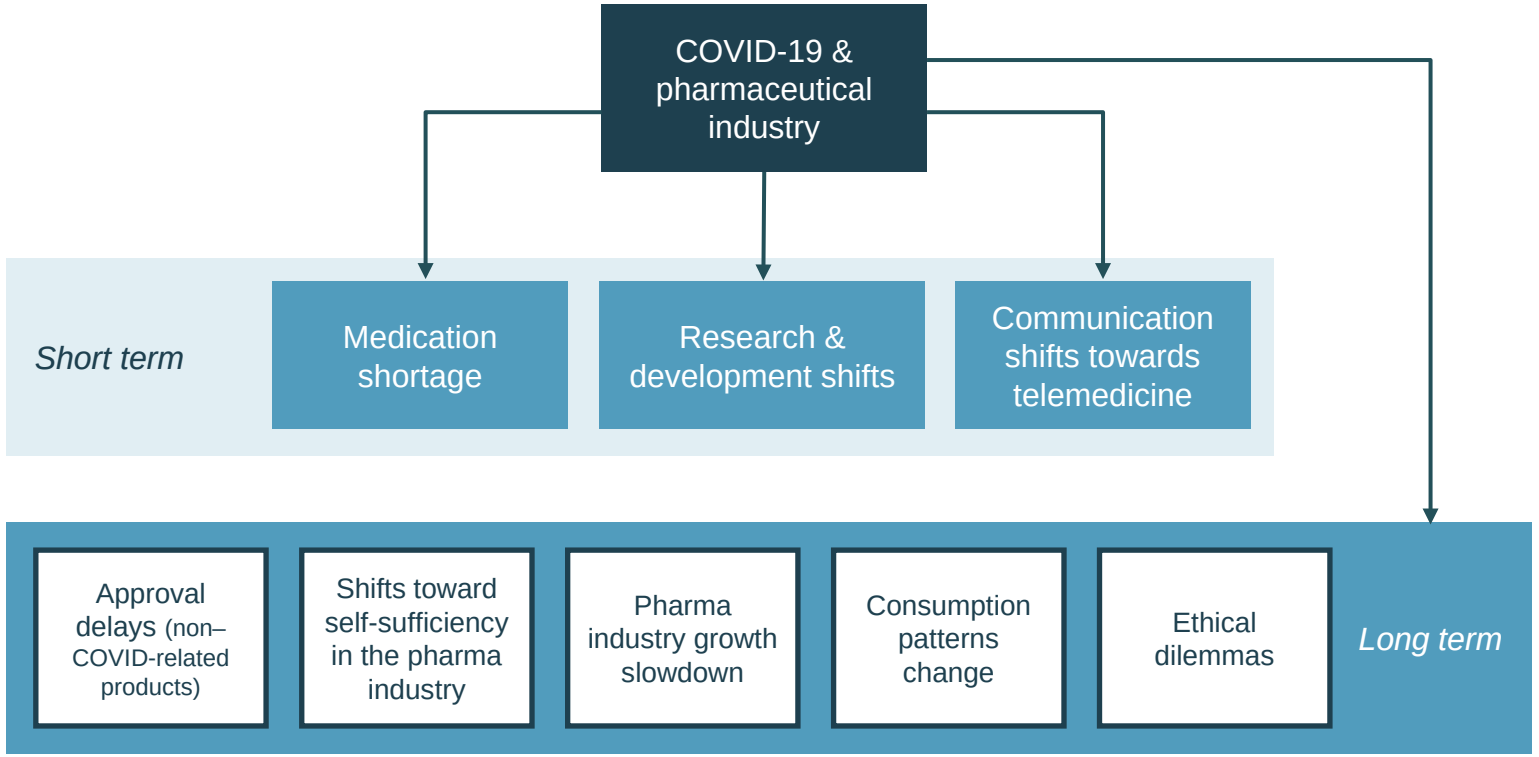
Senior Director, Health Economics

Overview

Shahnaz Khan

COVID-19: Impact and opportunity

Every part of the pharmaceutical value chain is affected by COVID-19, from drug development to sales and marketing



Although disruptions in the supply chain and clinical trials have had short-term negative impacts of COVID-19, the industry has also seen substantial growth opportunities, particularly the companies taking center stage in the race for vaccines and treatments for COVID-19

Source: Ayati et al., 2020

COVID-19 = coronavirus 2019

An all-hands approach

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Approved and authorized vaccine as of August 30, 2021

Vaccine name	Developer	Highest development stage for COVID-19	Regions
Ad26COVS1	Johnson & Johnson	EUA	US, Canada, EU, UK
Sputnik V	Gamaleya Center of Epidemiology and Microbiology	EUA	Russia, Argentina, Bolivia, UAE, etc.
EpiVacCorona	Vector State Virology and Biotechnology Center	EUA	Russia
mRNA-1273	Moderna	EUA	US, EU, UK, Canada, Israel, Japan
Comirnaty (BNT162b2)	Pfizer/BioNTech	Approved	US, EU, UK, Canada, Israel, Japan etc.
AZD-1222	AstraZeneca/Oxford University	EUA	EU, UK, India, Japan, Mexico, etc.
BBIBP-CorV	Sinopharm Group	Approved	China, Bahrain, UAE
CoronaVac	Sinovac Biotech	Approved	China, Indonesia
Covaxin	Bharat Biotech	EUA	India
Ad5-CoV	CanSino Biologics	EUA	Mexico
CoviVac	Chumakov Centre	EUA	Russia
Recombinant COVID-19 Vaccine	Chinese CDC and Chinese Academy of Sciences	EUA	China, Uzbekistan

CDC = Center for Disease Control and Prevention; EU = European Union; EUA = emergency use authorization; UK = United Kingdom; US = United States; UAE = United Arab Emirates
Source: Global data, 2021

An all-hands approach

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Approved and authorized therapies as of August 30, 2021

Drug name	Developer	Highest development stage for COVID-19	Regions
Veklury (remdesivir)	Gilead Sciences Inc	Approved	Global
Dexamethasone	None (generic)	Approved	Global
Favipiravir	Fujifilm Toyama Chemical	Approved (as generics)	Russia, India
Bamlanivimab & etesevimab	Eli Lilly	EUA	US
Casirivimab and imdevimab (REGN-COV2)	Regeneron/Sanofi	EUA	US
Olumiant (baricitinib)	Eli Lilly	EUA	US
Sotrovimab	Vir Biotechnology/GSK	EUA	US

Drug repurposing

Products with regulatory approval for other conditions being tested to treat COVID-19

World Health Organization

ACTIV-6

Product has already have been tested in humans and approved; therefore, repurposing could help discover COVID-19 treatment options sooner

ACTIV-6: COVID-19 Study of Repurposed Medications

ivermectin, fluticasone, and fluvoxamine

https://clinicaltrials.gov/ct2/show/NCT04885530

WHO Solidarity Trial

https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments

remdesivir, hydroxychloroquine, lopinavir, interferon beta-1a; artesunate; imatinib and infliximab for treatment of COVID-19 in hospitalize patients (WHO Solidarity Trial Consortium, 2021)

ACTIV = Accelerating COVID-19 Therapeutic Interventions and Vaccines; WHO = World Health Organization

The drug and vaccine pipeline is crowded, with more than 1,000 vaccines or therapeutics in development at various stages

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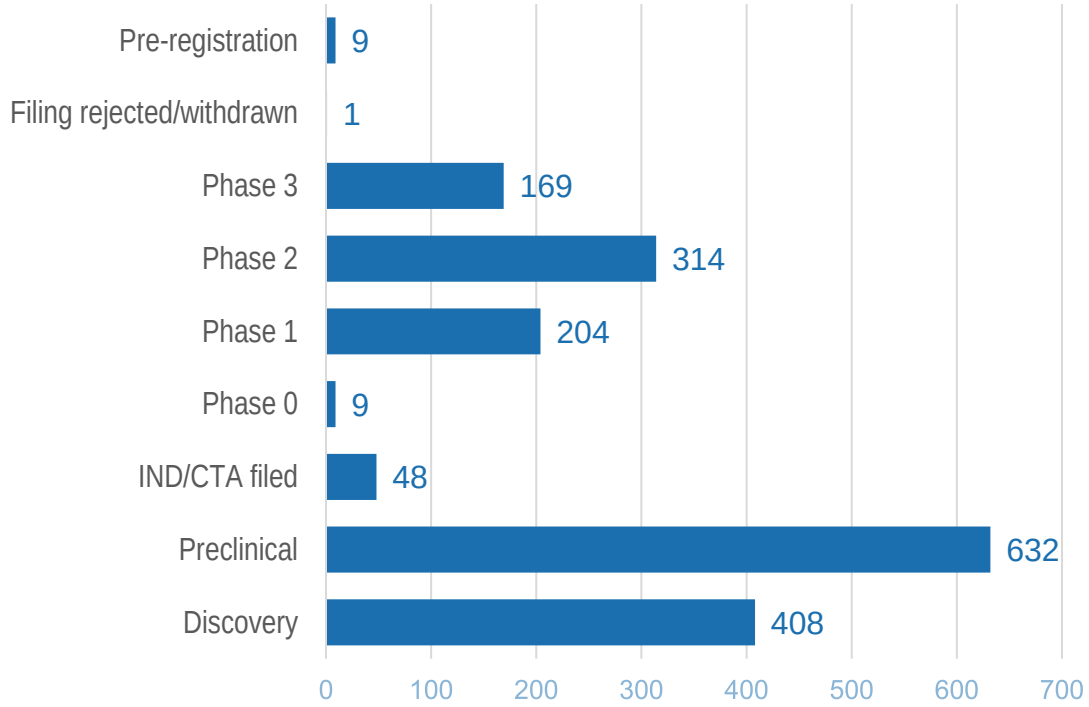
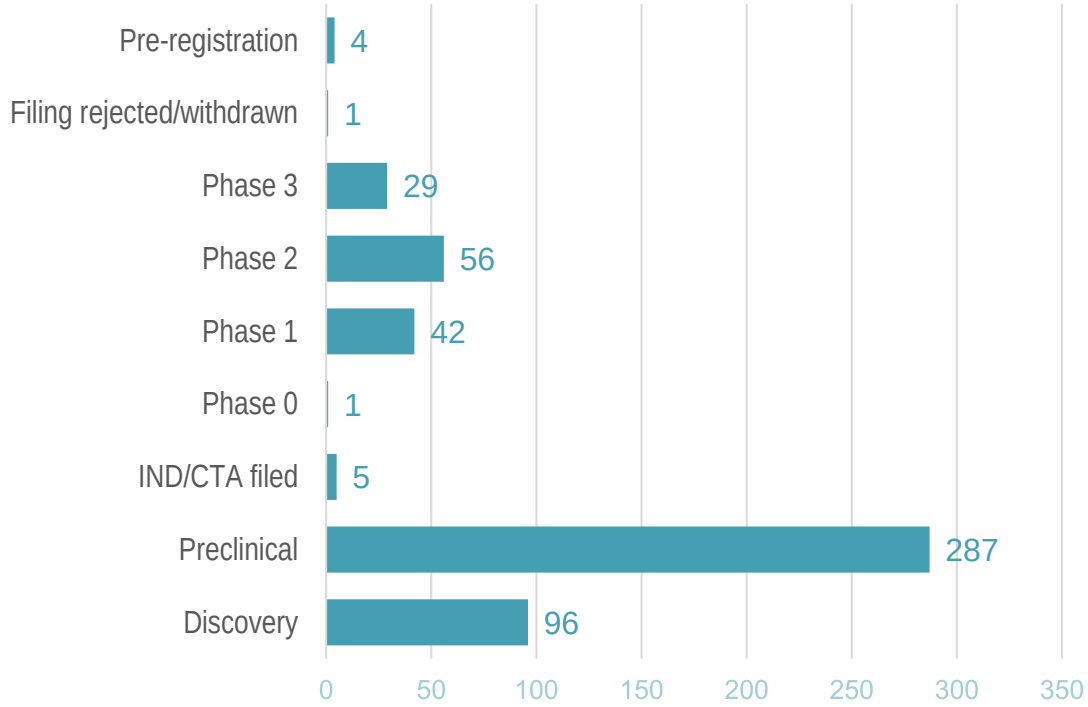
Landscape of *pipeline* candidates for COVID-19, by phase



Landscape of *vaccine* candidates for COVID-19, by phase



Source: GlobalData, 2021. CTA = Clinical Trials Application; IND = Investigational New Drug.

Product support

In order to support market access for new products, a number of HEOR/MA materials are needed, including:

- Literature reviews
- Product value story
- Global value dossier
- AMCP unapproved product dossier (US market)
- Preapproval information exchange (PIE) deck (US market)
- AMCP approved product dossier
- HE models
- Country-level submissions/HTA reviews

COVID projects provide a unique case study in that the information is rapidly changing and timelines are very uncertain within the context of EUAs

AMCP = Academy of Managed Care Pharmacy; HTA = health technology assessment

Key challenges across all materials

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Clinical picture of the disease evolves as knowledge evolves
(e.g., variants, long-term effects, changing population characteristics [primarily age])

Rapidly changing burden information
(rates of infections, deaths, economic burden, humanistic burden, etc.)

Rapidly changing competitor landscape

Changing reimbursement/who is paying for vaccines

Testing and testing methodology are constantly changing

Literature Reviews

Anne Heyes

Difference between the body of literature on COVID-19 and other therapy areas

The large number of publications is unprecedented

~10,000

new articles are added to the PubMed database alone each month

Difficult to keep up with the

latest research

Lack of

peer review

(particularly 2020)

Short time scale

2020 **2021**

Change in characteristics of the literature during the pandemic

- Many small studies
  - Single-center studies and case reports
- Guidelines very local (to hospital)
- Large number of preprints
- Information often restricted to specific geographies (e.g., China and US)
- Population with severe COVID-19–related disease (hospitalized)
- Short-term outcomes only

- Larger studies, reviews, & meta-analyses
- Full publications
- Information available from a much wider range of countries
- Information on patients with mild and moderate disease
- Longer follow-up of patients

Early stages → *More recently*

2020 **2021**

Meeting the challenges:
Designing the search strategy

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Design search strategy appropriately

(relevant yet manageable numbers in search results)

- Define a clear objective for the search
- ***Indexing terms, free-text search terms, and limits should be combined strategically***
- Conduct pilot searches to be refined strategically

Meeting the challenges:
Changing terminology

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Important to use common and new terminology to identify relevant articles

- Make use of publicly available resources
  - The US National Library of Medicine created some resources in order to help researchers
  - PubMed developed a series of search strings to capture relevant information on vaccines, diagnosis, transmission, etc.
  - LitCovid is a curated literature hub for tracking up-to-date scientific information
  - Epidemiology: desktop research of publicly available surveillance websites (e.g., WHO, CDC)

Recommendations

- Define a clear purpose for the literature review and refine the search strategy so that the outcome is manageable (e.g., reviews vs. single studies, date limits [by month])
- Partner with an experienced librarian to develop the search strategy and test different options
- Make use of available resources to ensure inclusion of appropriate terminology
- Plan the review schedule appropriately, including updates

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Global Value Dossiers

Kati Copley-Merriman

Developing the value story and GVD

What's the best approach?

- Value story: understand the evolving target population
  - May change over time based on trial results
  - Will be different for various geographic regions, nonhospitalized vs. hospitalized patients, vaccines vs. treatments, younger vs. older patients, immunocompromised patients, patients with comorbidities
- Competitor landscape/key comparators change rapidly
- Timing considerations
  - Good to start early but may want to pause if launch timelines are moved out to avoid redoing work repeatedly
- Modular approach works best, so some sections can be finished before others
- Clarify to local country affiliates which sections they need to research themselves and what the known resources are

Proposed GVD sections

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Section 1:
Executive summary and value story of treatment or vaccine

Section 2:
Disease background

- Pathophysiology related to the treatment/vaccine
- Epidemiology (sources and data cut dates)
- Clinical burden (acute and long-term outcomes)
- Humanistic burden (acute and long-term outcomes
- Economic burden

Section 3:
Disease management and competitor landscape

- Treatment guidelines and patterns
- Key competitors (including anticipated future treatments)
- HTA assessments, if available
- Unmet needs

Section 4:
Clinical evidence for Product X

- Product profile and mechanism of action
- Overview of the clinical development program
- Clinical efficacy
- Safety

Section 5:
Economic evidence for Product X

- Description of economic models
- CEM results
- BIM results

BIM = budget-impact model; CEM = cost-effectiveness model

Recommendations

- Design the GVD so local country affiliates can use the sections that apply to all countries but also identify which sections need to be customized for their setting and provide data website links
- If developing literature reviews, a GVD, and reimbursement dossiers simultaneously, extensively coordinate and communicate internally across project teams
- Anticipate changes in the target population, infectious disease variants, comparators, and outcomes data; plan timelines accordingly
- Discuss the value story upfront with payers and understand the reimbursement environment for each country

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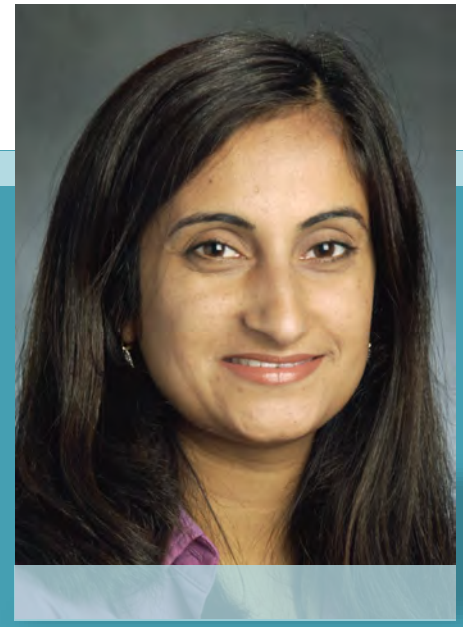
AMCP Dossiers

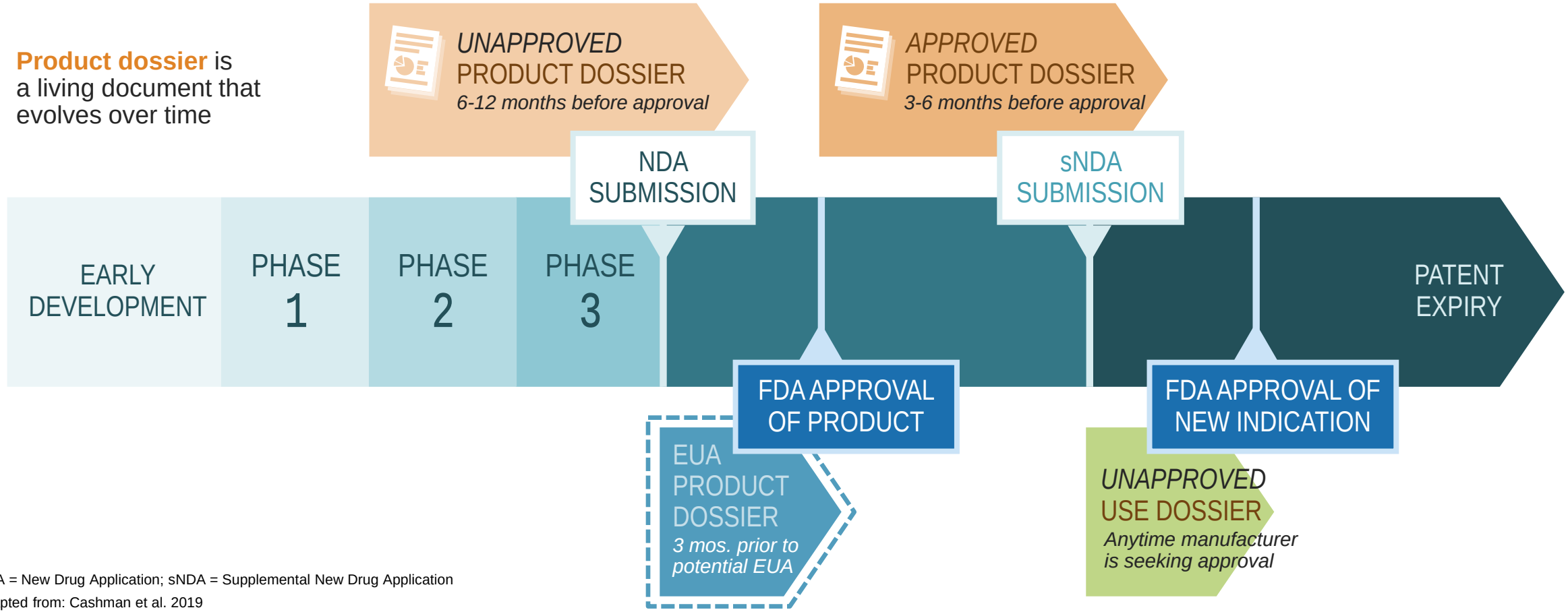
Shahnaz Khan



AMCP unapproved and approved product dossiers

Communicate clinical and economic evidence of product or vaccine before and after approval

Product dossier is a living document that evolves over time



NDA = New Drug Application; sNDA = Supplemental New Drug Application

Adapted from: Cashman et al. 2019

AMCP dossiers

Consider unapproved product dossier for early communications with payers

- Provides early product Information (including date EUA was granted, if applicable)
- If an EUA dossier, have a clear statement similar to UPD regarding lack of approval and proven efficacy and safety but also a statement listing the exact EUA language
- Materials: fact sheet, investigator's brochure, core data sheet, and internal slide decks
- Provides early product Information (including date EUA was granted, if applicable)
- Sets up the disease information and unmet need, with links to resources for most up-to-date information such as data on epidemiology, emerging variants, new treatment and vaccine approvals, and treatment guidelines
- Internal consensus on clinical evidence
- Introduce early clinical data in support of the product
  - Study design summaries of key trials
  - Preliminary results (based on availability and internal consensus; often only what is in the public domain)
- Similar to previous deliverables, information is rapidly changing, and timelines are uncertain, so innovative solutions and flexibility are a must
- A completed, internally approved EUA dossier facilitates development of a postapproval AMCP dossier

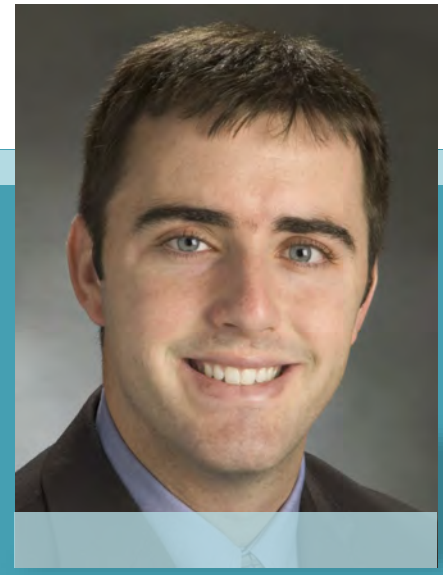
AMCP dossier

- **Timing:** start once BLA/NDA submitted (closer to approval)
- **Updates:** confirmation of indication, availability of PI, new disease information, updated clinical analyses, and economic evaluation
- ***Flexibility:***
  - Timelines may shift
  - Target population may shift
  - Emerging variants may become critical
  - Competitor landscape may shift
  - Additional resources to obtain updated materials

BLA = Biologic License Application

Economic Models

Mickey Wilson



Infectious disease models

Most HE models consider the impact of an intervention on the people who receive it (i.e., the direct effect)

- Typically built in Excel for ease of client use
- Examples: Markov, decision tree, patient-level simulation
- Can be used for modeling the impact of treatments in certain circumstances

In infectious diseases, contacts (and contacts of contacts…) of people who receive the intervention may also benefit (i.e., indirect effect which can lead to herd immunity)

- We can estimate the indirect effect or model interaction and transmission so that the indirect effect is endemic
- Examples: compartmental models, individual-based models, agent-based models, typically built using specialized software (e.g., MATLAB, R, Julia)
- Can be used to model impact of vaccines or treatments

Modeling Challenges in COVID-19

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Rapidly changing understanding of the disease

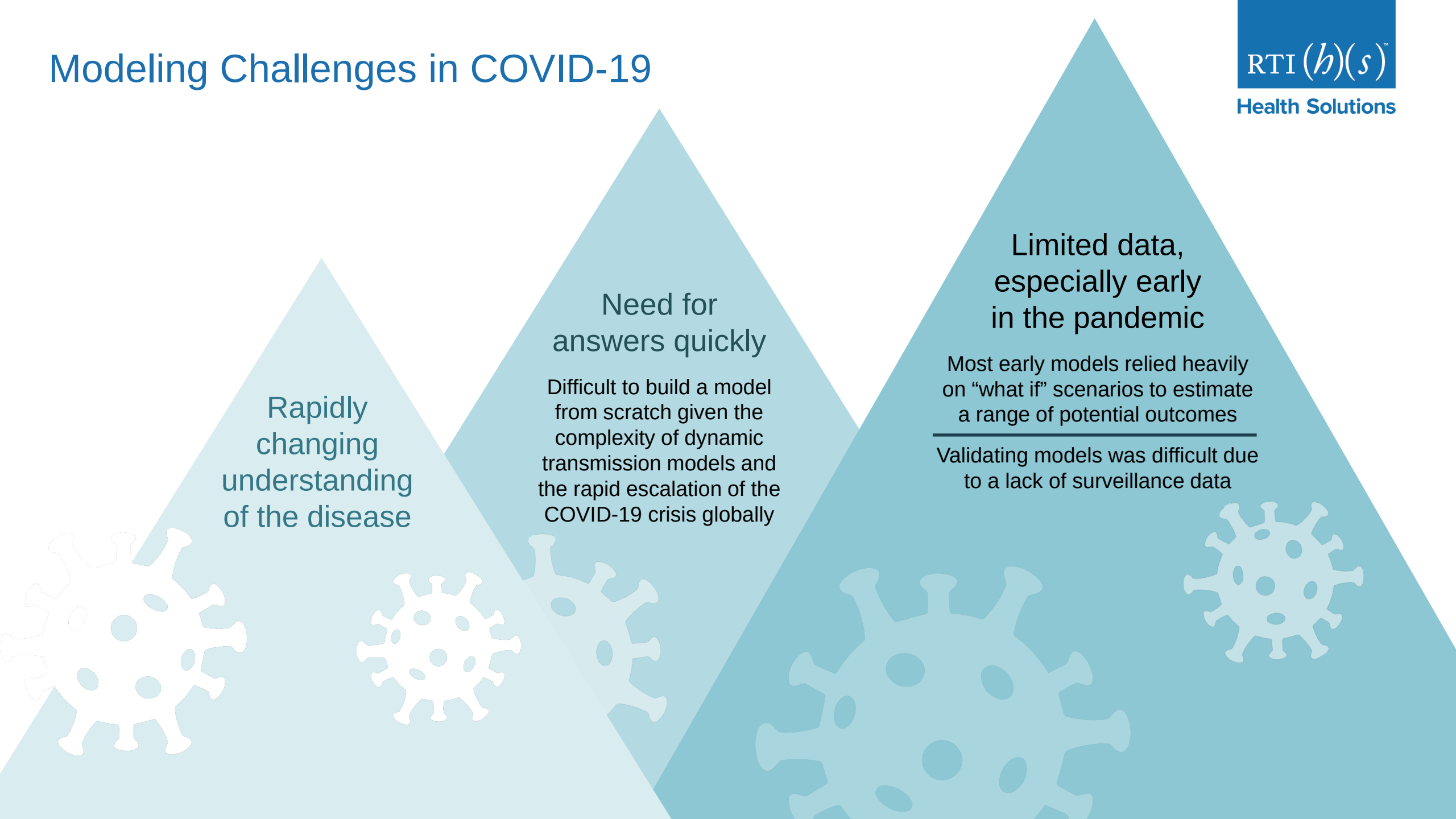
Need for answers quickly

Difficult to build a model from scratch given the complexity of dynamic transmission models and the rapid escalation of the COVID-19 crisis globally

Limited data, especially early in the pandemic

Most early models relied heavily on “what if” scenarios to estimate a range of potential outcomes

Validating models was difficult due to a lack of surveillance data



Examples of solutions to COVID Modeling challenges

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Publicly available data repositories

Sources for both latest data and economic models

Identifying simpler strategies for modeling

Modeling based on reproduction number using simplified population assumptions

Repurposing previously developed models for COVID-19

Given time constraints, the only feasible way to build the more complex models such as simulations or compartmental models

Core recommendations

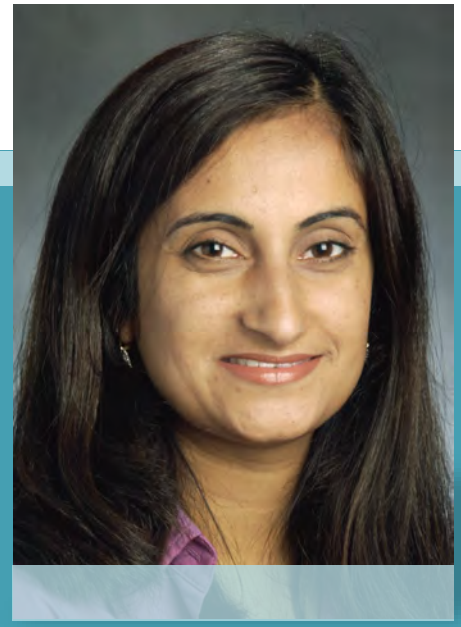
- Be sure to develop a model in accordance with local reimbursement/market access requirements
- Models should be designed to capture the epidemiological or clinical impact in addition to economic parameters
  - For vaccines, this requires capturing the indirect effects
  - For treatments, estimating indirect effects may or may not be necessary
- Outcomes should be validated as best as possible with available data

Additional recommendations

- Consider collaborations/partnerships/repurposing existing models
- Consider epidemiological models for other business needs (e.g., early business decisions, landscape analysis, above-brand messages)
- Consider sharing pharma-developed models in online model repositories
- Think outside the box for supporting “above-brand” value messages for COVID-19 vaccination in general (instead of or in addition to focusing only on the value of a specific COVID-19 vaccine)

Best Practices

Shahnaz Khan



Best practices for staying up to date

Familiarize yourself with the EUA Pathway in the US:

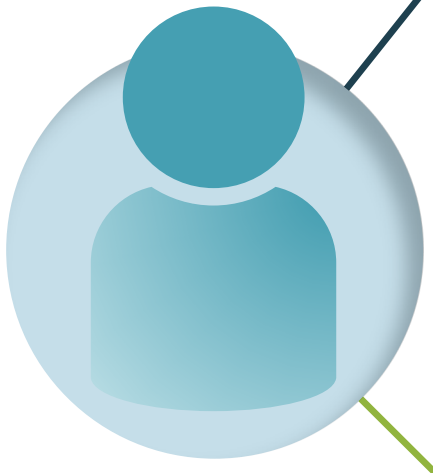
https://www.fda.gov/media/143890/download

and Conditional Marketing Authorization in the EU:

https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/conditional-marketing-authorization

In the US, engage payers early and proactively using PIE deliverables such as unapproved product dossier and PIE slide decks and/or webinars

Engage experienced librarian(s) to keep up to date with rapidly evolving literature



Use publicly available sources for the latest epidemiology information and provide links in documents for the audience or affiliates to obtain the most current information

Flexibility is key in an everchanging and evolving landscape; be prepared with resources to accommodate changing needs

Planning & Organizing: It's important to have your team aligned internally on which data you will want to include

Budgeting: Reserve some budget for unforeseen scenarios (as EUA gets pushed, you many need to update epidemiological and other information more often than expected; uncertainty; change in focus/strategy)

Team coordination: Critical that all team members coordinate closely (GVD, AMCP, model) and communicate regularly when there are updated data. It sort of becomes an everyone-helping-everyone situation

Thinking outside the box:

- Cross-links to the latest epidemiological data
- Economic burden must consider global economic impact of businesses closing, etc.
- Humanistic burden must consider isolation due to restrictions

Question & Answer

Thank you

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