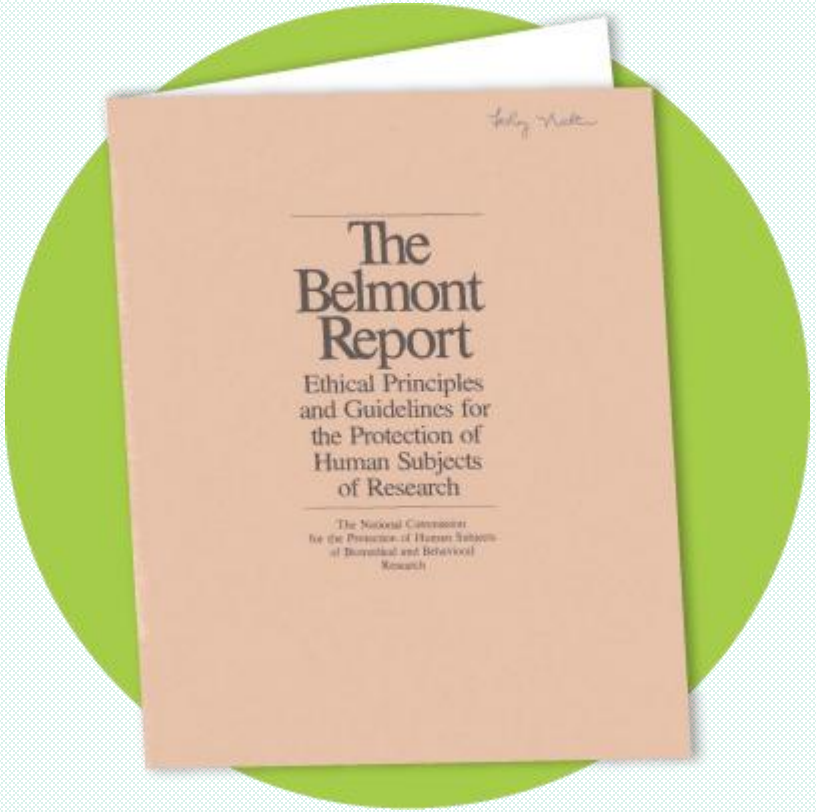
The Belmont Report (1979)



The three basic ethical principles

- Respect for persons (Autonomy)
- Beneficence
- Justice

Do pandemics impact ethical principles?

Vaccine - a key prevention strategy of any contagion

People often mandated to take a vaccine for the 'greater good' of humanity

Can impact autonomy

Vaccine Hesitancy – The Silent Killer?

COVID-19 vaccine phased roll-out in India: 16 Jan 2021

Covishield ® and Covaxin ® were available

Despite multiple COVID deaths, vaccine uptake not brisk as expected

Huge economic impact

Hesitant to take a new vaccine – concerns regarding safety, effectiveness, *etc*.

IHEA 2023 Congress

Track: Preferences and willingness-to-pay for care and insurance (12 July 2023)

Can a Discrete Choice Experiment (DCE) help understand COVID-19 vaccine hesitancy? A study from India

Speaker: Dr. Jeffrey Pradeep Raj, Assistant Professor, Seth GS Medical College & KEM Hospital, Mumbai, India
Email: jpraj.m07@gmail.com

Can a Discrete Choice Experiment (DCE) help understand COVID-19 vaccine hesitancy? A study from India

Jeffrey Pradeep Raj[1], Thenmozhi Mani[2], Melvin Joy[2], Sukant Pandit[1], Charuta Godbole[1], Shital Bendkhale[1], Dhruve Soni[1], Jeyaseelan Lakshmanan[2], Nithya Jaideep Gogtay[1]

1. Department of Clinical Pharmacology, Seth GS Medical College & KEM Hospital, Mumbai, India
2. Department of Biostatistics, Christian Medical College, Vellore, India

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Presentation Overview

- What is a DCE?
- Study Objectives
- Methods and Study procedures
- Results
- Discussion
- Conclusions

What is a DCE?

An experiment commonly used by companies (FMCG or white goods) for marketing purpose

A quantitative/ Statistical technique that elicits individual preferences regarding any goods or services. E.g., Whether vaccine A or Vaccine B

Preferences can be broken down into separate characteristics – called “attributes” [E.g., safety, effectiveness, etc.,] which vary across different levels (E.g., effectiveness - 50%, 70% or 90%).

Helps in identifying which attribute primarily influence the decision to take one vaccine over the other

Soekhai *et al*. Drug Discov Today. 2019;24(7):1324–31

Objectives

Primary:

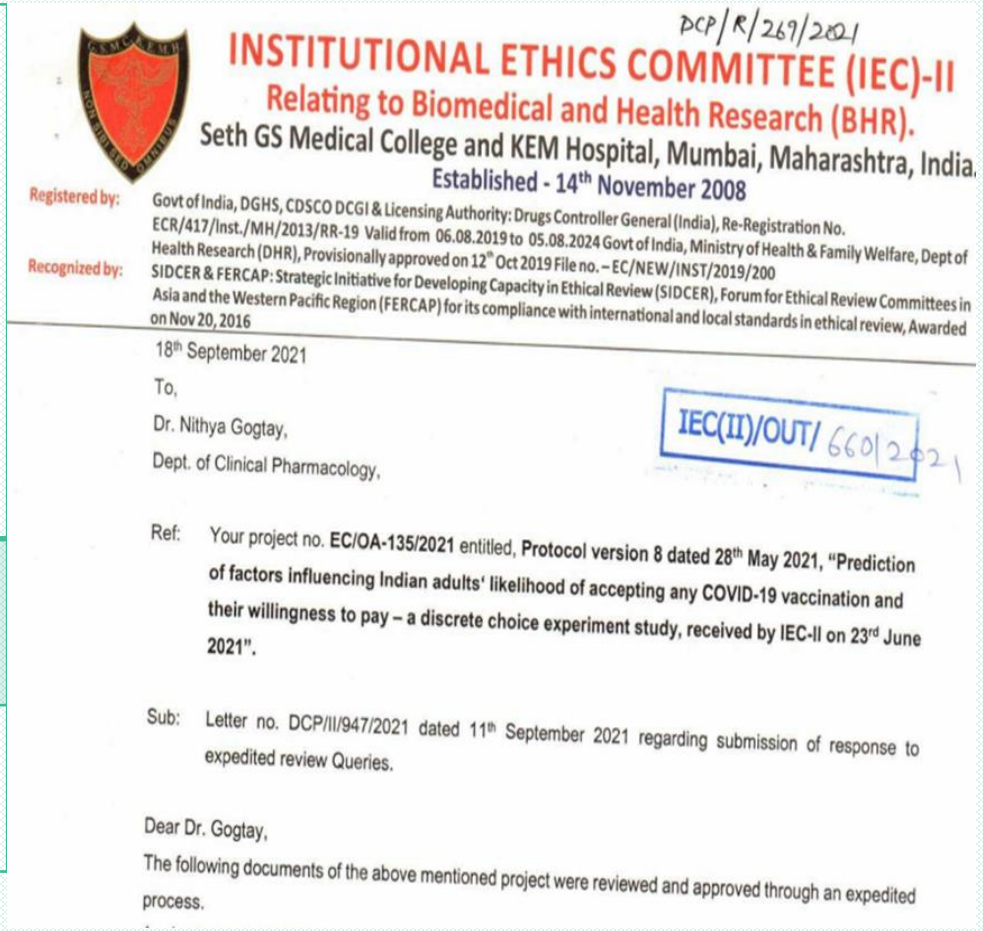
To identify the key attributes of COVID-19 vaccine for its acceptability and their willingness to pay (WTP) for the same in the face of an ongoing pandemic by the general population of India

Secondary:

To estimate the burden and predictors of vaccine hesitancy among the Indian public

Methods - overview

Ethics	IEC Reference Number: EC/OA-135/2021 CTRI Reference Number: CTRI/2021/09/036631. Written informed consent was obtained digitally Conducted in accordance with ICH-GCP, and ICMR ethics guidelines 2017
Study Design	Hybrid cross sectional survey at single time point
Sample size	Total of 10000 participants. No formal sample size estimation as it was a survey



DCP/R/269/2021

INSTITUTIONAL ETHICS COMMITTEE (IEC)-II

Relating to Biomedical and Health Research (BHR).

Seth GS Medical College and KEM Hospital, Mumbai, Maharashtra, India.

Established - 14th November 2008

Registered by: Govt of India, DGHS, CDSCO DCGI & Licensing Authority: Drugs Controller General (India), Re-Registration No. ECR/417/Inst./MH/2013/RR-19 Valid from 06.08.2019 to 05.08.2024 Govt of India, Ministry of Health & Family Welfare, Dept of Health Research (DHR), Provisionally approved on 12th Oct 2019 File no. – EC/NEW/INST/2019/200

Recognized by: SIDCER & FERCAP: Strategic Initiative for Developing Capacity in Ethical Review (SIDCER), Forum for Ethical Review Committees in Asia and the Western Pacific Region (FERCAP) for its compliance with international and local standards in ethical review, Awarded on Nov 20, 2016

18th September 2021

To,

Dr. Nithya Gogtay,

Dept. of Clinical Pharmacology,

IEC(II)/OUT/ 660/2021

Ref: Your project no. **EC/OA-135/2021** entitled, **Protocol version 8 dated 28th May 2021, "Prediction of factors influencing Indian adults' likelihood of accepting any COVID-19 vaccination and their willingness to pay – a discrete choice experiment study, received by IEC-II on 23rd June 2021".**

Sub: Letter no. DCP/II/947/2021 dated 11th September 2021 regarding submission of response to expedited review Queries.

Dear Dr. Gogtay,

The following documents of the above mentioned project were reviewed and approved through an expedited process.

Study Setting

The survey link was live from 02 October 2021 to 07 December 2021 (a little more than two months)

Corresponded to the interim period between the 2nd wave and 3rd wave of the COVID-19 pandemic in India

Predominant variant during these waves in India were Delta and Omicron respectively

Booster Dose was not approved for use then

Phases of the Study

I. Designing of the DCE

- Decide on the attributes and levels under each attribute
- Generate multiple vaccines pairs using various permutations and combinations of these levels
- Each of the vaccine (Vaccine A or Vaccine B) will have all the attributes mentioned but will have just one of the many levels

II. Conduct of the Survey

- Respondents assessed for eligibility to participate
- Survey containing the DCE was answered by the respondents and data analyzed

DCE Designing: Attributes and Levels for a COVID-19 vaccine

Attributes	Levels
Effectiveness	50% protection/70% protection/90% protection
Duration of protection	6 months/1 year/2 years/5 years
Number of Injections	One/Two/Three
Side effects anticipated	No side effects/Injection site pain, redness and swelling for 1-2 days/Fever or body pain for 1-2 days
Risk of severe/serious side effect	1 in one lakh (1 in 1,00,000)/1 in one crore (1 in 1,00,00,000)
Vaccine origin	Indian product/Imported product
Cost per injection	Free/ Rs. 250/Rs. 500/Rs. 1000/Rs. 1500/Rs. 2000 [1USD = 77 INR]

DCE Designing: An example DCE question

Attributes	Vaccine A	Vaccine B
Effectiveness	70%	50%
Duration of protection	2 years	6 months
Number of Injections	One dose	Three doses
Common Side effects anticipated	No common side effects	Fever and body ache 1-2 days
Risk of severe/ serious side effects	One in one crore	One in one lakh
Vaccine origin	India	Imported
Cost per injection	Rs. 500	Rs. 2000

Which among the above vaccines would you prefer?

- Vaccine A
- Vaccine B
- Neither vaccine/No vaccine

DCE Designing: The final construct

Using permutations & combinations of levels, no. of unique vaccine pairs (choice sets) obtainable = 33,57,936

Of which 40 pair wise choice sets were constructed using a D-optimality algorithm using STATA software V 16.0

All choice sets checked for logical plausibility and no manual alterations were done

40 choice sets were randomly assigned to eight blocks, each of which had 5 choice sets; Each participant received one block randomly

Hainmueller *et al*. Polit Anal. 2014;22(1):1–30.

Validity of the DCE

I. Internal validity

- Trap Question
- Hypothetical vaccine pair with one of the vaccine pair unambiguously better than the other pair
- It was fixed for all participant and was the 6th DCE question

II. External Validity

- Opt-out option of neither vaccine
- Respondents not forced to fit their responses as per the given DCE → Generalizability issues

DCE Designing: The Trap Question

Attributes	Vaccine A	Vaccine B
Effectiveness	90%	50%
Duration of protection	5 years	6 months
Number of Injections	One dose	Three doses
Common Side effects anticipated	No common side effects	Fever and body ache 1-2 days
Risk of severe/ serious side effects	One in one crore	One in one lakh
Vaccine origin	India	India
Cost per injection	Free	Rs. 2000

Which among the above vaccines would you prefer?

- Vaccine A
- Vaccine B
- Neither vaccine/No vaccine

Conduct of Survey: Inclusion Criteria

All consenting adults of any sex, age 18 years and above

A citizen of India who has been residing in India at least past 6 months (self-reported).

Survey forms that are filled 100 percent

Conduct of Survey: Exclusion Criteria

Non-resident Indians (NRIs) and overseas citizen of India (OCIs) [despite having a Passport or dual citizenship]

Those who do not answer the trap question correctly

Incompletely filled survey forms [anything less than 100 percent]

Conduct of Survey: Study Procedures

1. Online link circulated in various digital platforms

   Hybrid Mode – Self administered / volunteer administered (kiosk)

2. On clicking the link → access to PIS & ICD document in 6 language choices

   After consent, access to survey

3. Survey had 3 sections (a) Socio-demographic (b) past medical and COVID- 19 related history (c) DCE with 5 hypothetical vaccine pairs + 1 trap question

Conduct of Survey: Statistical Analysis Plan

Socio-demographic characteristics summarized using descriptive statistics

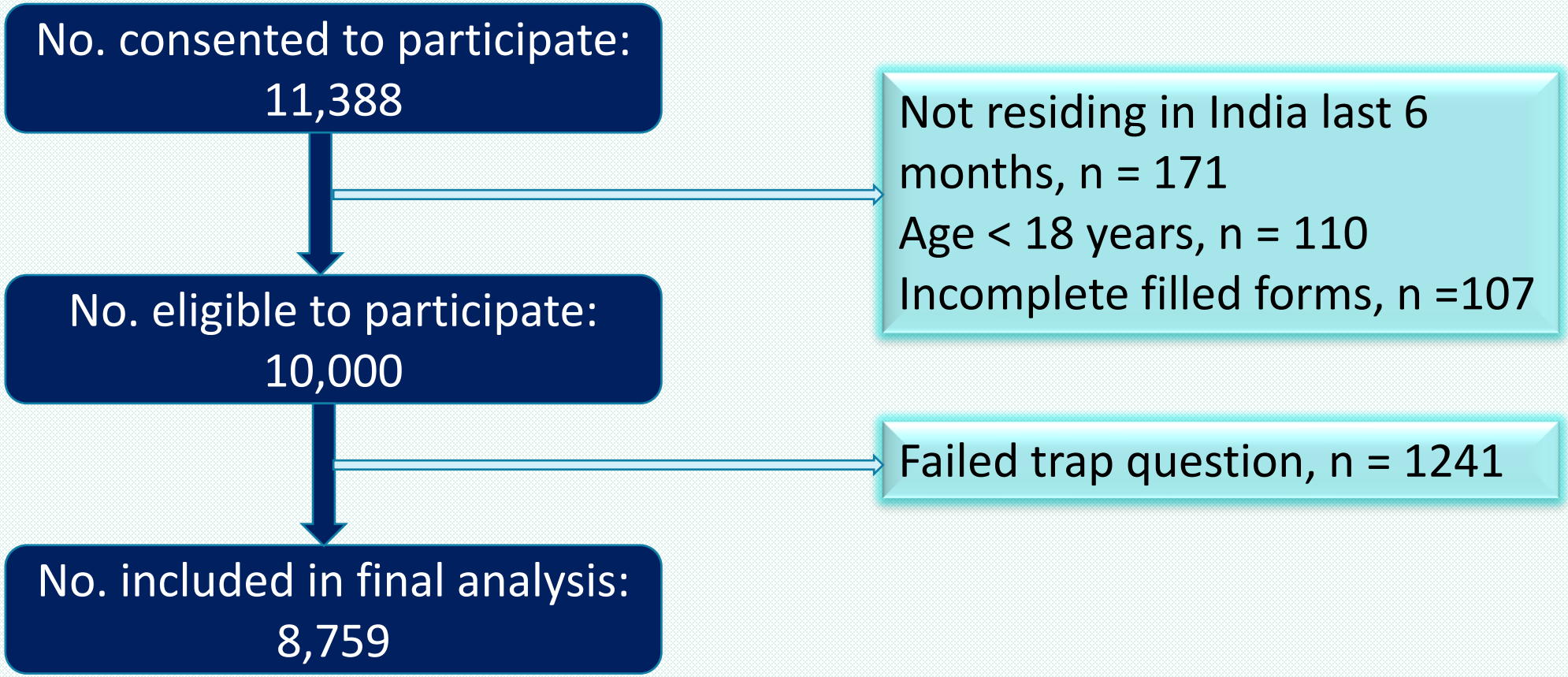
Mixed logit regression (MXL) - to identify the key attributes of COVID-19 vaccine for acceptability

Burden of vaccine hesitancy expressed as proportion of participants choosing the opt-out option

Predictors - univariate and multivariate binary logistic regression

Statistical significance $P < 0.05$

Results: Study Flow Diagram



Results

Demographic characteristics (1/2)

N=8759

	Number	Percentage
Age (Mean ± SD)	36.32 ± 12.61	
Sex		
Male	5346	61.03
Female	3411	38.94
Others	2	0.02
Marital status		
Unmarried	2951	33.69
Separated	76	0.87
Widow/ Widower	153	1.75
Married and living with spouse	5579	63.69
Locality of living		
City	5100	58.23
Town	2441	27.87
Village or Hamlet	1218	13.91
Education		
Illiterate	142	1.62
Primary School (Up to class 5th Pass)	169	1.93
Middle School (Class 6th, 7th & 8th Pass)	266	3.04
High School (Class 9th & 10th Pass)	498	5.69
Higher Secondary (PUC or Class11th & 12th Pass)	1140	13.02
Diploma / Certificate course	1155	13.19
Degree (UG / PG)	3460	39.50
Professional Degree, Lawyer, Chartered accountant, Engineer, PhD degree holder)	1929	22.02

Results

Demographic characteristics (2/2)

Health care worker		
Yes	1296	14.80
No	7463	85.20
If health care worker, role (n=1296)		
Doctor	334	25.77
Nurse	98	7.56
Ward boy/ sanitary worker/ Ward Clerk	43	3.32
Pharmacist	310	23.92
Lab technician	73	5.63
Other role involving patient interaction/ patient samples etc	164	12.65
Office /any other role that does NOT involve interaction with patient/patient samples etc.	274	21.14
Monthly total income of all family members		
Upper Class	312	3.56
Upper Middle Class	447	5.10
Middle Class	1496	17.08
Lower Middle Class	2760	31.51
Lower Class	3744	42.74

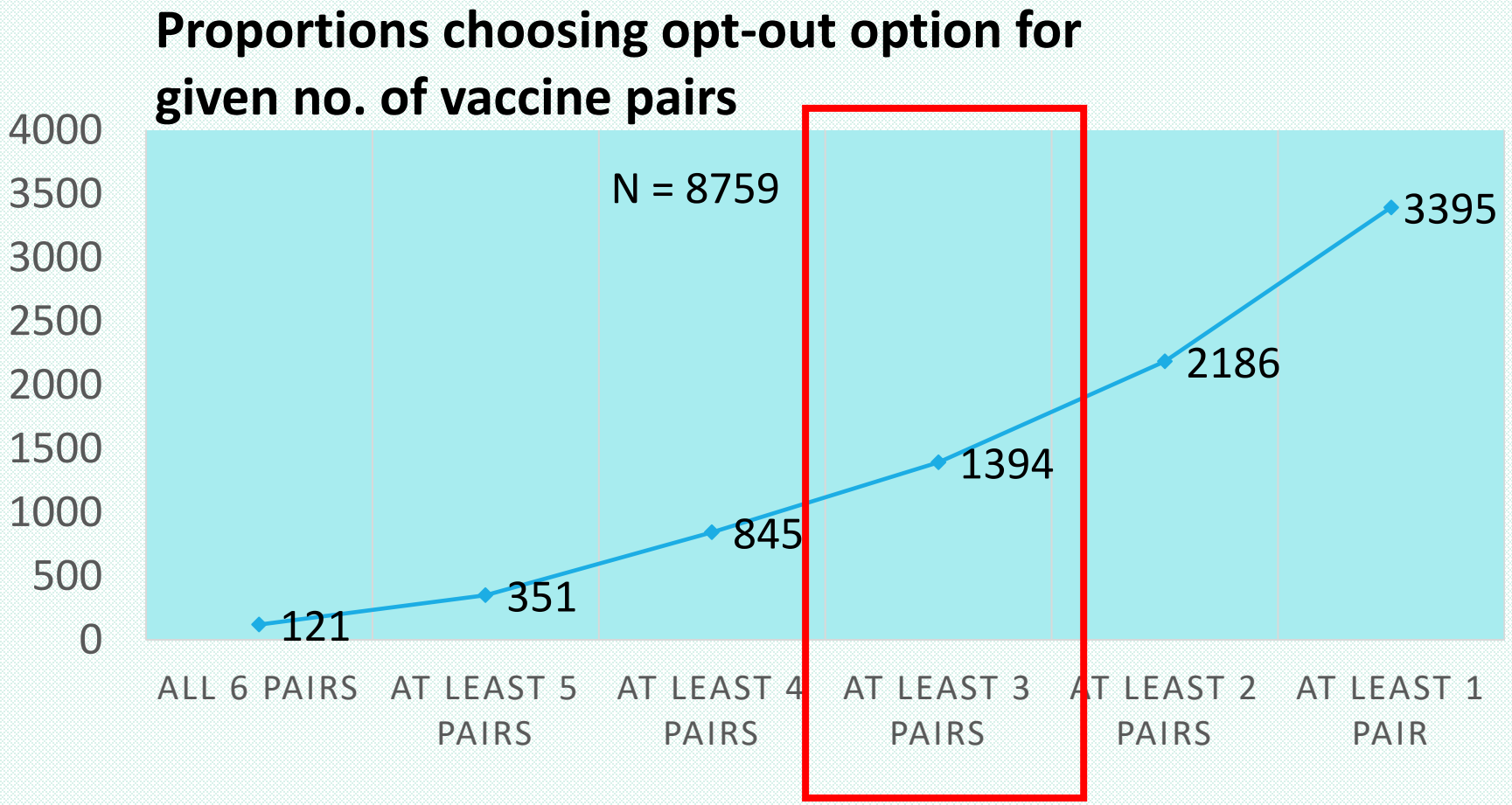
Results

DCE

N=8759

Attributes		Main Effects Model			Willingness to Pay	
		Coefficient (SE)	95% CI	P value	Coefficient (SE)	95% CI
Effectiveness	50% protection	-	-	-	-	-
	70% protection	0.658 (0.017)	0.624 - 0.691	<0.001	1013.065 (29.53)	955.186 - 1070.943
	90% protection	1.005 (0.018)	0.969 - 1.041	<0.001	1548.661 (35.964)	1478.173 - 1619.149
Duration of protection	6 months	-	-	-	-	-
	1 year	0.335 (0.022)	0.292 - 0.378	<0.001	515.634 (34.224)	448.557 - 582.712
	2 years	0.225 (0.02)	0.185 - 0.265	<0.001	346.720 (31.833)	284.329 - 409.112
	5 years	0.381 (0.02)	0.342 - 0.42	<0.001	586.542 (31.558)	524.69 - 648.394
Number of Injections	Three times	-	-	-	-	-
	One time	0.049 (0.017)	0.015 - 0.082	0.004	75.289 (26.436)	23.474 - 127.103
	Two times	0.045 (0.017)	0.011 - 0.079	0.009	69.370 (26.735)	16.971 - 121.769
Vaccine origin	Imported	-	-	-	-	-
	Indian	0.233 (0.012)	0.210 - 0.257	<0.001	359.560 (19.303)	321. 728 - 397.392
Common side effects anticipated	No side effects	-	-	-	-	-
	Injection site pain redness and swelling for 1-2 days	-0.123 (0.017)	-0.155 - (-0.09)	<0.001	-188.970 (25.721)	-239.382 - (-138.558)
	Fever, body pain for 1-2 days	-0.073 (0.017)	-0.106 - (-0.04)	<0.001	-112.751 (26.196)	-164.094 - (-61.407)
Risk of severe/serious side effect	One in one crore (10 million)	-	-	-	-	-
	One in one lakh (100 thousand)	-0.063 (0.012)	-0.087 - (-0.039)	<0.001	-96.488 (18.878)	-133.487 - (-59.488)
Cost per injection		-0.0006 (0.00001)	-0.0007 - (-0.0006)	<0.001	-	-

Results: Burden of Vaccine Hesitancy



Proportions
All 6 pairs: 1.38%
≥ 3 pairs: 15.92%
≥ 1 pair: 38.76%

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Discussion (1/2)

Our DCE suggested, highly effective, indigenous vaccine with lower side effects → most preferred. Cost least important attribute

Confirms the recently published results of a small study (N=1371) conducted in 5 Indian states by Bansal *et al*.

Effectiveness as single most important attribute of COVID-19 vaccine also reported from other countries such as the UK, USA and China

1. McPhedran *et al*. Econ Lett. 2021;200:109747
2. Dong *et al*. Heal Expect. 2020;23(6):1543–78
3. Kreps *et al*. JAMA Netw open. 2020;3(10):e2025594.

Discussion (2/2)

Cost of the vaccine was a significant but least important attribute → Similar to the report by Dong *et al*. from China

Burden of vaccine hesitancy (chose opt-out option for ≥ 3 / 6 pairs) = 15.92% → similar trend reported a decade ago during H1N1 pandemic (2009)

Despite a decade roll-by since last pandemic and despite a strikingly high mortality rate as compared to swine flu, issue of vaccine hesitancy unaddressed but vaccination made mandatory → ?autonomy

1. Dong *et al*. Heal Expect. 2020;23(6):1543–78
2. Schmid *et al*. PLoS ONE. 2017. 2005–2016 p

Strengths

Large Sample size (Final analyzed n = 8759)

Representative of entire nation (28 states and 8 union territories)

India is a nation of diverse cultures/ traditions and geographical topography → generalizable to other LMICs

Limitations

Non-probability sampling in a hybrid mode → unable to ascertain response rate

Although vaccine pairs were hypothetical → respondents could have linked one or more of the given attributes to the existing commercially available COVID-19 vaccines → Decision influenced based on other attributes not listed in this study

Conclusions

Most important attributes that influence decisions were effectiveness, duration of protection & Indian origin vaccines

The significant predictors of vaccine hesitancy were male sex, upper and middle socio-economic class, and presence of comorbidities such as diabetes, heart problems or asthma.

When in a pandemic, and while seeking to achieve close to 100% vaccination, understanding these individual issues becomes an ethical imperative

Acknowledgements

- The Dean, and Dept. of Clinical Pharmacology, Seth GSMC & KEMH, Mumbai
- Indian Council of Medical Research – Product Development Centre (PDC) – Partial funding
- Research Society, Seth GSMC & KEMH, Mumbai – Partial funding
- SIRO ClinPharm – Questionnaire development in Survey Monkey
- Klinera India – Data collection
- Vaividhya Foundation, New Delhi, India – Data Collection