Meta-Analysis On Effectiveness Of Janssen Vaccination In Prevention Of Corona Virus Disease In Some Countries

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***Abstract* — The reported outcome of the COVID-19, classified by World Health Organization (WHO) as pandemic, was very disruptive. This study was intended to evaluate the effectiveness of Janssen vaccination in the prevention of COVID-19 in three different world regions namely: North America, South America and Africa using a comprehensive meta-analysis version 3 software. Data used for this research was secondary data sourced on 1st November 2021, via google search engine as reported from Fact sheet for healthcare providers administering vaccine on emergency use authorization of the Janssen covid-19 vaccine to prevent COVID-19. Samples were obtained from the laboratory for analysis on 12th February 2021.Our findings from the results using fixed and random effect models show a summery effect of 0.000 indicating that the Janssen vaccination, based on the studies included in the meta-analysis, neither favored mortality nor survival. I-square statistic is zero indicating the total absence of bias. The variant of the Covid-19 as at the time the vaccine was tried may have been overwhelming to be put under control, considering the deadly nature of the pandemic. However, the mere fact that the results do not favour mortality, is a testament to the theory that getting vaccinated could mean milder symptoms in patients.**

Keywords – *Meta-analysis, COVID-19, Risk, Janssen.*

I. INTRODUCTION

A highly transmissible and virulent coronavirus known as syndrome coronavirus 2 (SARS-CoV-2) developed in late 2019 and was followed by a pandemic of acute respiratory sickness known as COVID-19 (Harcourt, 2020).

There were approximately 326 million confirmed COVID-19 cases and over 5.5 million fatalities globally as of January 1, 2022, impacting 192 nations and regions (Center, 2022). Vaccines that can protect humans from viral infections in an efficient and long-term way, according to (Jeroen Luyten, 2016), have played a significant role in human history against infectious illnesses. As the COVID-19 pandemic rages on, fostering the development of effective vaccinations is crucial to preventing more illness and mortality, as well as, ideally, limiting and even stopping COVID-19's global expansion (Tregoning J. S., 2021).

The US Food and Drug Administration (FDA) licensed an mRNA vaccine (Pfizer-BioNTech/Comirnaty) as a 2-dose series for symptomatic COVID-19 prophylaxis in people aged 16 and above on August 23, 2021. This vaccination can also be used to prevent COVID-19 in people aged 12 to 15 years old, according to an Emergency Use Authorization (EUA). Under an EUA, a second mRNA vaccine (Moderna) and a recombinant, replication-incompetent adenovirus serotype 26 (Ad26) vector vaccine (Janssen vaccine [Johnson & Johnson]) are approved for use in people over the age of 18. Both mRNA vaccines are also approved for an extra dosage to be given to immuno-compromised people. When people are 2 weeks after receiving the second dosage of a 2-dose series (mRNA vaccines) or 2 weeks after receiving a single-dose vaccination of (Janssen vaccine), they are considered completely immunized (Anonymous, Penn Medicine News, 2021).

Clinical studies with COVID-19 vaccines approved for emergency use in the United States (Pfizer-BioNTech, Moderna, and Janssen [Johnson & Johnson]) show great effectiveness against symptomatic sickness, including moderate to severe illness (Heidi L. Moline, 2021). Real-world studies of COVID-19 vaccination efficacy, in addition to clinical trials, are crucial in directing vaccine

policy and establishing vaccine confidence, particularly among populations at higher risk for more severe COVID-19 disease, such as older individuals. Data on 7,280 patients from the COVID-19–Associated Hospitalization Surveillance Network (COVID-NET) were analyzed with vaccination coverage data from state immunization information systems (IISs) for the COVID-NET catchment area to determine the real-world effectiveness of the three currently authorized COVID-19 vaccines among persons aged 65 years from February 1 to April 30, 2021 (Heidi L. Moline, 2021). Approximately 4.8 million persons for Pfizer-BioNTech, 96 percent for Moderna, and 84 percent for Janssen vaccine products were efficacious in reducing COVID-19 associated hospitalization among people aged 65–74 years. Pfizer-BioNTech reported 91 percent effectiveness of complete immunization in reducing COVID-19 associated hospitalization in individuals aged 75 years, while Moderna reported 96 percent, and Janssen vaccination products scored 85 percent. COVID-19 vaccinations that are now approved in the United States are quite successful at avoiding COVID-19 related hospitalizations in the elderly. Given the strong efficacy of COVID-19 vaccinations among older persons, efforts to boost immunization coverage in this age group are crucial for lowering the risk of COVID-19–related hospitalization (Heidi L. Moline, 2021).

JANSSEN VACCINE/AD26.COV2.S

This is a non-replicating recombinant human adenovirus type 26 that carries the full-length SARS-CoV-2 S protein and generates an anti-SARS-CoV-2 antibody response. Antibody against the S protein stops the SARS-CoV-2 virus from invading type 2 alveolar cells in the lungs, lowering infection severity and morbidity (Jerome Custers, 2021).

On the negative, in an epidemic situation, as with current pandemic, vaccine manufacture is likely to be slower since these facilities must meet biosafety level 2 requirements. Furthermore, there is the possibility of pre-existing immunity to viral vectors, which would reduce the vaccine's efficacy. Oxford/AstraZeneca was able to overcome this obstacle by employing the Chimpanzee adenovirus (ChAdOx1), which is a non-human adenovirus that lacks pre-existing immunity in humans (Van Doremalen N., 2020)

JOHNSON & JOHNSON (J&J)/JANSSEN COVID-19 VACCINE INGREDIENTS

According to (Rachael Zimlich, 2022), the COVID-19 vaccination from J&J/Janssen contains a portion of a modified virus that is not the COVID-19 virus. The vector virus is the name given to this modified virus. COVID-19 cannot be caused by the vector virus since it cannot proliferate. This vector virus instructs the body's cells to produce an immunological response. This reaction helps you avoid being ill with COVID-19 in the future. Following an immune reaction, the body discards all vaccination components, just as it would any information that cells no longer require. This is a regular element of the body's operation. All COVID-19 vaccines are made with as few chemicals as feasible and only the amount of each ingredient that is required. Almost all of the constituents of COVID-19 vaccines – fats, sugars, and salts – are also found in numerous meals.

ADVERSE EVENTS OF JANSSEN VACCINATION

1) 1. FAINTING AFTER VACCINATION

After receiving any vaccination, you may experience fainting (syncope) and other anxiety-related symptoms such as fast breathing, low blood pressure, numbness, or tingling (Rachael Zimlich, 2022). Although rare, these occurrences are not unheard of, and they are usually minor. There were 653 reports of fainting events (fainting and near-fainting) among roughly 8 million doses of J&J/Janssen COVID-19 vaccine delivered in the United States in March and April 2021, according to data from (Rachael Zimlich, 2022). This equates to around 8 fainting occurrences per 100,000 doses of the J&J/Janssen COVID-19 vaccine administered. During the specified 15-minute delay after immunization, these incidents happened. It's unclear if these occurrences were caused by the vaccination or by anxiety, which might be connected to previous fears about needles or injections that some individuals who elected to obtain the one-dose J&J/Janssen COVID-19 vaccine may have. In 2019–2020, the rate of fainting following flu vaccination was 0.05 per 100,000 doses.

2. THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME (TTS)

TTS is an uncommon yet dangerous side effect that results in blood clots in large blood arteries and low platelet counts (blood cells that help form clots). More than 18.0 million doses of the J&J/Janssen COVID-19 vaccine have been administered in the United States as of January 20, 2022. The CDC and FDA found 57 verified cases of patients who received the J&J/Janssen COVID-19

vaccination and had TTS later (Brit Long, 2021). TTS caused or was directly attributable to nine deaths, according to the CDC, following J&J/Janssen COVID-19 vaccine. Women between the ages of 30 and 49 should be especially mindful of the increased risk of this uncommon adverse occurrence.

3. GUILLAIN-BARRÉ SYNDROME (GBS)

GBS is an uncommon disease in which the immune system attacks nerve cells, resulting in muscular weakness and paralysis. The majority of people recover completely from GBS, but others have lifelong nerve damage. As of January 20, 2022, there were roughly 302 early reports of GBS in VAERS after more than 18.0 million J&J/Janssen COVID-19 vaccination doses were given (MedlinePlus, 2022). These instances have primarily been recorded approximately 2 weeks after immunization, and they have mostly been documented in men, with many of them being in their 50s and older. The rate of GBS within the first 21 days after J&J/Janssen COVID-19 vaccination was found to be 21 times greater than after Pfizer-BioNTech or Moderna COVID-19 immunization (MedlinePlus, 2022).

Pfizer-BioNTech and Moderna COVID-19 vaccines received Emergency Use Authorizations (EUAs) from the FDA in December 2020, while Janssen (Johnson & Johnson) COVID-19 vaccine received a EUA in February 2021. The Advisory Committee on Immunization Practices (ACIP) published interim recommendations for vaccine usage following each EUA; presently, Pfizer-BioNTech is approved and recommended for children aged 12 to 18, while Moderna and Janssen are authorized and recommended for children aged 18 to 20 (Anonymous, FDA Authorizes Pfizer-BioNTech Covid-19 Vaccine for Emergency use in Children 5 through 11 Years of Age, 2021).

Both the Pfizer-BioNTech and Moderna COVID-19 vaccines are mRNA-based, whereas the Janssen COVID-19 vaccine is a recombinant replication-incompetent adenovirus-vector vaccine that is given as a single dose. COVID-19 vaccine had been administered to at least 187 million people in the United States as of July 22, 2021 (Heidi L. Moline, 2021) and close safety observation has revealed that major adverse events following COVID-19 immunization are uncommon.

II. METHODOLOGY

This research is a meta-analysis on effectiveness of Janssen vaccination in the prevention of COVID-19 in the United States of America (United States), Latin America (Brazil) and Southern Africa (South Africa).

The data used in this research work was a secondary data sourced on the 1st November 2021 as reported from Fact sheet for Healthcare providers administering vaccine on emergency use authorization of the Janssen covid-19 vaccine to prevent coronavirus disease 2019 (COVID-19) conducted in the United States of America (United States), Latin America (Brazil) and Southern Africa (South Africa) (www.jassenCOVID19Vaccine.com/EUA-factsheet). The data was analyzed using Comprehensive Meta-Analysis version 3.

Base on the objectives of the study, the methods employed for analyzing the data was Fixed and Random effects Meta-analysis (MA) developed by (Michael Borenstein, 2009) and utilized in (Mohammed Rilwan, 2021). The data were analyzed using comprehensive mete-analysis program, version 3.

MODELLING OF OBSERVED EFFECT

The model for observed effect for any study is given by the population mean plus the sampling error in that study. thus is:

$$Y_i = \theta + \varepsilon_i \quad (1)$$

Where:

Y_i is the observed effect size; $\theta = \mu + \zeta_i$ and is the population mean; ε_i is the sampling error in the study

ESTIMATION OF EFFECT SIZES

The effect sizes are standardized mean differences and can be arrived at by dividing the mean difference in each study by that study's standard deviation to create an index.
The standardized mean difference can be estimated using the formula:

$$d = \frac{\bar{X}_1 - \bar{X}_2}{S_{within}} \quad (2)$$

where
$\bar{X}_1$ and $\bar{X}_2$ are the sample means in the two groups; S_{within} is the within-groups standard deviation, pooled across groups,

$$S_{within} = \sqrt{\frac{(n_1-1)S_1^2+(n_2-1)S_2^2}{n_1+n_2-2}} \quad (3)$$

Where
n_1 and n_2 are the sample sizes in the two groups, and S_1 and S_2 are the standard deviations in the two groups.
The variance of d is given (to a very good approximation) by:

$$V_d = \frac{n_1-n_2}{n_1 n_2} + \frac{d^2}{2(n_1+n_2)} \quad (4)$$

Where,
The first term on the right of the equals sign reflects uncertainty in the estimate of the mean difference and the second reflects uncertainty in the estimate of S_{within}
The standard error of d is the square root of V_d:

$$SE_d = \sqrt{V_d} \quad (5)$$

PERFORMING A FIXED-EFFECT META-ANALYSIS

In order to obtain the most precise estimate of the population effect (to minimize the variance) we compute a weighted mean, where the weight assigned to each study is the inverse of that study's variance. The weight assigned to each study in a fixed-effect meta-analysis is:

$$W_i = \frac{1}{V_{Y_i}} \quad (6)$$

Where:

where V_{Y_i} is the within-study variance for study (i). The weighted mean (M) is then computed as:

$$M = \frac{\sum_{i=1}^{k} W_i Y_i}{\sum_{i=1}^{k} W_i} \quad (7)$$

that is, the sum of the products WiYi (effect size multiplied by weight) divided by the sum of the weights.

The variance of the summary effect is estimated as the reciprocal of the sum of the weights, or

$$V_M = \frac{1}{\sum_{i=1}^{k} W_i} \quad (8)$$

and the estimated standard error of the summary effect is then the square root of the variance,

$$SE_M = \sqrt{v_M} \quad (9)$$

Then, 95% lower and upper limits for the summary effect are estimated as

$$LL_M = M - 1.95 \text{ X } SE_M \quad (10)$$

and

$$LL_M = M + 1.95 \text{ X } SE_M \quad (11)$$

Finally, a Z-value to test the null hypothesis that the common true effect θ is zero, can be computed using

$$Z = \frac{M}{SE_M} \quad (12)$$

For a one-tailed test the p-value is given by

$$P = 1 - \phi(\pm/Z/) \quad (13)$$

where we choose '+' if the difference is in the expected direction and '–' otherwise, and for a two-tailed test by

$$P = 2[1 - \phi(\pm/Z/)] \quad (14)$$

where $\phi(Z)$ is the standard normal cumulative distribution.

COMPUTATION OF Q-STATISTIC

The first step in partitioning the variation is to compute Q defined as:

$$Q = \sum_{i=1}^{k} W_i Y_i^2 - \frac{(\sum_{i=1}^{k} W_i Y_i)^2}{\sum_{i=1}^{k} W_i} \quad (15)$$

where Wi is the study weight (1/Vi), Yi is the study effect size, and k is the number of studies. In words, we compute the deviation of each effect size from the mean, square it, weight this by the inverse-variance for that study, and sum these values over all studies to yield the weighted sum of squares (WSS), or Q.

with a degree of freedom (df) as:

$$df = k - 1 \quad (16)$$

where k is the number of studies.

ESTIMATING TAU-SQUARED (τ^2)

The parameter tau-squared (τ^2) is defined as the variance of the true effect sizes. In other words, if we had an infinitely large sample of studies, each, itself, infinitely large (so that the estimate in each study was the true effect) and computed the variance of these effects, this variance would be τ^2.

Since we cannot observe the true effects, we cannot compute this variance directly. Rather, we estimate it from the observed effects, with the estimate denoted T^2. To yield this estimate we start with the difference (Q – df) which represents the dispersion in true effects on a standardized scale. We divide by a quantity (C) which has the effect of putting the measure back into its original metric and also of making it an average, rather than a sum of squared deviations. Concretely,

$$T^2 = \frac{Q - df}{C} \quad (17)$$

$$C = \sum_{i=1}^{k} W_i - \frac{\sum_{i=1}^{k} W_i^2}{\sum_{i=1}^{k} W_i} \quad (18)$$

If Q<df. In this case, T^2 is simply set to zero.

If Q>df then T^2 will be positive, and it will be based on two factors. The first is the amount of excess variation (Q–df), and the second is the metric of the effect size index.

To estimate the standard deviation, we simply take the square root of T^2,

$$T = \sqrt{T^2} \quad (19)$$

THE I^2-STATISTIC

I^2 is the ratio of true heterogeneity to total variation in observed effects, a kind of signal to noise ratio. The qualities that make it useful for this purpose are that it is not sensitive to the metric of the effect size, and it is not sensitive to the number of studies.

It is important to understand that T^2 and T (on the one hand) and I^2 (on the other) serve two entirely different functions. The statistics T^2 (and T) reflect the amount of true heterogeneity (the variance or the standard deviation) while I^2 reflects the proportion of observed dispersion that is due to this heterogeneity.

I^2 reflects only the proportion of variance that is true, and says nothing about the absolute value of this variance and it is computed as:

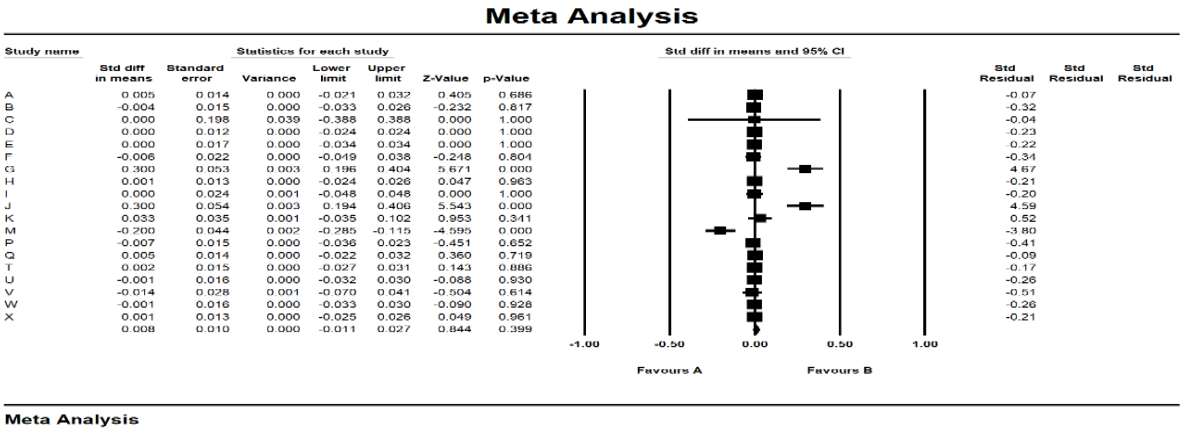
$$I^2 = \left(\frac{Q - df}{Q}\right) \text{ X } 100\% \quad (20)$$

The scale of I^2 has a range of 0 – 100%, regardless of the scale used for the meta-analysis itself.

II. Applications

Table 1 shows the information about the meta-analysis conducted on the Samples obtained from the laboratory for analysis on 12th February 2021 to evaluate the effectiveness of Janssen vaccination in the prevention of COVID-19 in three different world regions namely: North America, South America and Africa.

Table 1: Forest plot showing the effectiveness of Janssen vaccination in the prevention of COVID-19



III. Conclusion

Based on the samples obtained from the laboratory for analysis on 12th February 2021. Our findings from the results using fixed and random effect models show a summery effect of 0.000 indicating that the Janssen vaccination, based on the studies included in the meta-analysis, neither favored mortality nor survival. I-square statistic is zero indicating the total absence of bias. The variant of the Covid-19 as at the time the vaccine was tried may have been overwhelming to be put under control, considering the deadly nature of the pandemic. However, the mere fact that the results do not favour mortality, is a testament to the theory that getting vaccinated could mean milder symptoms in patients.

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