Sheba Ivermectin Project (SIP)

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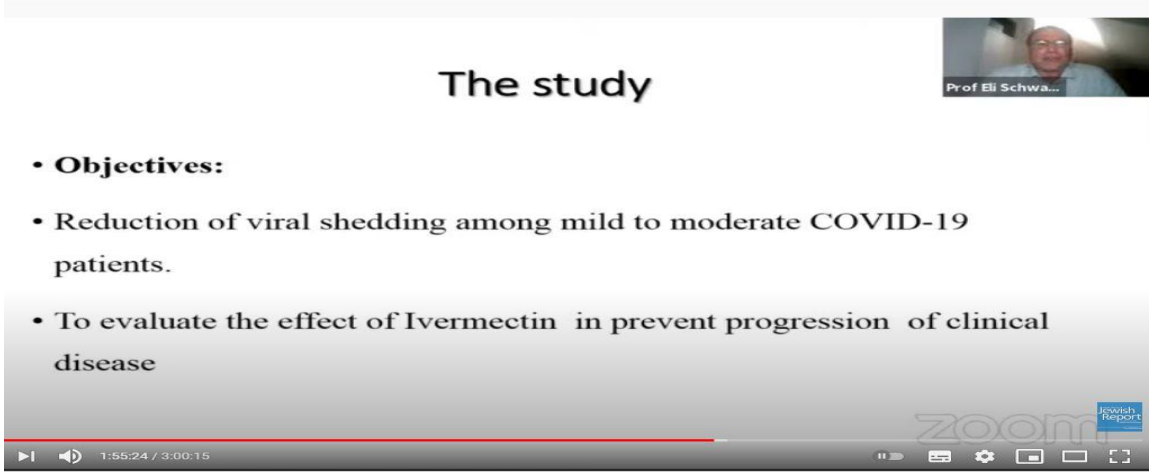
These summary notes are a draft on 14 February 2021 and are taken from a pre-publication video discussion by Prof. Eli Schwartz on 12 February 2021 and are not the official notes.
Please see the video yourself, which starts after 1 hour and 49 minutes at https://www.youtube.com/watch?v=amflCYOsF34&ab_channel=TheSAJewishReport.

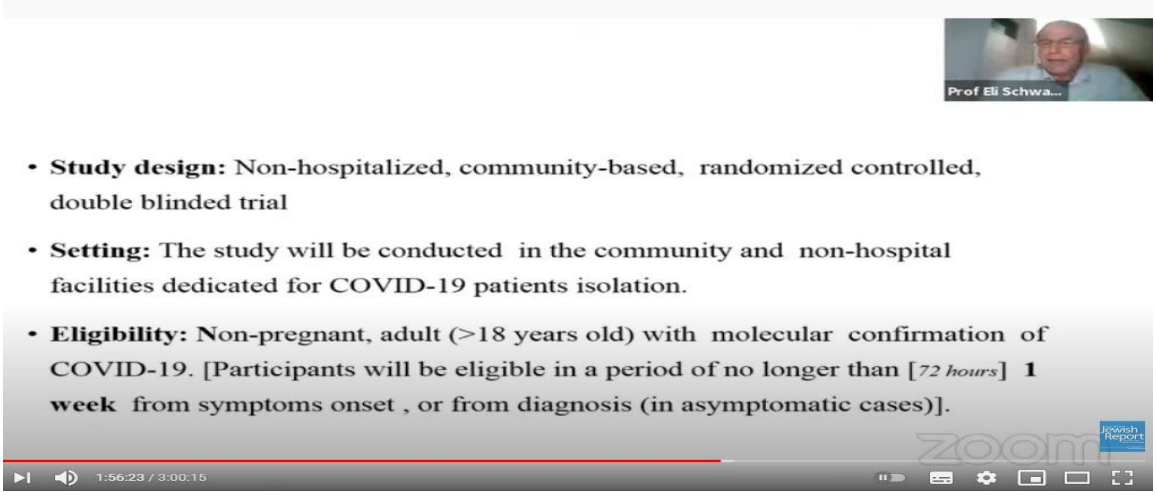
Although previous studies were done in third world countries, Prof Eli Schwartz led a study in Israel of Ivermectin vs. Placedo in non-hospitalized patients with COVID-19. This report is probably the first double-blind RDC study to be published.

Although an excellent drug Ivermectin is not well known and is not registered in many Western countries, including Israel, it is possibly the reason for the doctors' hesitation with Ivermectin. There is research worldwide on Ivermectin against certain parasites.
Ivermectin is one of only 6 Nobel Prizes for medicine for its effect against parasitic diseases. With the Coronavirus epidemic, individuals started studies, the first in Australia, which showed high activity against the coronavirus, which triggered more work on its efficacy, not only in in-vitro studies.

This study was Ivermectin vs. Placebo treatment in non-hospitalized patients with Covid-19 – A double-blind, randomized controlled trial, looking only at mild patients.
The Objectives were a study that reduced viral shedding among mild to moderate COVID-19 patients and evaluated the effect of Ivermectin in preventing clinical disease, registered Clinical trials Identifier NCT04429711



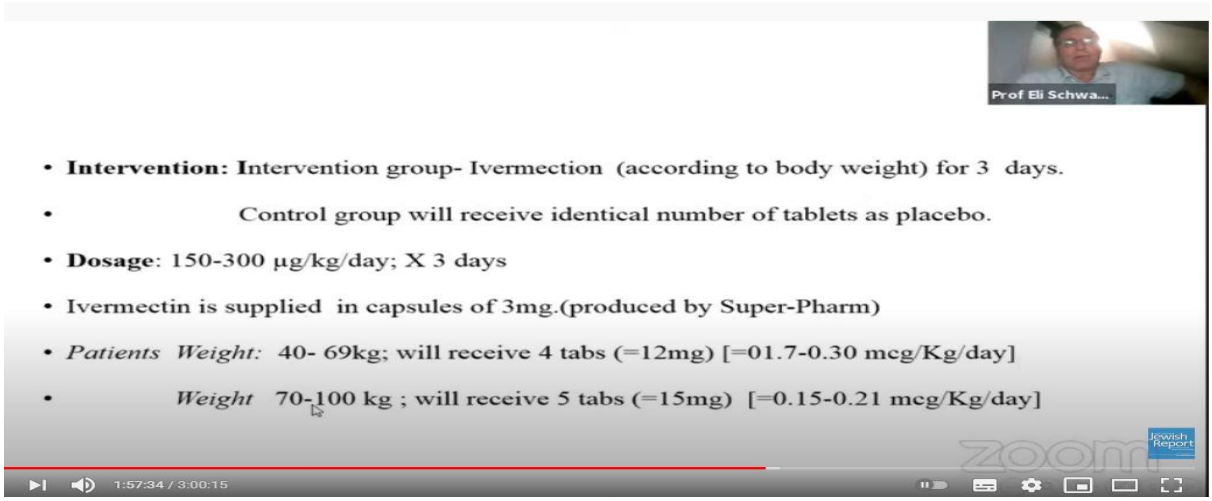
The study concentrated on patients who were not severe, not hospitalised, not oxygenated at the beginning of the disease to show that in these patients, the Ivermectin would slow viral shedding and to prevent the progression of this mild to severe disease. Prof Eli Schwartz started planning the study in March 2020 when far less was known about the disease. Since only a small fraction progress to severe disease, they cannot answer the second question conclusively.



Study Design and Setting

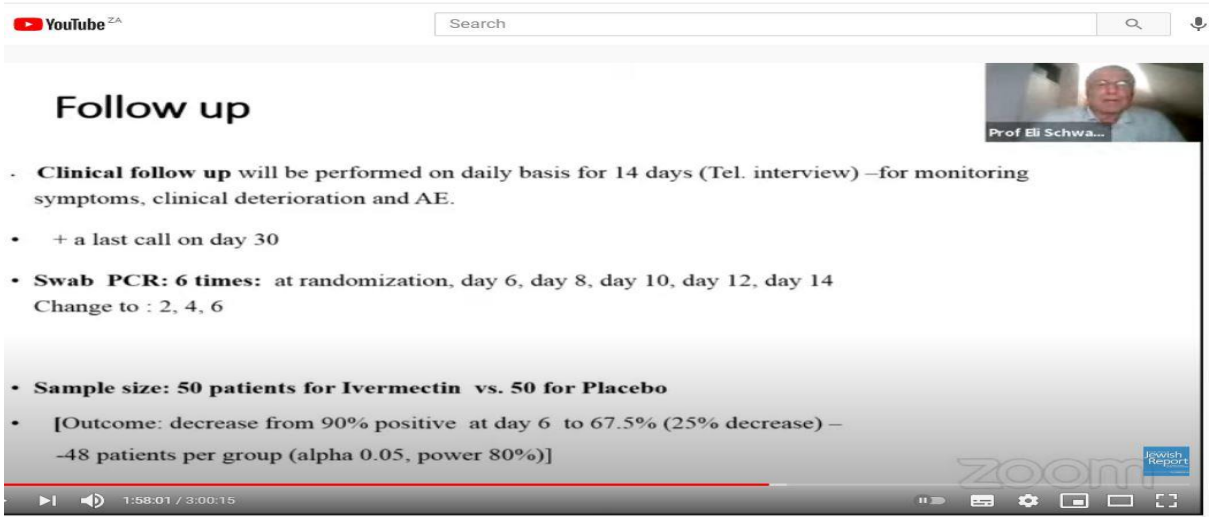
• **Study design:** Non-hospitalized, community-based, randomized controlled, double-blinded trial
• **Setting:** In Israel, patients who could not be isolated at home were being moved to dedicated hotels, so from the manpower saved, we concentrated on these isolated patients. Therefore, the study was to be conducted in the community and non-hospital facilities dedicated to isolation for COVID-19 patients.
• **Eligibility:** Non-pregnant, adult (> 18 years old) with molecular confirmation of Covid-19. [participants will be eligible in a period of no longer than [72 hours,] 1 week from symptoms onset, or diagnosis (in asymptomatic cases)]. For asymptomatic cases, the intention was to check how quickly the virus disappeared in each group.

Ivermectin Dosage



• **intervention:** Intervention group- Ivermectin (according to body weight) for 3 days.
• Control group will receive identical number of tablets as a placebo.
• **Dosage**: 150-300 ug/kg/day; X 3 days
• Ivermectin is supplied in capsules of 3mg. (produced by Super-Pharm)
• *Patients Weight:* 40- 69kg: will receive 4 tabs (-12mg) [=01.7-0.30 mcg/IKg/day]
• *Weight* 70-100 kg: will receive 5 tabs (=15mg) [=0.15-0.21 mcg/Kgday]

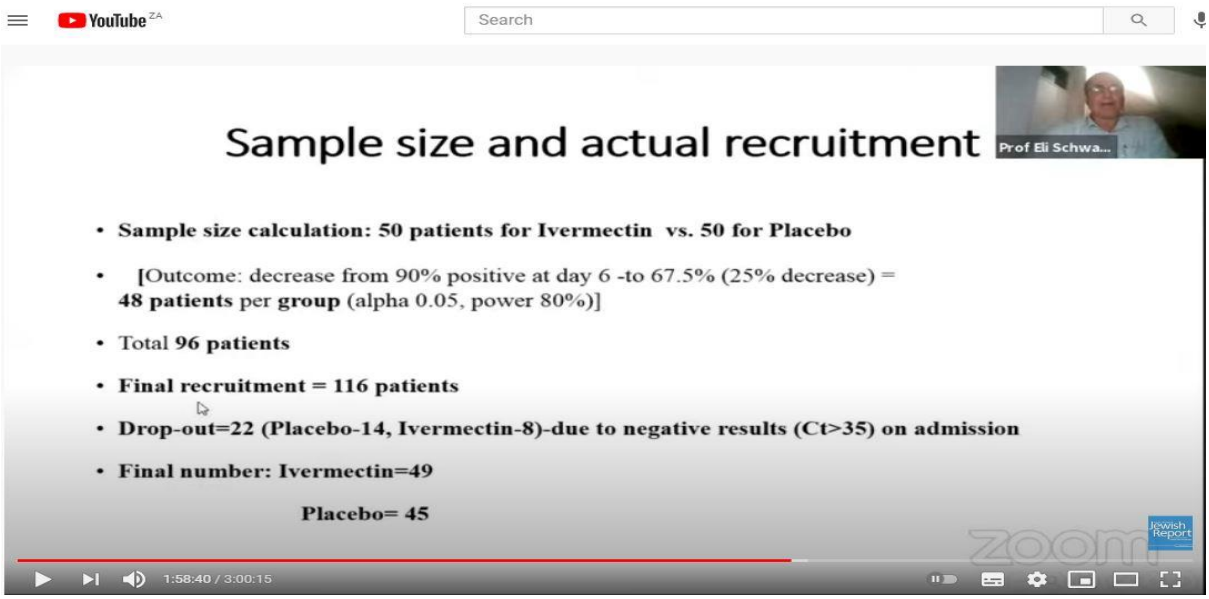
They were completely blinded as the placebo looks the same as the Ivermectin. The usual ivermectin dosage is once only, but it was given for 3 days in the trial.



Follow up

• **Clinical follow-up** originally planned to be performed daily for 14 days (Tel interview) - for monitoring symptoms, clinical deterioration, and AE.
• + a last call on day 30
• **Swab PCR: 6 times**: at randomisation, day 6, day 8, day 10. day 12. day 14
Which was changed to days: 2, 4, 6 in the trial.
• **Planned sample size was 50 patients for Ivermectin vs. 50 for the Placebo**
• [Planned outcome: decrease from 90% positive at day 6 to 67.5% (25% decrease) - 48 patients per group (alpha 0.05, power 80%)]

The idea was to see whether after 6 days there was any difference between the groups and hoping for a 25% decrease after 6 days.



Sample size and actual recruitment

• Sample size calculalion: 50 patients for Ivermectin vs. 50 for Placebo

• [Outcome: decrease from 90% positive at day 6 to 67.5% (25% decrease) = 48 patients per group (alpha 0.05. power 80%)]

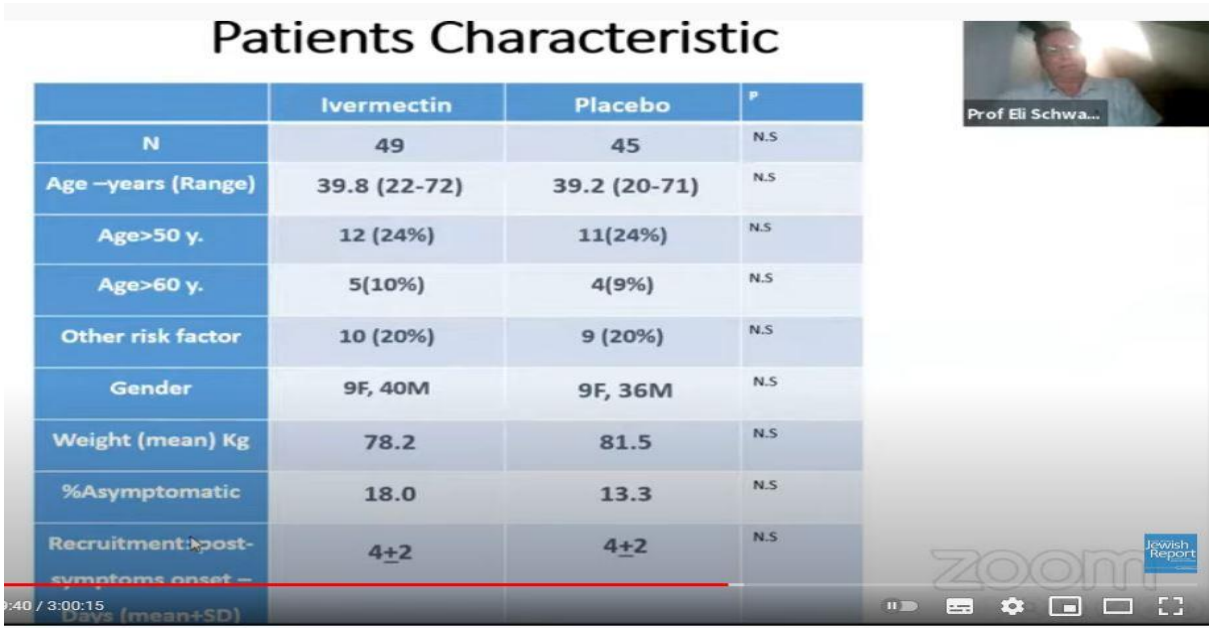
• Total **96 patients**

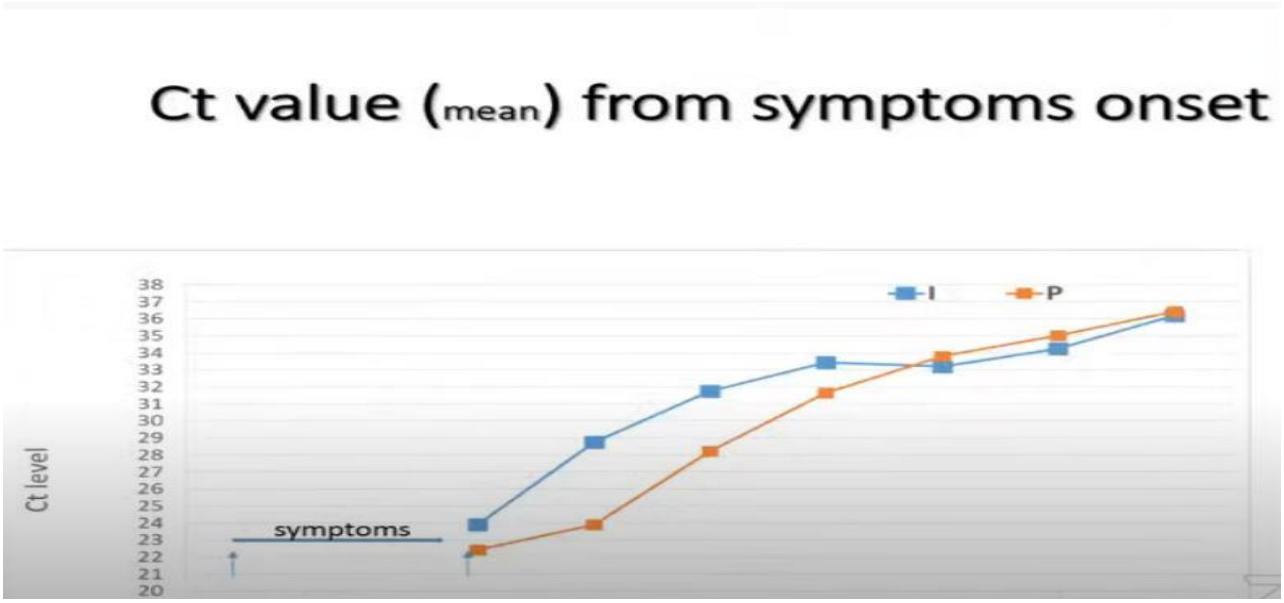
• Final recruilment = 116 patieots

• **Drop-out=22 (Placebo-I4, Ivermeclin-8}-due to negative resulls (Ct>35) on admission**

• **Final number: Ivermectin = 49 Placebo = 45**

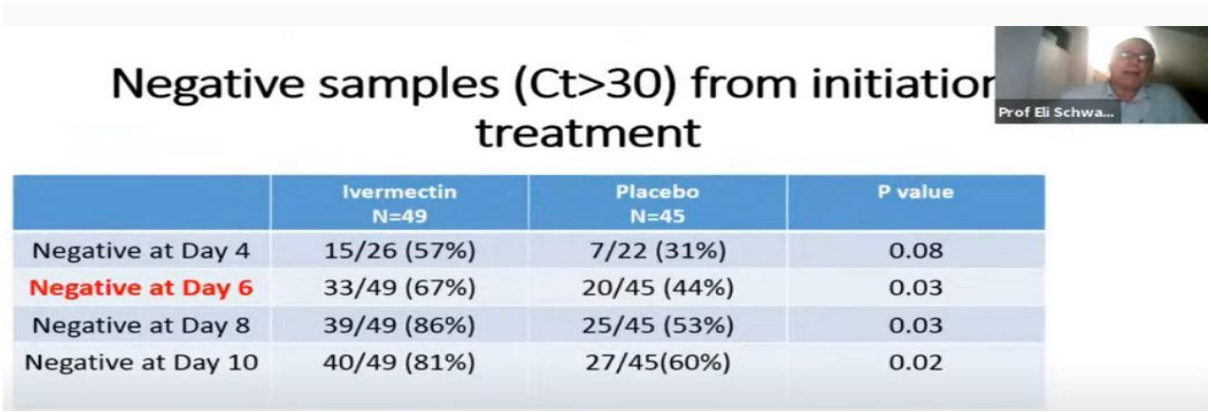
Drop out as those were too late in the disease. Tried to get patients as early as possible, and the average was 4 days after the beginning of symptoms.





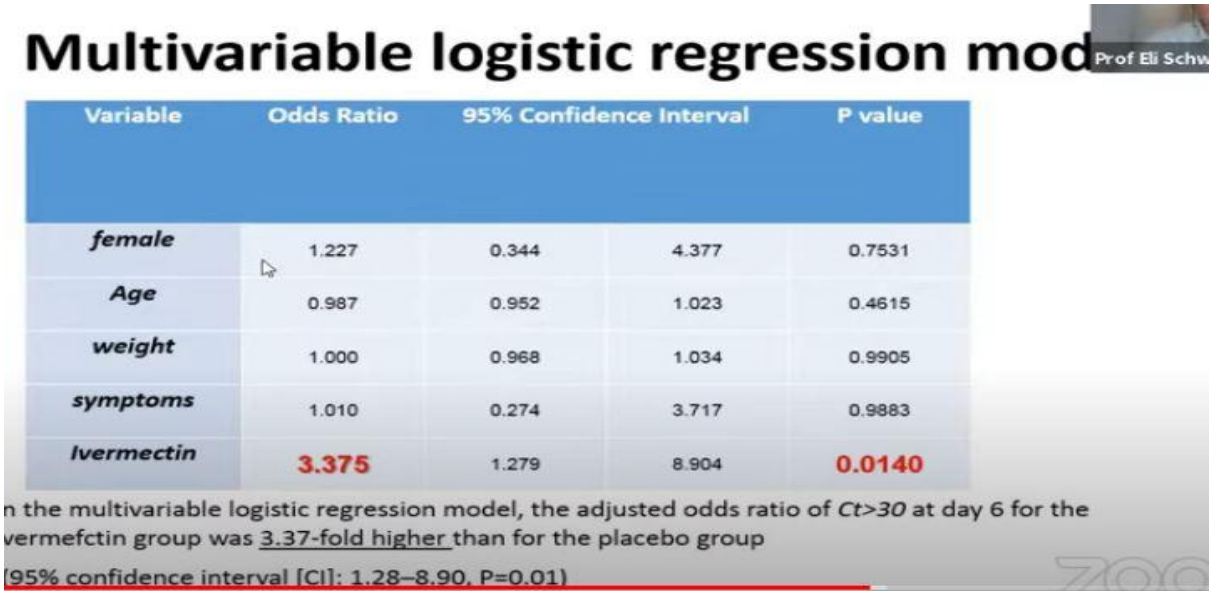
The first four days are the time taken to determine the patients' suitability in the trial, so although the graph starts at day zero, the trial starts on day 4.
At the beginning of the pandemic, it took time to diagnose patients, so it was harder to find suitable patients.
The CT value is the number of cycles required in the PCR test to detect the patient's virus.

The higher the Ct level, the lower the viral load, the higher the Ct level is good since it shows that the virus was harder to find in those patients.
The Ct level chart shows that both groups start at about the same Ct level. Looking at the chart, we see that 6 days from detection of the virus or 2 days from using ivermectin, we see a higher cycle level and lower viral load for the Ivermectin group, continuing at four days from using Ivermectin, almost equal after eight days using ivermectin or 12 days from starting symptoms.
This chart shows a much more rapid drop in infection and spreading with Ivermectin.
This result shows that Ivermectin has an impact on the infection.

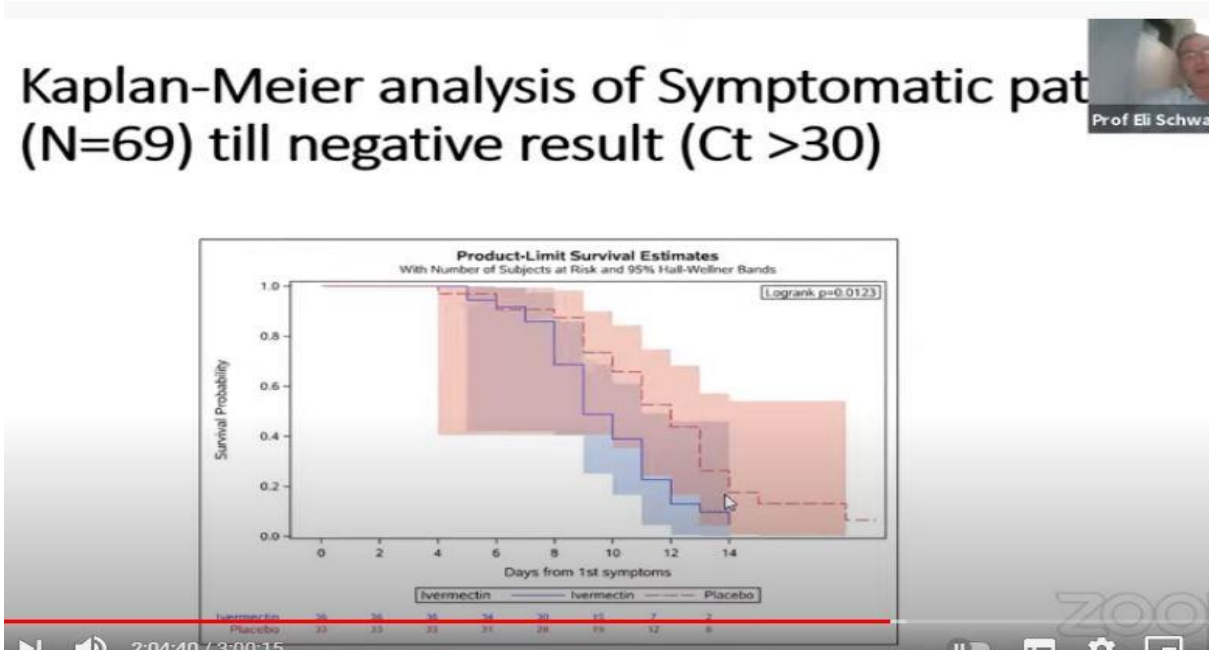


	Ivermectin N=49	Placebo N=45	P value
Negative at Day 4	15/26 (57%)	7/22 (31%)	0.08
Negative at Day 6	33/49 (67%)	20/45 (44%)	0.03
Negative at Day 8	39/49 (86%)	25/45 (53%)	0.03
Negative at Day 10	40/49 (81%)	27/45(60%)	0.02

This chart shows that Ivermectin had an impact on viral shedding.



In the Ivermectin Multivariable Logistics Regression Model, the adjusted odds ratio of Ct>30 at day 6 for the Ivermectin group was 3.37-fold higher than for the placebo group. These results prove that Ivermectin will reduce the viral load, and the patient more quickly becomes non-infectious.



The Ivermectin group, shown as the blue line, becomes more negative quicker than the red line, the placebo group. The primary goal was to prove whether Ivermectin reduces viral shedding, and this was proven.

Clinical deterioration

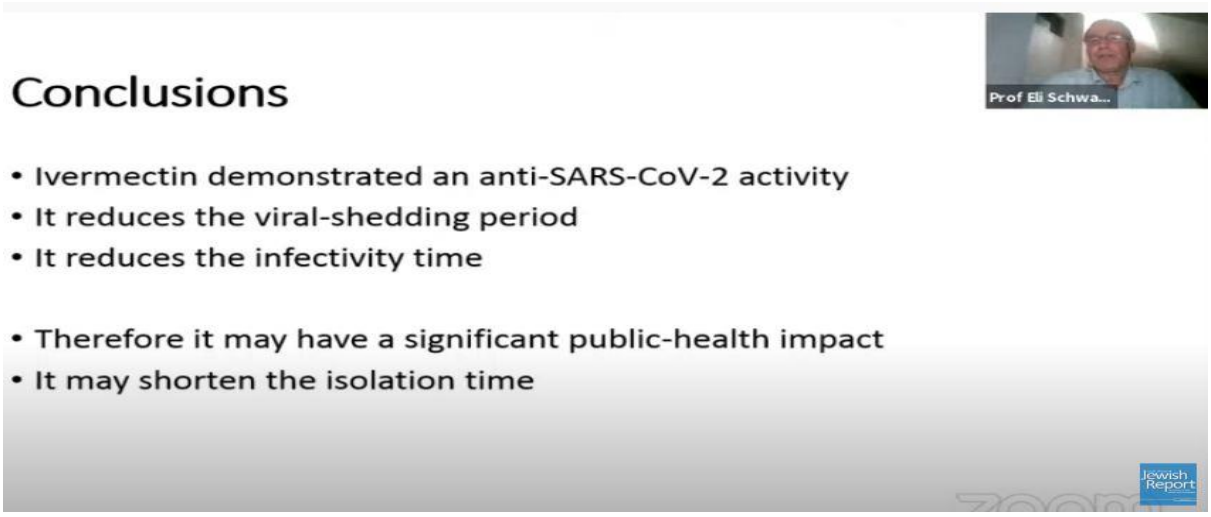
	Ivermectin	Placebo	P
N	49	45	N.S
Age –years (Range)	39.8 (22-72)	39.2 (20-71)	N.S
Age>50 y.	12 (24%)	11(24%)	N.S
Age>60 y.	5(10%)	4(9%)	N.S
Other risk factor	10 (20%)	9 (20%)	N.S
Hospitalization	0	2	

Looking at Clinical deterioration, none in the Ivermectin group required hospitalisation, while two in the placebo group did. This result, although encouraging, was too small a sample to draw any conclusions, which is an indication that more research is needed. However, should Ivermectin reduce progression to severe illness? This would reduce the pressure on hospitals?

Safety

- No Safety issues were reported
- Total dose/patients ~ 0.6 mg/kg (given in 3 days)

We know from past usage that Ivermectin is a safe drug. No safety issues were reported despite the dosage of .6 mg/kg given in 3 days, being more than double the usual dosage for anti-parasitic usage.



Conclusions

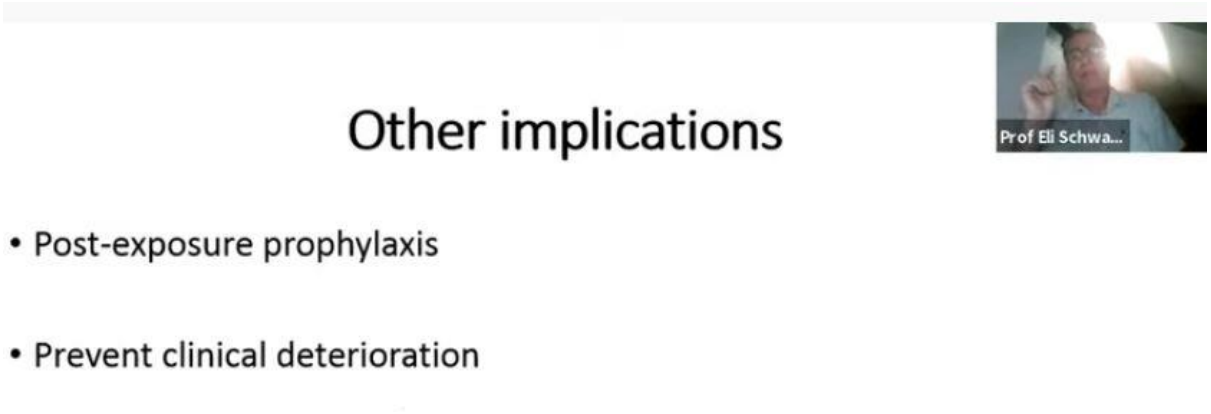
• Ivermectin demonstrated an anti-SARS-CoV-2 activity which is a very relevant conclusion. In the literature, it mentions that Ivermectin may have antiviral and may have anti-inflammatory activity. In this study, we show that ivermectin has antiviral activity at

the beginning of the disease and may reduce the virus's effects in the disease's later stages due to its anti-inflammatory activity, the cytokine storm.

• It reduces the viral-shedding period

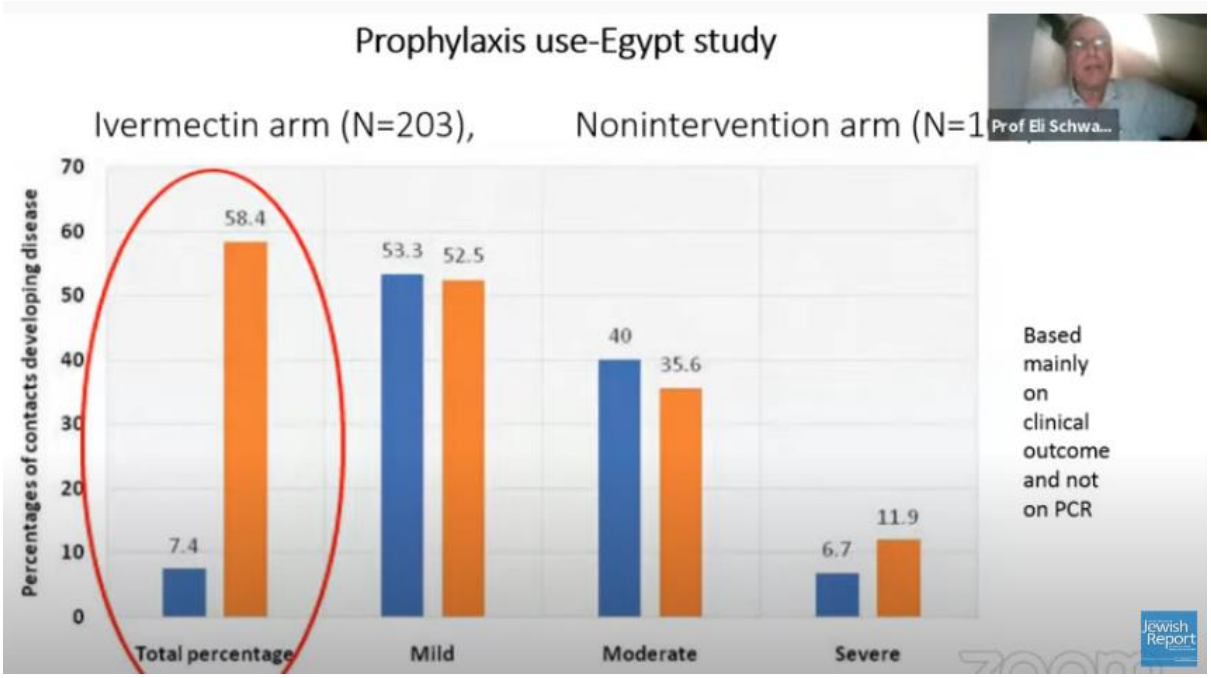
• It reduces the infectivity time

• Therefore, it may have a significant public-health impact since above 90% of the Covid-19 patients are mild cases, so considerable economic and social benefit in shortening the isolation time. Instead of 10 to 14 days of isolation in special accommodation and or away from work, with Ivermectin treatment for 3 days, the isolation is reduced considerably. Most counties do not have the vaccine, so the hope that the vaccine will solve the issue is a dream since many will not be vaccinated, such as children and those who resist the vaccine. There is a need for a drug that can shorten the viral load and activity time.



Ivermectin can be used in cases exposed to the virus, such as the rest of the household, especially those vulnerable.

Ivermectin prevents clinical deterioration, post-exposure prophylaxis for family members and health care workers.

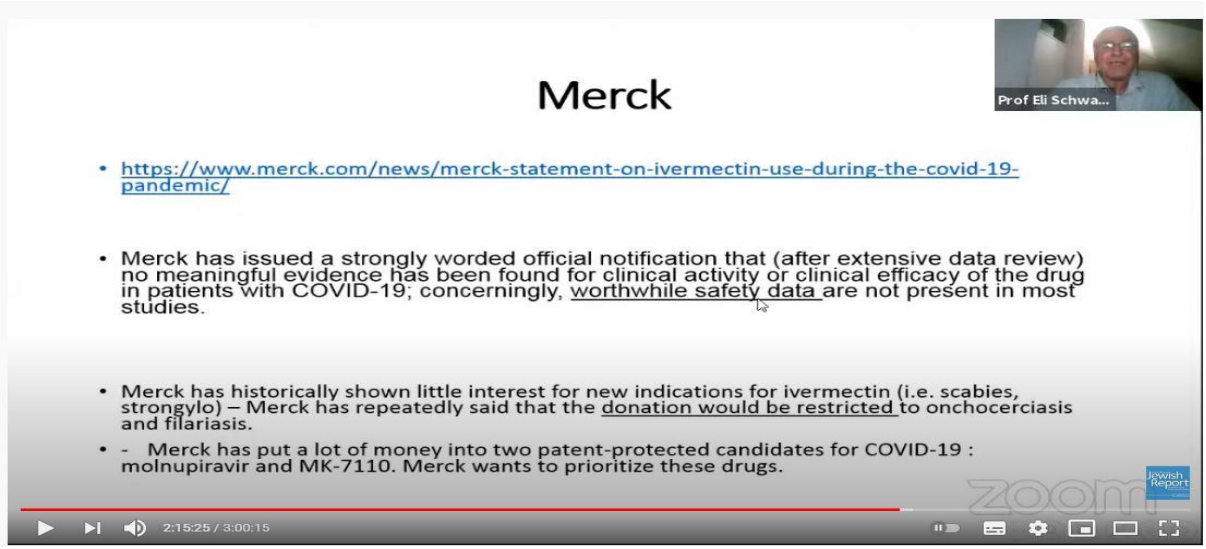


In a recent Egyptian study of contacts developing the disease, only 7.4% of 203 patients became sick, while 58.4% without Ivermectin became sick. This was not a double-blind study but rather an intervention study, and they were diagnosed using clinical outcomes due to Egypt's limited resources rather than PCR tests.

Due to Western countries' unfamiliarity with Ivermectin, some will be reluctant to accept these reports with an unwillingness to use it since they do not prove its effectiveness.

An evangelical group injected the veterinarian Ivermectin into 5,000 villages in Peru and claimed that they saved the village.

There is a reluctance to use Ivermectin in Western countries because of any acceptable proof, but it is used widely in endemic countries



Merck, the company that discovered and manufactured billions of Ivermectin doses, states that they only recommend Ivermectin for Onchocerciasis and filariasis. Merck is now concerned about the drug's safety, which is very strange since there were no safety concerns when used by billions for river blindness. It is illogical that changing the use should affect safety**. Still, it should be noted that Merck has put a lot of money into patent-protected molnupiravir and MK-7110 and wants to prioritise these drugs.** It would appear that science is not behind the latest Merck recommendation and that the truth is that Merck does not wish competition from an old patent expired cheaper drug. Unfortunately, not everything is science; it could be politics and business.
Prof Schwarz comments that the WHO has recently issued a paper recommending against the use of repurposed drugs such as remdesivir, hydroxychloroquine, lopinavir and interferon beta-1a for **hospitalised** patients. This reluctance to accept the repurposing of drugs without good science has possibly also contributed to the anti-Ivermectin movement in many Western countries to Ivermectin. *(Despite the American Journal of Medicine now including hydroxychloroquine as an effective drug against Covid-19 in the early-stage application. – Not mentioned in this presentation. Most successful studies using HCQ have been for early-stage use.)*

Dr Swartz comments.

This study proves Ivermectin works. With 120 patients, we had no side effects.
There have been reports that a stronger dosage has a better and faster effect.
You may be advised to take Ivermectin for incidental exposure, but you cannot take it indefinitely, so you should still be vaccinated. It could be used in households where there are already cases.
Many studies show better survival with Ivermectin.
This report focused more on Ivermectin's antiviral activity, and although Ivermectin also has anti-inflammatory activity, since this report was based on the beginning of the disease, the effect the report was on the antiviral effectiveness, not on the inflammatory cytokine storm
The economic effect can be lessened by three days of treatment instead of 10 days of isolation,
It can also be used for post-exposure prophylaxis and prevent clinical deterioration, especially for those vulnerable.

More about Ivermectin from Dr Paul Marik https://www.youtube.com/watch?v=n2MlliaLC0A
and [Dr Pierre Kory https://www.youtube.com/watch?v=PXh1yflndVE](https://www.youtube.com/watch?v=PXh1yflndVE)