Spain, Convincing Therapeutic Evidence
Dr. John Campbell – 13 Feb 2021
https://youtu.be/oYK9-zvJF_k

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Effect of calcifediol treatment and best available therapy versus best available therapy on intensive care unit admission and mortality among patients hospitalized for COVID-19: A pilot randomized clinical study (October 2020)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456194/

n = 76, Calcifediol treatment

50 patients treated with calcifediol

One required admission to ICU (2%)

No deaths

26 untreated patients

13 required admission to ICU (50 %)

2 deaths

Calcifediol treatment and COVID-19-related outcomes

(22nd January)

Barna-COVIDIOL

Barcelona

https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3771318

Effect of calcifediol treatment

In admitted patients

On ICU admission

and mortality

N = 930

Randomly assigned

Calcifediol treatment group n = 551

Day one, 532 ug (21,000 iu)

Days, 3, 7, 15, 30, 266 ug (10,640 iu)

No adverse effects reported

Required ICU, 30 (5.4%)

Deaths, 36 (6.5%)

Death RR = 0.36

64% reduced chance of death

Control group n = 379

Required ICU, 80 (21.1%), p less than 0.0001

Deaths, 57 (15%), p = 0.001

Adjusted for

Age

Sex

Comorbidities

Linearized 25(OH)D levels at baseline

Treated patients

Reduced risk to require ICU

RR 0.18

Baseline 25(OH)D levels

Inversely correlated with the risk of ICU

Predictors of reduced mortality

Higher baseline 25(OH)D levels

Predictors on increased mortality

Age

Obesity

Interpretation

In patients hospitalized with COVID-19, calcifediol treatment at the time of hospitalization significantly reduced ICU admission and mortality.

Early calcifediol after admission

Prior to ARDS development, is critical for mortality reduction

Initiation of calcifediol during ICU admission did not modify patient survival

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00:01 you're almost welcome to this talk and
00:02 i'm going to give you the bottom line
00:03 straight away in case you haven't got
00:05 time to listen and it's a really
00:07 important study it's on calcifidiol the
00:10 vitamin d derivative
00:11 it's been done in barcelona in spain now
00:14 these
00:15 researchers they admitted 930 people and
00:18 recruited them into the trial that is a
00:20 good
00:20 size 930 people in the trial now the
00:23 treatment group were given the calcified
00:25 eye or the vitamin d derivative
00:27 the control group were given exactly the
00:28 same treatment but they were not
00:30 given the calcified diet so what were
00:32 the results
00:33 well in the treatment group 5.4 percent
00:36 were admitted to the itu
00:38 in the control group it was 21 admitted
00:41 to the itu
00:43 big difference so 5.4 went to itu in the
00:45 treatment group
00:46 21.1 percent went to itu in the uh
00:50 control group
00:51 in the treatment group the death rate
00:53 and these are people that were already
00:54 admitted to hospital of course so
00:56 they're already poorly
00:57 in the treatment group 6.5 percent of
01:00 patients died in the control group
01:02 15 of patients died so it's 6.5
01:06 versus 15. this is massive this is a
01:09 huge result
01:10 all of these results were highly
01:12 significant
01:13 there was either one chance in a
01:15 thousand the results could have risen by
01:16 chance or one chance in ten thousand
01:18 that those results could have risen by
01:20 chance and
01:22 to be quite honest if national
01:24 regulators and
01:25 people that decide clinical policy
01:26 around the world don't start listening
01:29 to this data now
01:30 i think they're in breach of their duty
01:31 of care so that's the bottom line
01:34 massively significant study very
01:36 positive result
01:38 if you want to stick around we'll now go
01:39 into the detail
01:42 now you might remember that back in
01:44 october last year we reported on this
01:47 paper here
01:49 uh now this paper here is uh
01:52 is that this one the effect of a
01:54 calcifidiol treatment
01:56 versus best available therapy but it was
01:58 a pilot study now it was a randomized
02:00 clinical study so it was good
02:03 um but the number was only 76 patients
02:06 so
02:07 pretty small number of patients but the
02:09 results were impressive
02:10 50 patients treated with calcifidiol and
02:14 one that's two percent
02:15 required admission to the itu no deaths
02:18 in the treatment group in the 26
02:21 untreated
02:22 patients 13 that's 50 were admitted to
02:25 the itu
02:26 two deaths so that was um
02:30 really quite a a seminal paper really
02:33 that was a bit of a turning point
02:35 that was the first clinical trial data
02:38 and we covered that extensively at the
02:40 time and rightly so
02:42 but that stimulated a lot of interest
02:46 throughout spain and throughout spain
02:48 there's about a dozen centers now
02:49 researching this
02:51 now that was based in cordova in the
02:53 south of spain and andalucia
02:54 and they've been coordinating in close
02:57 collaboration with other universities
02:59 academics doctors and researchers
03:01 uh they're studying this all over spain
03:03 now and this is the first one to come
03:05 out so there are more to come out we
03:06 believe this is being done in
03:08 in 12 centres in spain already so it
03:11 it and the results as we've seen are are
03:14 totally convincing
03:16 now this wasn't quite a clinical trial
03:18 they described this as as a clinical
03:21 cohort study but i've read this paper
03:24 i'll by the way this paper here um
03:28 that this first one is peer-reviewed
03:30 this second one that we're looking now
03:32 is in lansing preprint so it's not
03:35 peer-reviewed
03:36 so i think it's important to emphasize
03:38 that the pilot study we looked at in
03:39 october is now fully pre-reviewed
03:41 what we're going to look at now is not
03:43 peer-reviewed but i've looked at it
03:45 and i i think it's a very high quality
03:48 study and it will be
03:49 it will be a pass for uh for full
03:52 publication pretty soon
03:54 and i suspect with minimal or no
03:56 modifications
03:58 because it is a very convincing study
04:00 and it's well conducted and the stats
04:02 are
04:02 really good um so this is the name of
04:06 the study here calcified dial so
04:08 do look at it for yourself always worth
04:10 going to the original source don't take
04:11 my word for things
04:13 you can download that's the abstract
04:15 there you can download the the full
04:16 paper
04:18 so it's all there now in the public
04:20 domain
04:21 now actually published on the 22nd of
04:23 january but i didn't
04:24 couldn't get access to this until
04:26 yesterday so i think the full paper
04:28 has just been put into the public domain
04:30 so this is pretty um
04:32 pretty new stuff calciferol treatments
04:34 and covered 19 related outcomes as the
04:36 title of the paper
04:37 22nd of january and it's the the banner
04:40 cover dial
04:42 study that's the this is the name of the
04:43 study
04:45 and this particular branch of the study
04:46 was conducted and i think it's called
04:48 the hospital by the sea
04:50 in barcelona northern spain of course
04:54 right pre-prints with the lancet um
04:57 now effects of calcified oil treatment
04:59 now these are patients that were already
05:01 admitted to hospital
05:03 so that's important to grasp these
05:05 patients were ready
05:07 poorly enough to be admitted to the
05:08 hospital and this was all during the
05:11 first wave
05:12 during the first wave of the pandemic
05:14 and this date is only just getting
05:15 fully assimilated and crunched now pity
05:17 has taken so long because the results
05:19 are so significant
05:21 so admitted patients already poorly
05:24 patients
05:25 is the point to grasp there so in
05:28 admitted patients
05:30 what difference did the calcified dial
05:32 have on icu admission
05:35 what difference did it have on mortality
05:37 what was what they were looking at and
05:38 the number in the study was 930
05:41 and they were randomly assigned either
05:43 into the treatment group
05:47 to get the actual calcifidiol or into
05:51 the control
05:52 group not to get the calcifidiol
05:56 in every other way these groups were
05:59 treated
05:59 in exactly the same way as per hospital
06:02 protocol so the only difference between
06:04 the two groups was the calcify dial
06:06 we call that the independent variable
06:09 and
06:10 these are the dependent variables the
06:12 question is were these dependent
06:13 variables i see your admission
06:15 and mortality dependent on the
06:17 independent variable
06:19 which was giving the calcify dial
06:22 so this is the way these clinical trials
06:25 and cohort studies clinical cohorts that
06:27 is in this case
06:29 work now just before we go on to the
06:32 details of the paper itself i just want
06:33 to give you a quick
06:35 um quick revision really so this
06:39 is um this is just one of my diagrams
06:41 that i do for for students
06:43 so here we have the skin and the uh
06:46 the calciferol which is the vitamin d3
06:49 is going to be synthesized mostly in the
06:51 lower parts of the
06:52 skin and the skin as you might remember
06:55 is in two parts this top part is the
06:57 epidermis this lower part is the dermis
06:59 so the uh the cholecalciferol the
07:02 vitamin d3 is synthesized in the
07:05 dermis when it's exposed to ultraviolet
07:07 b
07:09 radiation then this coley
07:12 uh this cholecalciferol that's been
07:14 synthesized
07:15 goes off in the blood to the liver the
07:18 biochemical factory of the body
07:20 and in the liver it's converted to
07:22 calcifidiol
07:24 now this is the form that is circulating
07:26 in the blood so this goes off into the
07:28 blood
07:31 so this is the form of the vitamin d
07:33 that when we're doing the blood levels
07:35 this is the form that we're looking at
07:37 but it's not actually the final form the
07:39 body uses now it's the best bio marker
07:41 to use
07:42 so when we're analyzing vitamin d levels
07:44 this is the best one to use
07:46 for quite a few reasons for example it's
07:47 got a long half-life
07:49 it stays in the circulation for weeks
07:51 the half-life is about 12 to 21 days so
07:54 it let's stick around sticks around for
07:55 a long time
07:56 and it's in much higher concentrations
07:58 than the final one but the final product
08:00 here is calcitrol
08:01 so it goes from the blood uh into the
08:04 kidneys
08:05 and in the kidneys it's converted into
08:08 calcitrol
08:09 which is the active hormone and then
08:12 it's this calcitrol hormone
08:14 that goes out to all of the tissues of
08:15 the body such as the immune system
08:18 and all the tissues in the body with
08:19 vitamin d receptors which is basically
08:21 most of the cells or indeed all of the
08:23 cells
08:24 in the body so that's the way it works
08:26 so this is important
08:28 because this keeps the liver supplied
08:30 with the calcifidiol
08:31 to convert into calcitrol which is the
08:33 active form
08:34 but obviously there's not enough of that
08:36 you can't make enough of that
08:38 but if you give more of that then you
08:40 end up with more of that so you end up
08:42 more of the active hormone which is what
08:45 we want
08:49 if we give if we give more now
08:53 if we give vitamin d of course this is
08:55 vitamin d made from the skun its sun if
08:57 we give vitamin d via the
08:58 gastrointestinal tract
09:00 um that will of course uh go to the
09:01 liver the colon calcium will go to the
09:03 liver to be converted to calcifidial
09:05 but this process of converting that
09:09 into that in the liver takes uh quite a
09:12 bit of time
09:13 um it's not like um a week or two to
09:16 convert it so there's always a delay
09:19 that's why when we give this in clinical
09:21 practice it's working straight away
09:24 so i think that's important to realize
09:26 anyway
09:28 let's get back to the back to the study
09:32 um so calcifidiol treatment group now
09:36 there was a
09:38 551 went into the treatment group
09:41 now on day one this is the first day of

09:43 admission to hospital so remember
09:45 poorly patients admitted to hospital
09:48 soon as they came into hospital
09:49 they started the treatment as soon as
09:51 they're admitted so day one
09:53 they gave them 532 micrograms that's 21
09:57 000 international units of calcified io
10:00 and then they gave 266 micrograms that's
10:04 10
10:06 640 international units of calcifidiol
10:09 on day 3 and day 7
10:12 and day 15 and day 30 if they were still
10:15 in hospital
10:16 so they had a total of one two three
10:19 four five doses of high doses it must be
10:23 said reasonably high doses of the
10:24 calcifidiol
10:26 the reason they use the calcified diol
10:28 as we've said
10:29 is it is absorbed very efficiently
10:31 through the gastrointestinal tract
10:32 100 of it's absorbed straight into the
10:34 blood it will stay in the blood for
10:37 several weeks it will be measurable it's
10:39 got a long half-life
10:40 and it means there's any amount of
10:43 calcifidiol
10:44 in the blood that the kidneys can
10:46 convert to the active form of calcitrol
10:49 so we'll get the effect of the active
10:51 hormone
10:52 in the blood so if we gave this first
10:55 we'd have to wait for a couple weeks to
10:57 get to this stage so by giving this we
10:59 save all that time
11:01 and convert this into this will just
11:03 take a matter of hours
11:05 rather than a matter of uh a week or
11:08 many days or a week and of course if
11:10 patient patients are already poorly
11:12 the whole point is we don't have a week
11:14 to wait they could die in that week
11:16 after they've been admitted to hospital
11:17 we certainly don't have a fortnight we
11:18 have to give the kalki for dial
11:20 to be quick acting and the spanish seem
11:23 to have realized this when everyone else
11:25 doesn't now let me ask you why don't
11:27 people get this is that is that is what
11:29 i've just told you they're complicated
11:31 you know is that is that hard to
11:33 understand it really is
11:35 why don't people get this and why isn't
11:36 everyone doing it really is
11:39 a bit of a mystery anyway back to the
11:41 study keep the emotion out of it
11:44 um now no adverse effects reported now
11:48 this is
11:48 staggering this is staggering
11:52 this appears to have no side effects
11:57 i mean every every every time you learn
11:59 about a drug you learn about the
12:00 indications contraindications and side
12:02 effects
12:02 this is we would memorize this like
12:04 parrots so you know you you give a drug
12:07 you learn what it's for the indication
12:09 the contraindications is when you must
12:10 not give it and all drugs have side
12:12 effects
12:12 so you have to memorize the side effects
12:14 nausea vomiting dry mouth whatever it
12:16 happens to be
12:18 um but this calcified diol had no
12:20 reported adverse effects
12:22 it appears to be completely safe
12:26 so that really alters the risk benefit
12:28 analysis
12:29 you know there's no identified risk from
12:31 this in in these hospitalized patients
12:33 from this study
12:35 no identified risks identified in this
12:37 study so
12:39 um you know if we can have some benefit
12:42 and you're taking essentially as far as
12:44 we know
12:44 essentially no risk at all what what's
12:47 not to like why not why not do it
12:50 because it's safe according to this
12:53 study no adverse effects reported
12:56 now the calciferol treatment group um
13:00 30 patients so 30 patients of the
13:04 551 had to go to the intensive care
13:07 that's 5.4 percent
13:10 now if we go down to the control group
13:12 uh there was uh
13:14 379 in the control group who did not
13:17 did not have the calcific aisle then 80
13:21 of those that's 21
13:23 had to go to the intensive care and the
13:25 chances of that difference arising by
13:27 chance are not one in
13:28 10 not 100 not one in a thousand but one
13:31 in ten thousand so there's a one in ten
13:33 thousand chance
13:35 that is not a genuine result but
13:38 uh it looks like it is a genuine result
13:41 so it's nine thousand nine hundred and
13:43 ninety nine out of ten thousand
13:44 likely to be a genuine result
13:48 greatly reduced admission to the
13:50 intensive care unit
13:52 now what about deaths well out of the
13:54 551
13:56 admitted patients already poorly
13:59 who were given the calcifidiol given the
14:01 treatment
14:04 36 of the 551 died
14:08 so 36 out of 551 died
14:12 giving a death rate of 6.5 percent
14:17 in the uh control group who were treated
14:19 in exactly the same way
14:21 but uh were not given the calcific dial
14:26 then uh 57 of those out of the 379 died
14:30 that's
14:31 15 died and the probability of that
14:35 arising by chance were one in a thousand
14:39 again massively significant
14:42 results these sort of results don't
14:45 happen by chance very often well they
14:48 happen when out of 10 000 times i think
14:50 we know that that happens one out of a
14:51 thousand times
14:52 so i'm happy that these are genuine
14:54 results
14:56 so the death relative risk was a 36
14:59 percent or to put it another way
15:01 64 reduced 64 reduced
15:04 chance of death that's the chance of
15:07 death
15:08 that's the likely adverse effects of the
15:09 drug why don't we use it it
15:12 really is quite incredible that this is
15:15 not widely adopted so that's the
15:16 difference between the
15:17 calcification treatment group 551
15:22 and the control group 379
15:26 huge difference between the two
15:29 groups massive uh massive difference
15:33 between the groups
15:35 um now they went on and did more more
15:38 analysis than this is pretty pretty
15:40 thorough study actually
15:41 um
15:45 now the they went back and they took the
15:46 data and they adjusted for
15:49 age sex comorbidities and this is quite
15:52 a clever bit
15:54 most of the people that were admitted
15:55 had relatively low vitamin d levels but
15:58 they uh they were able to linear
16:00 linearize that in other words they could
16:02 take account whether it was uh
16:04 very low levels or medium levels or
16:06 medium high levels or higher
16:08 levels and they're able to put that in a
16:10 linear structure to to account for that
16:13 now the treated patients another way
16:15 they worked it out was reduced risk to
16:17 itu the relative risk was 18
16:19 it was 0.18 so that means
16:22 if you're treated you've got 18 of the
16:24 chance of going to intensive care
16:26 compared to uh someone who's not treated
16:30 so massively reduced chance of going to
16:32 intensive care
16:33 and the other thing i like about this
16:35 they also so the this is calcify dial as
16:38 a treatment
16:39 but of course they measured calcified
16:41 levels in the patients they were
16:42 admitted
16:43 and the the calcified io levels in the
16:45 patients that were admitted would be as
16:46 a result of vitamin d they'd taken in
16:48 the weeks
16:49 before they were admitted so they looked
16:52 at that as well
16:52 the baseline levels of calcifidiol based
16:55 on the person's vitamin d
16:57 either sun exposure or dietary exposure
16:59 or supplement exposure
17:00 over the past few weeks and they found
17:02 an inverse correlation with the risk of
17:04 intensive care
17:07 in other words in other words as the
17:10 levels of vitamin d rose the probability
17:14 of going to intensive care
17:15 decreased whereas people with lower
17:18 levels of intensive care
17:20 low levels of lower levels of vitamin d
17:22 on admission were
17:23 more likely to go to intensive care they
17:25 were inversely
17:27 related so high levels of vitamin d less
17:30 likelihood to go to intensive care this
17:32 inverse
17:33 correlation was detected as well
17:39 predictions of reduced mortality
17:42 higher baseline levels so in in other
17:46 words um mortality was inversely related
17:48 as well
17:49 so to predict reduce mortality those
17:52 with higher baseline levels of vitamin d
17:55 were less likely to die
17:58 um but the reason to put that like that
18:01 is there was also predictors of
18:03 increased mortality
18:05 and the people that were more likely to
18:07 die were the older people
18:09 and the more obese people so high levels
18:13 of vitamin
18:14 d on admission less likely to die
18:17 greater age
18:18 greater body mass index uh
18:22 more more likely to die during the study
18:24 less likely to die
18:26 more likely to die in the study now
18:30 we've gone over this sort of fairly
18:32 quickly really but i
18:34 just want to just want to go back and
18:35 reflect on something really
18:37 in the control group
18:40 that didn't get the treatment there were
18:42 there was 57
18:43 deaths so in a sense that's
18:46 57 people that have given their lives
18:49 for us to have this information
18:51 this is how precious this information
18:55 is if those people have been given the
18:57 calcify dial which to be quite honest
18:59 the doctor suspected would work
19:02 um a lot less of them we believe from
19:05 this data
19:06 would have died and yet
19:09 with great nobility that they agreed to
19:11 take part in this trial so
19:14 uh we know we just read through these
19:15 numbers but these are human beings that
19:17 have sacrificed themselves essentially
19:19 for this data
19:21 and i think that gives us a real moral
19:23 responsibility
19:26 um to use this data to help
19:30 the rest of the human race to be quite
19:31 honest without being too melodramatic
19:33 about it
19:36 right the interpretation of this study
19:40 um direct quote
19:45 in patients hospitalized with covered 19
19:47 calcifidiol treatment
19:49 at the time of hospitalization that's
19:51 got to be given at the time of
19:51 hospitalization
19:53 reduces significantly reduces very
19:56 significantly reduces
19:58 intensive care admission and mortality
20:02 and as i said at the start i really feel
20:04 now
20:06 that groups like the nice in this
20:09 country and
20:10 whoever makes the rules around the world
20:13 now are going to fail in their duty of
20:16 care
20:17 if they don't take cognizance of this
20:20 safe treatment now how it's working is a
20:23 bit of a separate matter i mean
20:24 basically these people are already
20:26 admitted so they could have still some
20:27 of them could have still been in the
20:28 viral phase
20:30 and we know that vitamin d is important
20:31 for immunity but we also know that
20:33 vitamin d is an immunomodulator so it
20:35 would damp down the inflammation
20:38 in the inflammatory phase and the people
20:40 with the higher levels of calcifidiol
20:42 would have less acute respiratory
20:43 distress syndrome
20:45 the alveoli wouldn't be filling up with
20:47 fluid in the same way
20:49 therefore less likely to be admitted to
20:50 intensive care and less likely to
20:53 die so that seems to be the way that
20:55 this is uh
20:57 this is working now the calcific diol
20:59 treatment had to be early after
21:01 admission
21:03 these people were given the council for
21:05 dial as soon as they were admitted
21:07 and this is important because if you
21:10 waited
21:12 until these people deteriorated and went
21:14 on to intensive care
21:15 it was too late it didn't alter the
21:17 outcome
21:18 like many things in covered the the
21:21 treatment is
21:22 specific to a particular time
21:26 so early calciferol dial treatment was
21:28 necessary after admission
21:30 prior to the development of acute
21:32 respiratory distress syndrome
21:34 it's critical for mortality reduction so
21:36 if you wait for the ards
21:38 if you wait for the cytokine storm to
21:40 cause the acute respiratory distress
21:42 syndrome
21:43 if you wait for the alveoli to fill up
21:45 with fluid
21:46 the fluids already there it's too late
21:49 it needs to prevent the inflammation
21:51 it needs to promote the immunity and
21:52 prevent the inflammation as the immuno
21:54 modulated before
21:56 the alveoli fill up with inflammatory
21:58 fluid and you can't get the oxygen out
22:00 and you can't get the carbon dioxide
22:02 back in
22:03 needs to happen before that
22:06 phase indication
22:10 of calcifidiol diol so initiation of
22:12 calcifidiol during intensive care
22:14 admission did not modify patient
22:16 survival
22:17 so it needs to be done
22:20 so ideally ideally vitamin d
22:24 is going to be given at a much earlier
22:27 stage
22:27 so when patients are admitted if they
22:29 are admitted they've already got high
22:30 levels of calcifidiol in the blood
22:34 if they haven't it's not too late it can
22:36 be topped up the calcifidar can be
22:38 topped up
22:39 when they're first admitted but if you
22:41 wait for them to deteriorate then it
22:42 doesn't have a benefit it is too
22:45 late so i think that is just an
22:49 absolutely massive finding
22:51 treatment group 5.4 admitted to the itu
22:56 control group um so
22:59 treatment group 5.4 admitted to the itu
23:01 control group 21.1
23:03 admitted to the itu 5.4 versus 21
23:08 treatment group 6.5 deaths control group
23:12 15 deaths
23:17 those figures are now there in the
23:19 literature that will be peer reviewed
23:20 soon
23:21 more data will be coming out shortly to
23:23 be quite honest we've been anticipating
23:26 this on
23:27 this channel for example for a year now
23:30 over a year now actually um literally
23:33 over 12 months now
23:34 and um i really feel strongly now that
23:38 if international um bodies are not
23:41 taking cognizance of this
23:42 um well they're failing in their duty of
23:46 care and
23:46 that's the mildest way i can put it so
23:49 we call on the
23:50 the national institute for health and
23:52 care excellence in the uk to review this
23:54 data
23:56 urgently and other people around the
24:00 world this this treatment is
24:01 uh very cheap when i say it costs
24:04 pennies literally
24:06 it costs pennies it probably costs about
24:08 10 cents per tablet or something if that
24:10 um it's off license
24:14 pharmaceutical companies won't make any
24:15 money from it
24:17 because it's off license but it's freely
24:19 available to
24:20 to the world this is this is a gift to
24:22 the world it's a really really cheap
24:25 and from this we believe highly
24:27 efficacious
24:30 intervention and uh i look forward to
24:34 rapid um review of these results
24:38 but by national bodies as you and me
24:40 have just done
24:41 on this video um
24:45 given past performance i'm not too
24:48 hopeful but the data now is so strong i
24:50 really feel
24:51 they will start to have to act uh soon
24:55 okay well that's us it's a weekend so uh
24:57 we'll leave it there for today now i
24:58 don't want to dilute that that's such an
25:00 important message so um
25:02 so we'll leave it there so thank you for
25:04 watching and have a great
25:05 rest of your weekend