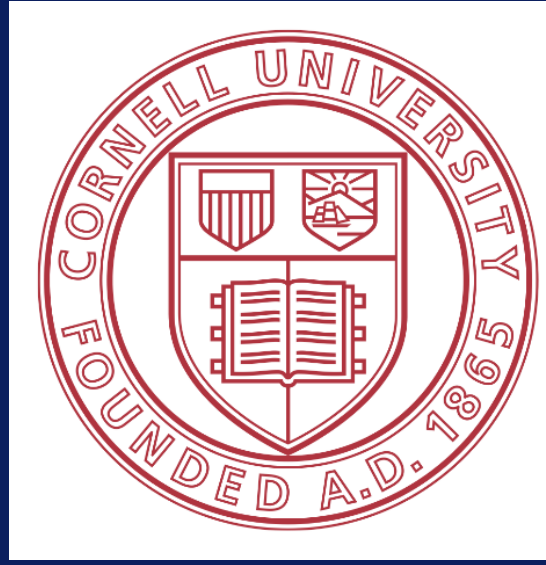


# Protocols designed to improve a man's overall health are linked to increased capacitation ability: a multicentric, prospective, blinded analysis

Fady Sharara, Eric Seaman, Anna Lysenko-Brockman, Haneen Taha, Cristina Cardona, G. Charles Ostermeier, Alexander J. Travis.



## Abstract

**Objective:** Traditional semen analysis (SA) parameters are declining; hypotheses as to the cause focus on worsening men's health due to environmental exposures and/or lifestyle. SA evaluates ejaculate volume, sperm motility, concentration, and morphology, but doesn't assess sperm fertilizing ability, which causes half the cases of male infertility. It is therefore unknown whether reported declines in SA values have any impacts on actual male fertility. Prior to fertilizing, sperm must capacitate. Cap-Score™ measures the capacitation ability of a man's sperm and prospectively predicts his probability of generating a pregnancy (PGP). Here, we evaluate the effects of protocols designed to improve a man's overall health on his SA and capacitation ability.

**Materials and Methods:** 55 men questioning their fertility were evaluated for Cap-Score and SA at two independent clinics. Recommendations were made to improve overall health: Clinic 1) quit use of tobacco, marijuana, or alcohol; avoid laptops on laps or Jacuzzis/saunas; lose weight if obese; increase Vitamin D intake ( $\geq 2k$  IU/day); and start supplements (Androferti; n=30; vitamins C, E, B12, Folate, Zinc, selenium, L-carnitine, & coenzyme Q10), or Conception XR (n=8; vitamins C, E, D, Folate, Zinc, selenium, & Lycopene); Clinic 2) limit alcohol, tobacco, marijuana; exercise  $\sim 20$ min/d; increase sleep, avoid foods with pesticide residues; & start supplements N acetyl cysteine & Proxeed Plus (n=17; Vitamins C, B<sub>12</sub>, Folic Acid, Zinc, Selenium, L-Carnitine, Acetyl-L-Carnitine, & coenzyme Q10). A second blinded analysis was done  $\sim 13$  weeks later; paired Wilcoxon signed rank tests were done to compare before and after lifestyle changes.

**Results:** All supplements impacted measures similarly ( $p > 0.05$ ; ANOVA). An increase in Cap-Score from  $23.5 \pm 0.9$  to  $27.6 \pm 1.0$  ( $p = 0.001$ ; n=55), corresponding to a 25% increase in a man's PGP, was observed. Recommended lifestyle changes had no impact on semen volume ( $p = 0.479$ ; n=54), sperm concentration ( $p = 0.562$ ; n=54), or sperm motility ( $p = 0.112$ ; n=54). Strict normal morphology was available from Clinic 1 and improved ( $1.7 \pm 0.2$  to  $3.3 \pm 0.5$ ;  $p = 0.001$ ; n=38). No relationship was detected between Cap-Score and strict normal morphology before ( $p = 0.566$ ) or after ( $p = 0.156$ ) lifestyle changes.

**Conclusions:** Similar lifestyle changes recommended by two independent clinics improved capacitation ability.

**Impact Statement:** Promoting a man's overall health through lifestyle change and nutritional supplementation increased capacitation ability and PGP.

## Objective

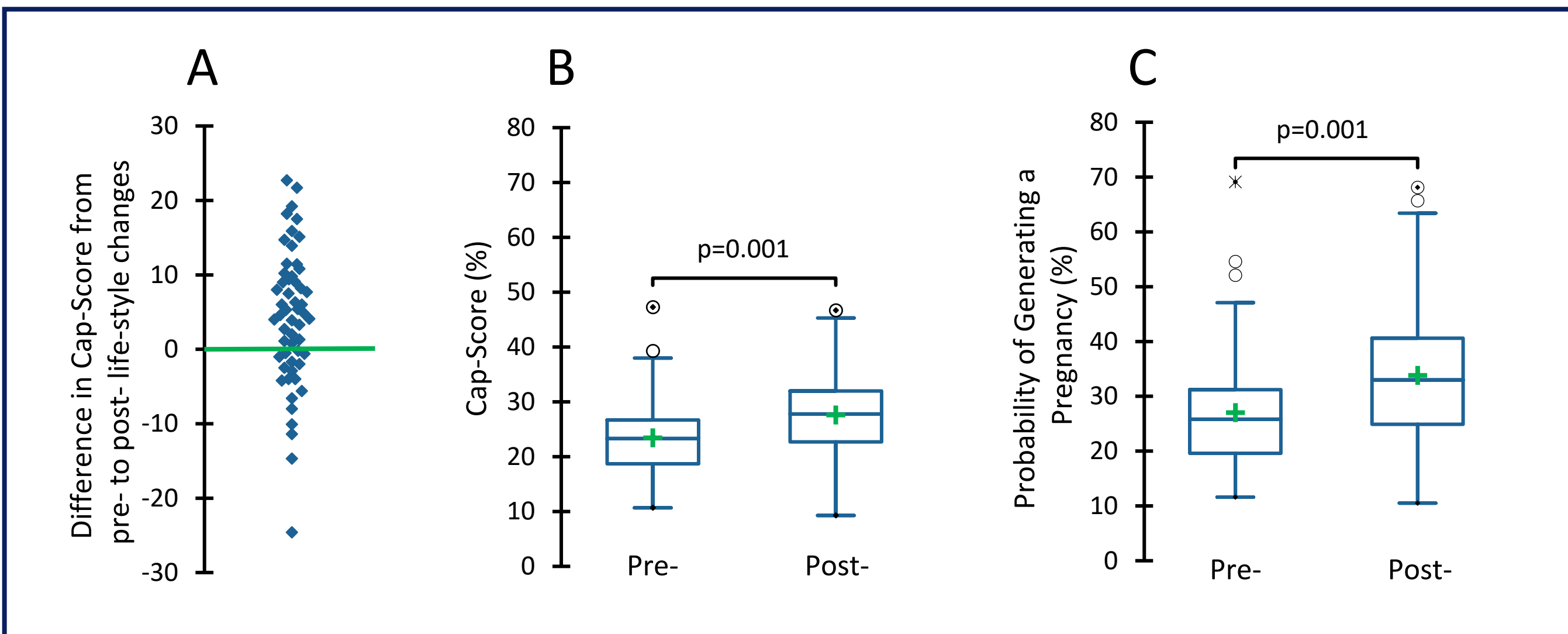
Determine if improving a man's overall health, through lifestyle changes and nutritional supplementation, can enhance capacitation ability and semen analysis measures.

## Materials and Methods

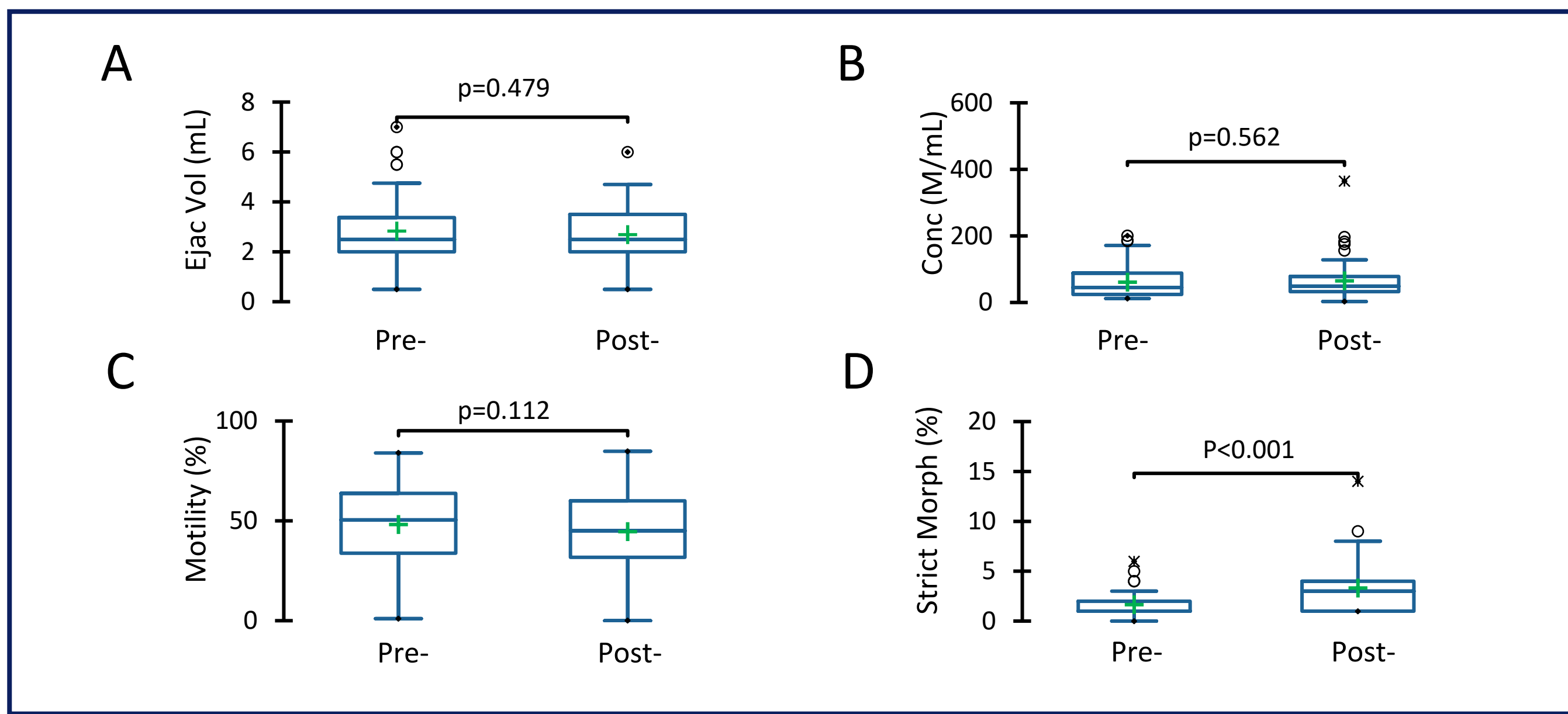
Clinic #1	<ul style="list-style-type: none"> <li>Quit:                             <ul style="list-style-type: none"> <li>tobacco</li> <li>marijuana</li> <li>alcohol</li> </ul> </li> <li>Avoid:                             <ul style="list-style-type: none"> <li>laptops on laps</li> <li>Jacuzzis/saunas</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>Lose weight if obese</li> <li>Increase Vitamin D intake (at least 2000 IU/day)</li> <li>Start 1 of 2 supplements                             <ul style="list-style-type: none"> <li>Androferti (n=30; vitamins C, E, B12, Folate, Zinc, selenium L-carnitine, and coenzyme Q10)</li> <li>Conception XR (n=8; vitamins C, E, D, Folate, Zinc, selenium, and Lycopene)</li> </ul> </li> </ul>
	<ul style="list-style-type: none"> <li>Limit:                             <ul style="list-style-type: none"> <li>tobacco</li> <li>marijuana</li> <li>alcohol</li> </ul> </li> <li>Avoid foods w/ pesticide residues</li> <li>Exercise <math>\sim 20</math> min/d</li> </ul>	<ul style="list-style-type: none"> <li>Increase sleep</li> <li>Start supplements                             <ul style="list-style-type: none"> <li>N acetyl cysteine</li> <li>Proxeed Plus (n=17; vitamins C, B12, Folic Acid, Zinc, selenium, L-carnitine, Acetyl-L-carnitine and coenzyme Q10)</li> </ul> </li> </ul>
Clinic #2	<ul style="list-style-type: none"> <li>Limit:                             <ul style="list-style-type: none"> <li>tobacco</li> <li>marijuana</li> <li>alcohol</li> </ul> </li> <li>Avoid foods w/ pesticide residues</li> <li>Exercise <math>\sim 20</math> min/d</li> </ul>	<ul style="list-style-type: none"> <li>Increase sleep</li> <li>Start supplements                             <ul style="list-style-type: none"> <li>N acetyl cysteine</li> <li>Proxeed Plus (n=17; vitamins C, B12, Folic Acid, Zinc, selenium, L-carnitine, Acetyl-L-carnitine and coenzyme Q10)</li> </ul> </li> </ul>

**Figure 1. Study design.** Cap-Score was determined for 55 men seeking fertility assistance at two different clinics. Their lifestyle was subsequently changed, as outlined above. A second blinded analysis was done approximately  $\sim 13$  weeks after initiating these changes.

## Results

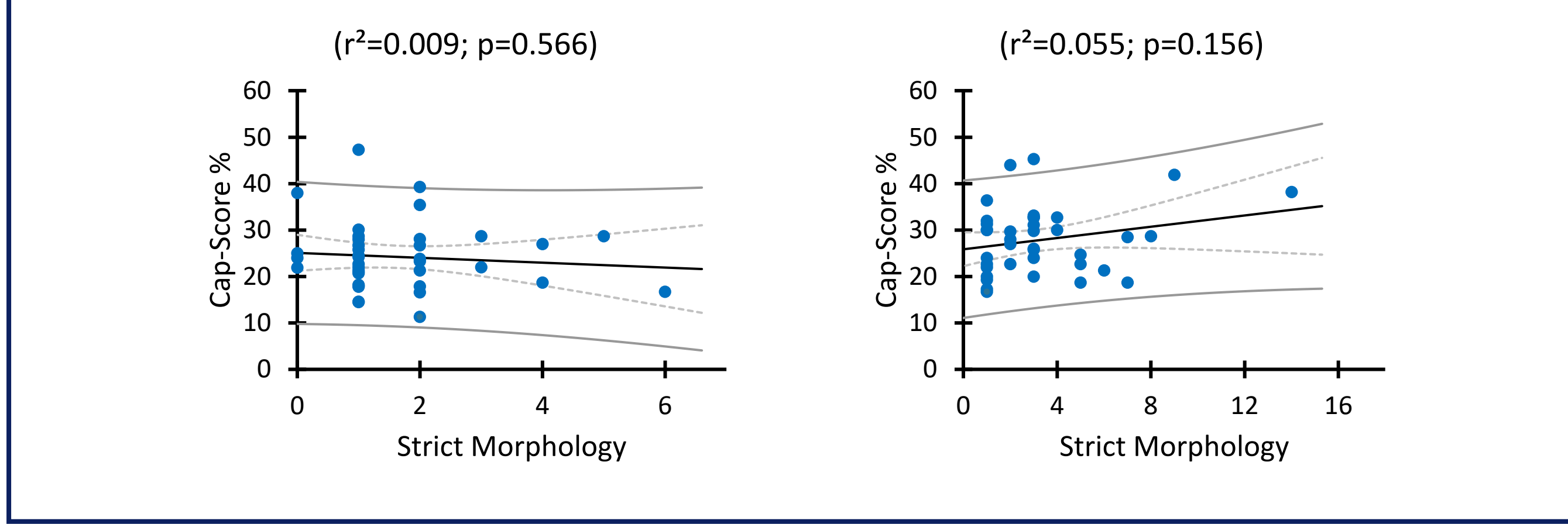


**Figure 2. Impacts of improving a man's overall health on his capacitation ability.** Panel A, shows the difference in Cap-Score between pre- and post- life-style change. Note that 67% (37/55) of patients showed an increase, as their difference was above the horizontal green line. This suggested that improving a man's overall health can increase his sperm capacitation ability. In fact, these improvements corresponded to an increase in Cap-Score from  $23.5 \pm 0.9$  to  $27.6 \pm 1.0$  ( $p = 0.001$ ; n=55; **panel B**), representing a 25% increase in a man's probability of generating a pregnancy (**Panel C**). In the "box whisker" plots, the green crosses correspond to the mean. The central horizontal bars are the medians. The lower and upper limits of the boxes are the first and third quartiles, respectively. Points above or below the whiskers' upper and lower bounds may be considered as outliers.



**Figure 3. Impacts of Life-Style changes on traditional semen analysis measures.** Lifestyle changes had no impact on semen volume ( $p = 0.479$ ; **Panel A**), sperm concentration ( $p = 0.538$ ; **Panel B**), or sperm motility ( $p = 0.112$ ; **Panel C**). In contrast, strict normal morphology improved ( $p < 0.001$ ; **Panel D**). In the "box whisker" plots, the green crosses correspond to the mean. The central horizontal bars are the medians. The lower and upper limits of the boxes are the first and third quartiles, respectively. Points above or below the whiskers' upper and lower bounds may be considered as outliers.

## A. PRE-LIFE-STYLE CHANGES      B. POST-LIFE-STYLE CHANGES



**Figure 4. Assessment of relationship between morphology and capacitation ability.** No relationship was detected between Cap-Score and strict normal morphology before (**panel A**) or after lifestyle changes (**panel B**). This would suggest that the two measures are evaluating separate and unique features and that strict morphology is not necessarily predictive of a sperm's ability to capacitate and thus fertilize. In these charts, the blue dots represent unique data points. The solid black line shows the regression equation, while the dotted and solid gray lines represent the 95% confidence intervals for the mean and observed values, respectively.

## Conclusions

- Similar lifestyle changes recommended by two independent clinics:
  - Improved capacitation ability.
  - Had little impact on traditional semen analysis measures.
- Strict morphology and Cap-Score evaluate separate and unique sperm features.
- Strict morphology is not predictive of the ability of sperm to capacitate and thus fertilize.
- Capacitation ability and probability of generating a pregnancy were improved by promoting a man's overall health.

**Funding/disclosures:** Androvia LifeSciences performed the Cap-Score as part of patient standard of care. Physicians received no compensation from Androvia.