# Quality of Life in Early-Stage HCM: A Secondary Analysis of the VANISH Trial

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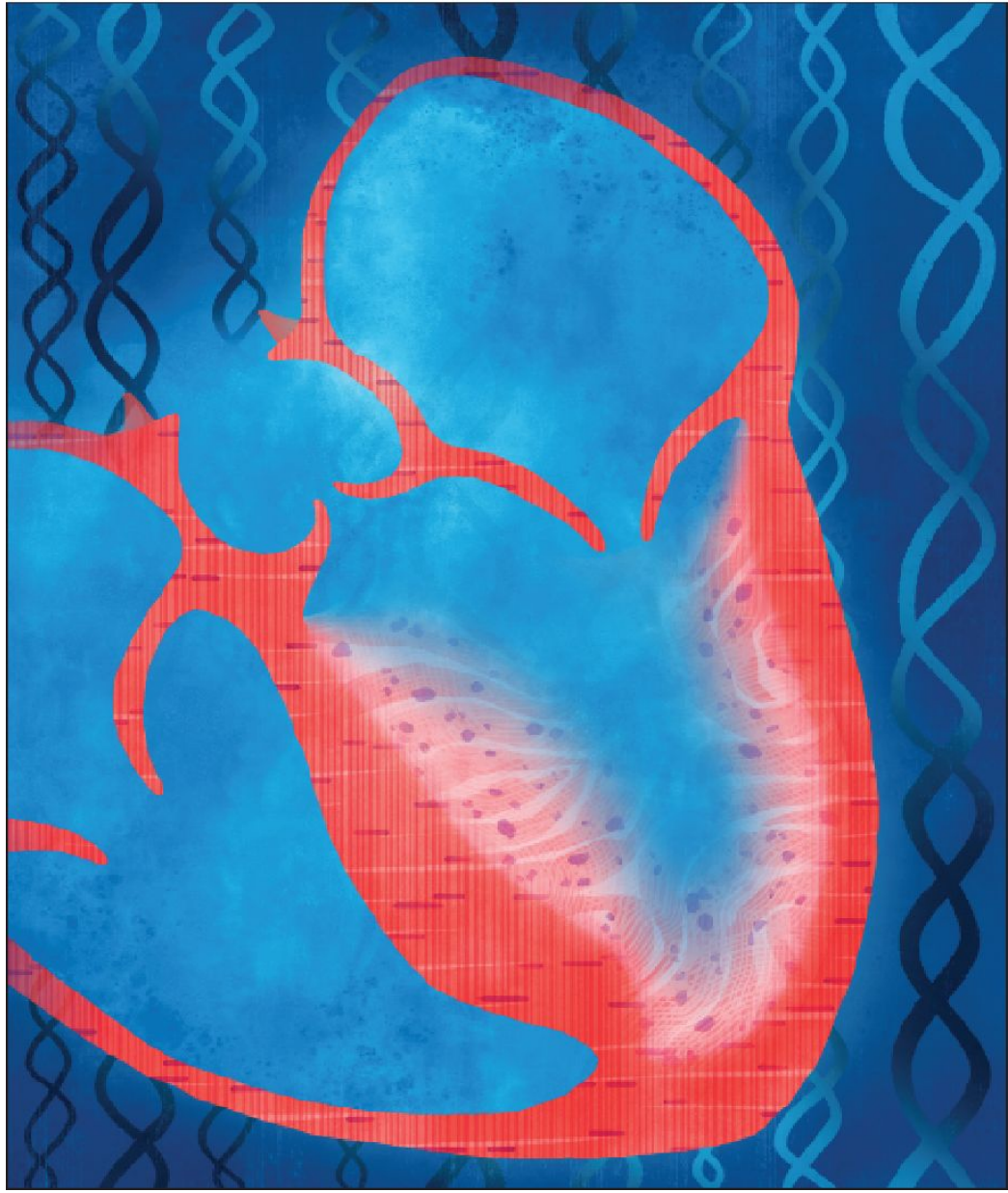
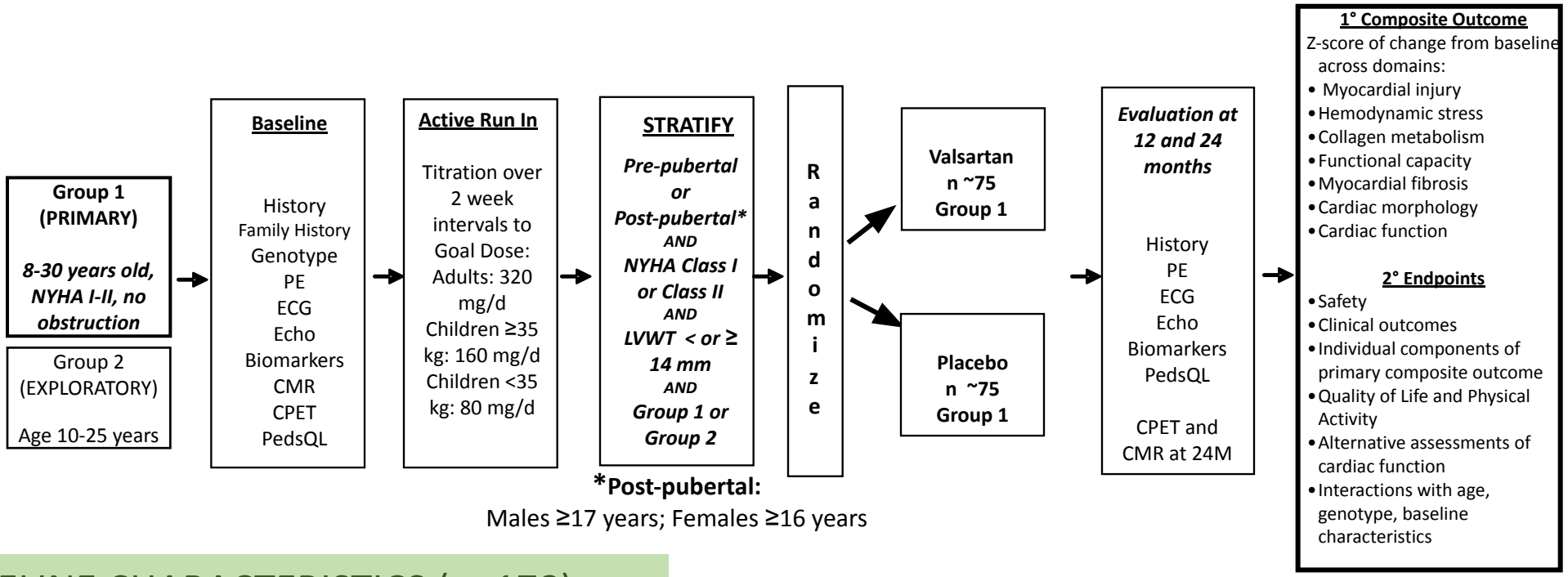


Cardiovascular Genetics Center

BRIGHAM AND WOMEN'S HOSPITAL

# Phase II Randomized, Placebo-controlled, Double-Blind Clinical Trial of Valsartan for Attenuating Disease Evolution in Early Sarcomeric HCM




***Post-pubertal:**
Males ≥17 years; Females ≥16 years

24 months treatment

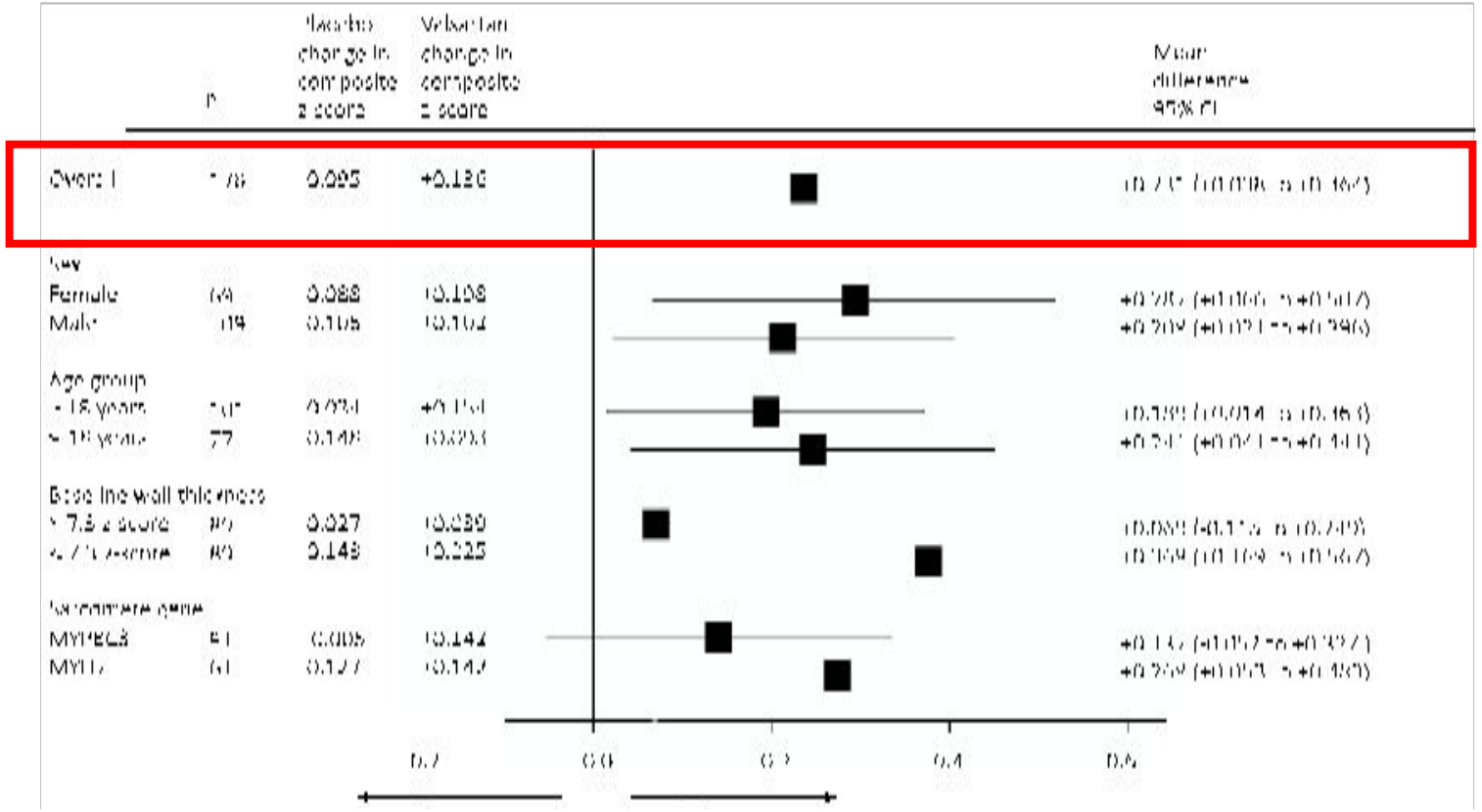
## BASELINE CHARACTERISTICS (n=178)

Mean Age 23 years
< age 18yrs 43%
Female 39%
Mean LVWT 17 mm, z-score 8

ClinicalTrials.gov NCT01912534

Ho CY, et al. *Am Heart J.* 2017

# Primary endpoint and prespecified subgroup analysis




Ho CY, et al, *Nature Medicine*, 2021

# Secondary QOL analysis

Do QoL scores vary between subclinical and early-stage HCM?

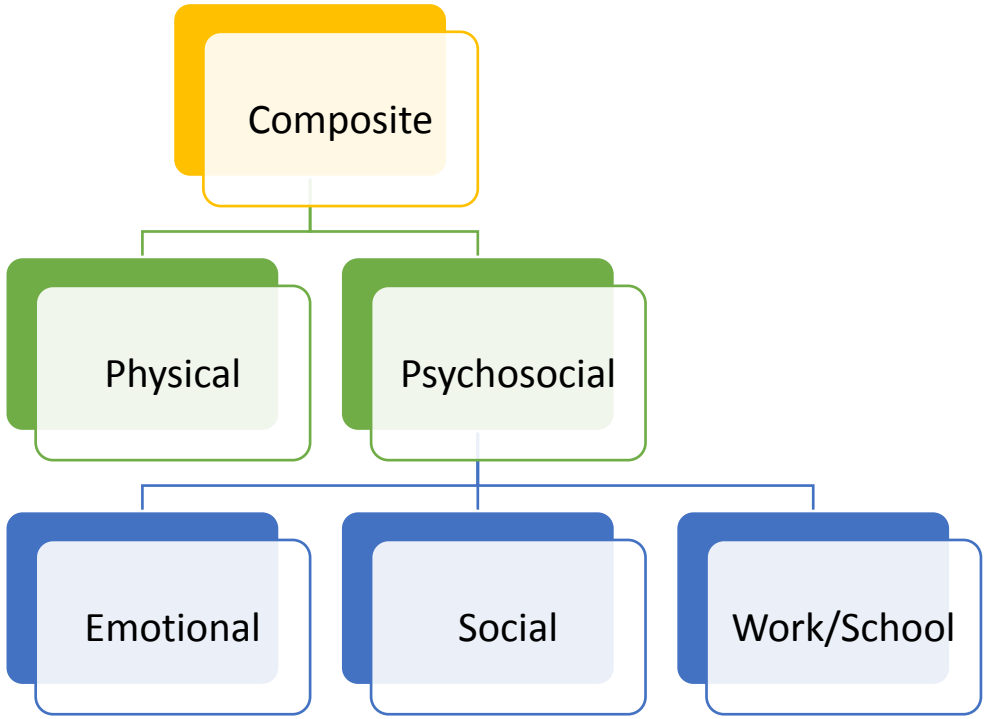
Are there baseline correlates of QoL in patients with early-stage HCM?

Does valsartan impact QoL in early-stage HCM?

# PedsQL structure

- 23 question Likert scale survey, reverse-scored and transformed to 0-100 scale (higher better)
- We used 4 versions by age:
  - Child: 8-12
  - Teen: 13-18
  - YA: 19-25
  - Adult: ≥26

Parent + child options



# In the past month, how often have you had a problem … (always, often, sometimes, never)

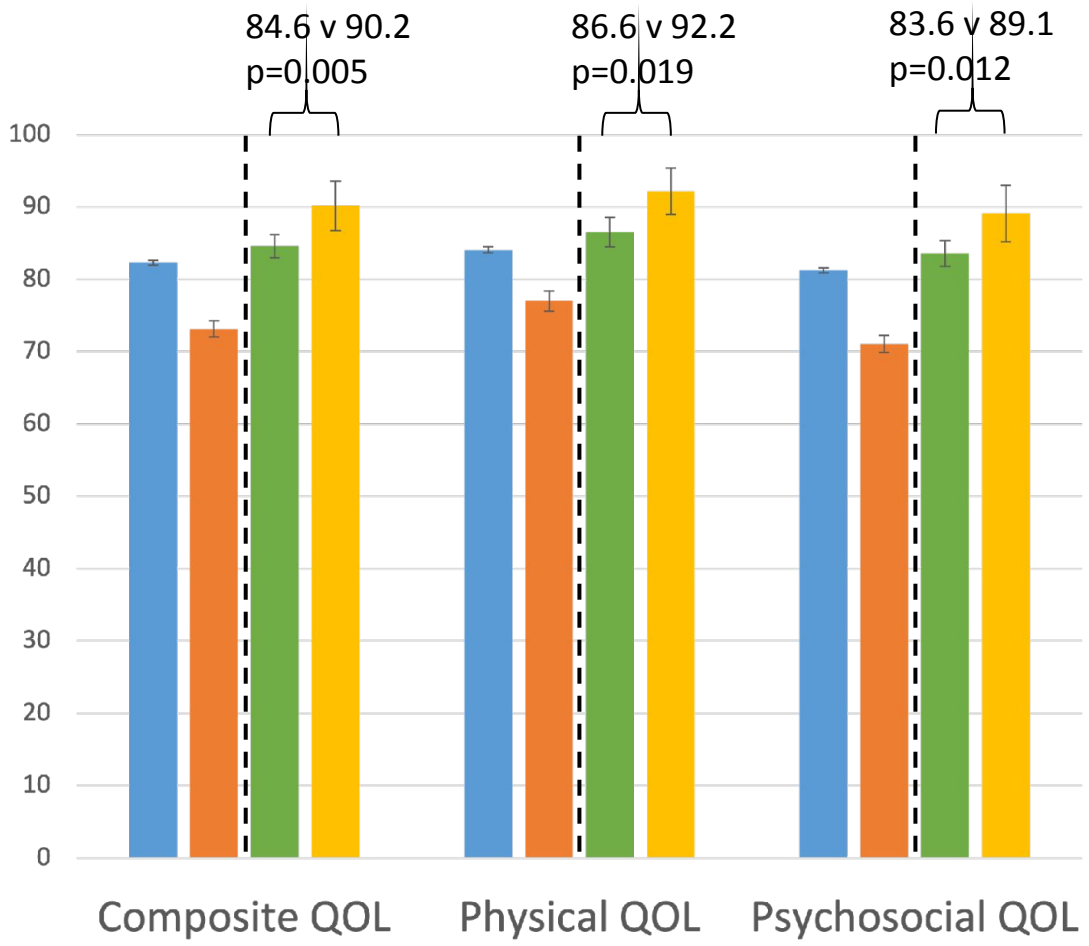
**Physical Function:**
- Walking >1 block
- Running
- Sports/exercise
- Lifting something heavy
- Bathing independently
- Household chores
- Low energy
- Having aches/pains

**Emotional Function:**
- Feeling afraid/scared
- Feeling sad/blue
- Feeling angry
- Trouble sleeping
- Worrying about what will happen to you

**Social Function:**
- Getting along with peers
- Peers not wanting to be a friend
- Getting teased by peers
- Not able to do things peers can do
- Keeping up playing with peers

**Work/School Function:**
- Paying attention
- Forgetting things
- Keeping up with assignments
- Missing time because not feeling well
- Missing time for medical care

# QOL in early-stage HCM is diminished compared to subclinical HCM




| Domain | Difference | MCID |
|---|---|---|
| Composite | 5.6 | 4.50 |
| Physical | 5.6 | 6.92 |
| Psychosocial | 5.5 | 5.49 |

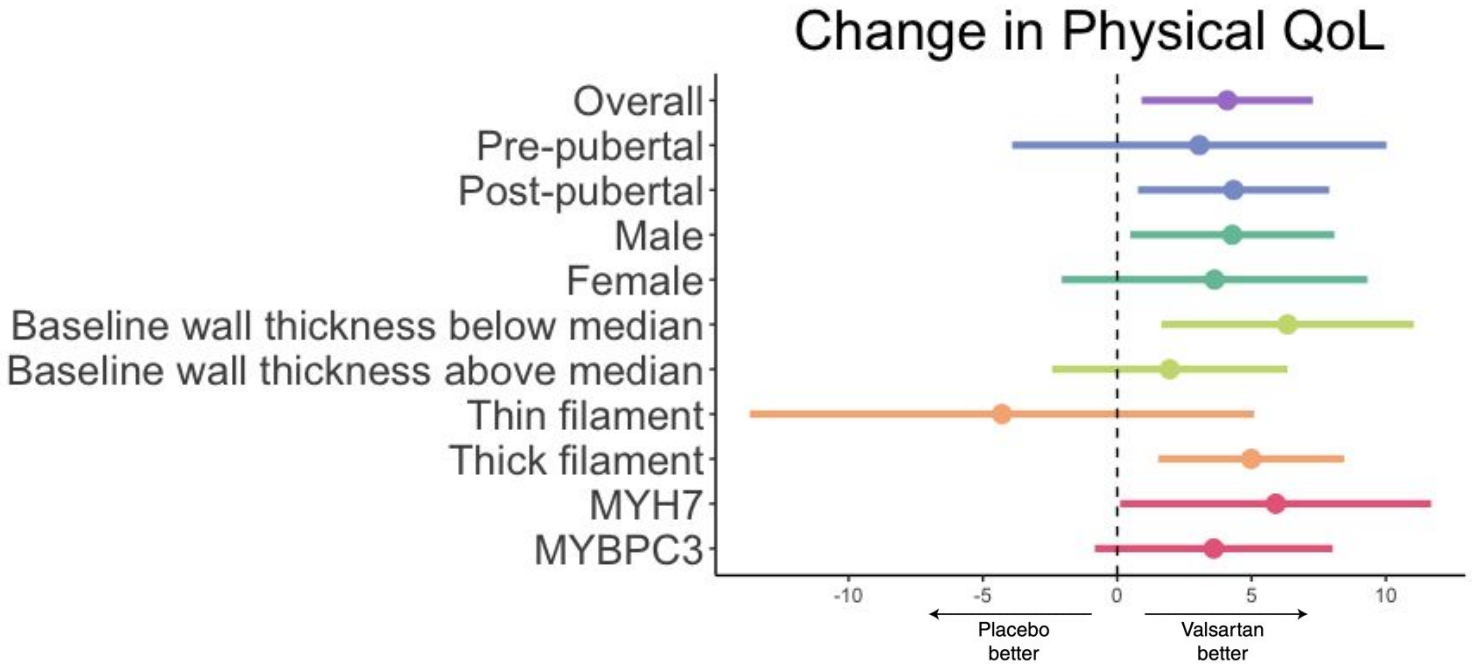
- Healthy validation cohort
- Chronically ill validation cohort
- VANISH early-stage HCM
- VANISH subclinical HCM

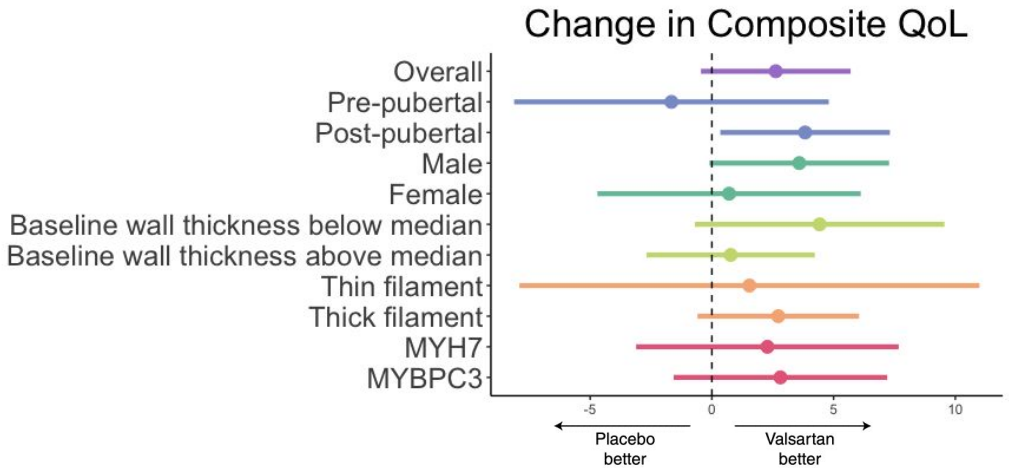
# Baseline correlates of QOL

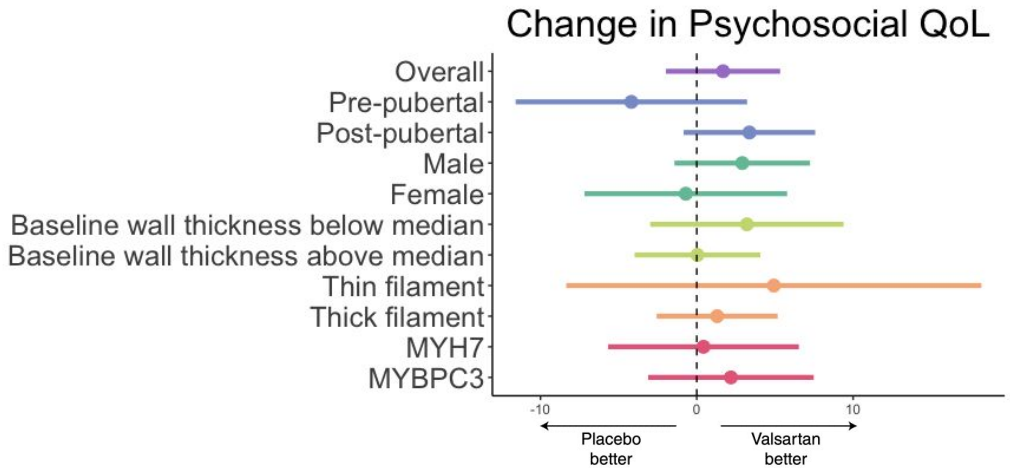
| | Composite QOL | | Physical QOL | | Psychosocial QOL | |
|---|---|---|---|---|---|---|
| | Estimate (95% CI) | p-value | Estimate (95% CI) | p-value | Estimate (95% CI) | p-value |
| Age, per 10 years | -0.3 (-2.0, 1.3) | 0.69 | **-3.5 (-5.4, -1.5)** | **<0.001** | 1.3 (-0.5, 3.1) | 0.14 |
| Pre-pubertal (vs post) | -0.3 (-3.7, 4.3) | 0.88 | 3.5 (-8.4, 1.3) | 0.15 | -2.4 (-2.0, 6.7) | 0.29 |
| Female sex (vs male) | -0.3 (-3.7, 3.0) | 0.85 | -3.4 (-7.5, 0.7) | 0.10 | 1.3 (-2.4, 5.0) | 0.49 |
| White race (vs non-white) | **13.9 (4.6, 23.2)** | **0.004** | **20.3 (8.9, 31.7)** | **<0.001** | **10.6 (0.1, 21.0)** | **0.048** |
| Non-Hispanic ethnicity (vs Hispanic) | **6.0 (2.1, 9.8)** | **0.003** | **8.3 (3.6, 13.1)** | **<0.001** | **4.7 (0.4, 9.1)** | **0.032** |
| Thick filament mutation (vs thin filament) | -3.8 (-8.8, 1.2) | 0.13 | -4.6 (-10.8, 1.5) | 0.14 | -3.3 (-8.9, 2.2) | 0.24 |
| Composite primary outcome z score, per 0.6 | 1.3 (-0.4, 2.9) | 0.13 | **3.7 (1.8, 5.6)** | **<0.001** | 0.0 (-1.8, 1.8) | 0.98 |
| Log NT-proBNP, per SD | -0.7 (-2.2, 0.9) | 0.41 | -2.1 (-4.0, -0.1) | 0.038 | 0.0 (-1.7, 1.8) | 0.98 |
| LV mass index, per 25 g/m$^2$ | -0.9 (-2.5, 0.8) | 0.30 | -1.2 (-3.2, 0.9) | 0.25 | -0.7 (-2.5, 1.1) | 0.45 |
| LA volume index, per 15 mL/m$^2$ | **-1.6 (-3.2, 0.0)** | **0.047** | **-3.4 (-5.3, -1.5)** | **<0.001** | -0.6 (-2.3, 1.2) | 0.51 |
| LV end diastolic volume index, per 17 mL/m$^2$ | 1.0 (-0.7, 2.6) | 0.26 | 1.6 (-0.4, 3.7) | 0.12 | 0.7 (-1.2, 2.5) | 0.49 |
| LV end systolic volume index, per 8 mL/m$^2$ | -0.3 (-1.8, 1.3) | 0.75 | -0.1 (-2.0, 1.8) | 0.92 | -0.3 (-2.0, 1.4) | 0.75 |
| Maximum LV wall thickness (BSA-adjusted z-score), per 5 | -0.3 (-2.1, 1.4) | 0.71 | **-2.7 (-4.8, -0.5)** | **0.014** | 0.9 (-1.0, 2.8) | 0.36 |
| E' velocity, per 3.2 cm/s | 0.9 (-0.7, 2.6) | 0.26 | **3.9 (1.9, 5.8)** | **<0.001** | -0.6 (-2.4, 1.2) | 0.52 |
| S' velocity, per 1.5 cm/s | 1.3 (-0.4, 2.9) | 0.14 | **3.6 (1.6, 5.7)** | **<0.001** | 0.0 (-1.9, 1.9) | 0.98 |
| Peak $VO_2$, per 9 ml/(kg min) | **2.2 (0.6, 3.8)** | **0.007** | **5.1 (3.2, 7.0)** | **<0.001** | 0.7 (-1.1, 2.5) | 0.44 |
| Percent predicted peak $VO_2$, per 16 % | **2.5 (0.9, 4.0)** | **0.003** | **3.6 (1.7, 5.5)** | **<0.001** | **1.9 (0.1, 3.6)** | **0.040** |
| $VE/VCO_2$ slope, per 5 | **-1.8 (-3.5, 0.0)** | **0.044** | **-3.3 (-5.4, -1.2)** | **0.003** | -1.0 (-3.0, 0.9) | 0.31 |

Estimate is represented as the beta-value in regression analysis. Positive effect size indicates increasing QOL; negative indicates decreasing QOL.

# Valsartan improves physical QOL



# Summary

- PedsQL allows evaluation of QOL domains across pediatric and adult age groups.
- Patients with early-stage HCM have a good baseline QOL, although reduced compared to those with only subclinical disease.
- QOL can vary with race and ethnicity, but larger and more diverse cohorts are needed to understand full impact.
- Valsartan improves physical QOL in early-stage HCM.

# Participating Sites

| Trial site | Principal investigator |
|---|---|
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| University of Michigan | Sharlene Day, MD |
| | Mark Russell, MD |
| Cleveland Clinic Foundation | Harry Lever, MD; |
| | Kenneth Zahka, MD |
| Boston Children's Hospital | Steven Colan, MD; |
| | Renee Margossian, MD |
| Yale University (virtual site) | Kevin Hall, MD |
| Vanderbilt University | Jason Becker, MD |
| Cincinnati Children's Hospital Medical Center | John Lynn Jeffries, MD |
| University of Chicago | Amit Patel, MD |
| Northwestern University (virtual site) | Lubna Choudhury, MD |
| Johns Hopkins University | Anne Murphy, MD |
| Washington University School of Medicine | Charles Canter, MD; |
| | Richard Bach, MD |
| University of Colorado, Denver | Matthew Taylor, MD; |
| | Luisa Mestroni, MD |
| Stanford University | Matthew Wheeler, MD |
| Toronto Hospital for Sick Children | Lee Benson, MD |
| Hospital of the University of Pennsylvania | Anjali Owens, MD |
| Children's Hospital of Philadelphia | Joseph Rossano, MD; |
| | Kim Lin, MD |
| Lurie Children's Hospital of Chicago | Elfriede Pahl, MD |
| INCOR (Instituto do Coração) | Alexandre Pereira, MD |
| Rigshospitalet | Henning Bundgaard, MD; |
| | Anna Axelsson Raja, MD |

VANISH

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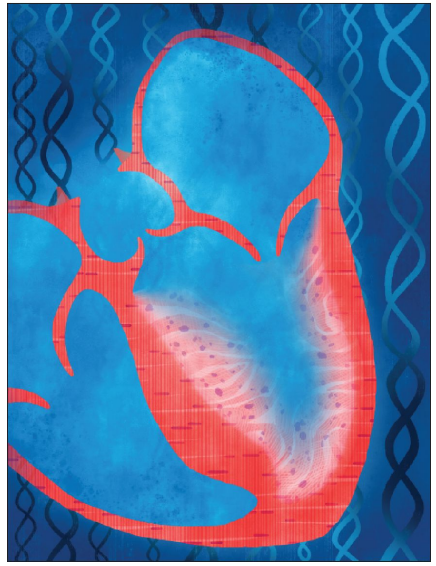


# Supplemental slides

# PedsQL scoring varies with age, reporter, and domain

**Table 2.** Scale Descriptives for PedsQL 4.0 Generic Core Scales: Child Self-Report and Parent Proxy-Report

| Scale | Scale Descriptives | | | | | Minimal Clinically Important Difference |
|---|---|---|---|---|---|---|
| | Number of items | N | Mean | SD | Range | SEM* |
| Child self-report | | | | | | |
| Total Score | 23 | 5972 | 82.87 | 13.16 | 0–100 | 4.36 |
| Physical Health | 8 | 5962 | 86.86 | 13.88 | 0–100 | 6.66 |
| Psychosocial Health | 15 | 5963 | 80.73 | 14.70 | 0–100 | 5.30 |
| Emotional Functioning | 5 | 5961 | 78.21 | 18.64 | 0–100 | 8.94 |
| Social Functioning | 5 | 5948 | 84.04 | 17.43 | 0–100 | 8.36 |
| School Functioning | 5 | 5908 | 79.92 | 16.93 | 0–100 | 9.12 |
| Parent proxy-report | | | | | | |
| Total Score | 23 | 10 070 | 81.34 | 15.92 | 0–100 | 4.50 |
| Physical Health | 8 | 10 050 | 83.26 | 19.98 | 0–100 | 6.92 |
| Psychosocial Health | 15 | 10 071 | 80.22 | 15.84 | 0–100 | 5.49 |
| Emotional Functioning | 5 | 10 044 | 80.28 | 16.99 | 0–100 | 7.79 |
| Social Functioning | 5 | 10 036 | 82.15 | 20.08 | 0–100 | 8.98 |
| School Functioning | 5 | 8466 | 76.91 | 20.16 | 0–100 | 9.67 |

*SEM indicates Standard Error of Measurement and was derived by multiplying the standard deviation by the square root of 1-alpha (Cronbach alpha reliability coefficient). The PedsQL 4.0 scores in the column represent the transformed value of 1 SEM. For example, a change in PedsQL 4.0 Total Scale Score for child self-report of 4.36 represents a minimal clinically important difference.

# Table 1: Baseline characteristics by cohort and treatment group

| | Early-stage HCM | | | Subclinical HCM |
|---|---|---|---|---|
| | Placebo (n=84) | Valsartan (n=82) | Full cohort (n=166) | Full cohort (n=34) |
| **Mean age, years** | 23.7 (10.1) | 23.1 (10.1) | 23.4 (10.1) | 16.4 (4.9) |
| **Pre-pubertal, n (%)** | 19 (22.6) | 17 (20.7) | 36 (21.7) | 14 (41.2) |
| **Female, n (%)** | 34 (40.5) | 32 (39.0) | 66 (39.8) | 17 (50.0) |
| **White, n (%)** | 82 (97.6) | 79 (96.3) | 161 (97.0) | 34 (100.0) |
| **Hispanic, n (%)** | 21 (25) | 15 (18.3) | 36 (21.7) | 1 (2.9) |
| **Country of enrollment, n (%)** | | | | |
| **USA** | 65 (77.4) | 65 (79.3) | 130 (78.3) | 32 (94.1) |
| **Brazil** | 15 (17.9) | 12 (14.6) | 27 (16.3) | 0 (0.0) |
| **Denmark** | 4 (4.8) | 5 (6.1) | 9 (5.4) | 2 (5.9) |
| **BMI, kg/m$^2$** | 25.6 (5.7) | 24.9 (5.7) | 25.2 (5.7) | 22.7 (4.8) |
| **Systolic BP, mmHg** | 118 (12) | 118 (10) | 118 (11) | 114 (12) |
| **NYHA class I, n (%)** | 79 (94.1) | 74 (90.2) | 153 (92.2) | 34 (100.0) |
| **NYHA class II, n (%)** | 5 (6.0) | 8 (9.8) | 13 (7.8) | 0 (0.0) |
| **LVEF, %** | 66.8 (7.1) | 66.2 (5.7) | 66.5 (6.5) | 64.1 (4.4) |
| **Beta blocker use, n (%)** | 14 (16.7) | 16 (19.5) | 30 (18.1) | 2 (5.9) |
| **Calcium channel blocker use, n (%)** | 1 (1.2) | 4 (4.9) | 5 (3.0) | 0 (0.0) |

# Table 2: Baseline quality of life, biomarker, imaging and exercise metrics

| | Early-stage HCM | | | Overall cohort | | |
|---|---|---|---|---|---|---|
| | Placebo (n=84) | Valsartan (n=82) | p-value | Early-stage HCM (n=166) | Subclinical HCM (n=34) | p-value |
| **Composite QOL, pts** | 85.0 (10.0) | 84.2 (11.3) | 0.62 | 84.6 (10.6) | 90.2 (9.8) | 0.005 |
| **Physical QOL, pts** | 86.3 (12.8) | 86.9 (13.6) | 0.77 | 86.6 (13.2) | 92.2 (9.2) | 0.019 |
| **Psychosocial QOL, pts** | 84.4 (10.9) | 82.7 (12.6) | 0.37 | 83.6 (11.8) | 89.1 (11.1) | 0.012 |
| **Composite primary outcome z-score** | 0.041 (0.548) | -0.055 (0.654) | 0.31 | -0.006 (0.603) | 0.000 (0.313) | 0.95 |
| **NT-proBNP, pg/ml (median, IQR)** | 88 (40, 201) | 124 (46, 427) | 0.06 | 101 (434, 294) | 32 (20, 63) | 0.003 |
| **LV mass index, g/m$^2$** | 73 (26) | 75 (24) | 0.61 | 74 (25) | 55 (10) | <0.001 |
| **LA volume index, ml/m$^2$** | 39 (16) | 39 (14) | 0.92 | 39 (15) | 30 (6) | 0.001 |
| **LV end diastolic volume index, ml/m$^2$** | 74 (16) | 75 (17) | 0.82 | 75 (17) | 77 (11) | 0.39 |
| **LV end systolic volume index, ml/m$^2$** | 25 (9) | 25 (8) | 0.65 | 25 (8) | 27 (6) | 0.20 |
| **Maximum LV wall thickness, mm** | 15.5 (3.7) | 16.5 (4.7) | 0.15 | 16 (10) | 4.2 (0.1) | <0.001 |
| **Maximum LV wall thickness, BSA-adjusted z-score** | 8.3 (4.2) | 9.5 (5.1) | 0.09 | 8.9 (4.7) | 2.6 (0.7) | <0.001 |
| **E' velocity, cm/s** | 9.5 (2.6) | 9.4 (3.7) | 0.82 | 9.4 (3.2) | 12.9 (2.1) | <0.001 |
| **S' velocity, cm/s** | 8.0 (1.4) | 7.7 (1.5) | 0.11 | 7.8 (1.5) | 8.2 (0.9) | 0.15 |
| **Peak $VO_2$, ml/(kg min)** | 31.9 (8.8) | 31.8 (9.3) | 0.92 | 31.9 (9.0) | 38.5 (8.8) | <0.001 |
| **Percent predicted peak $VO_2$, %** | 72 (15) | 71 (17) | 0.51 | 72 (16) | 78 (16) | 0.046 |
| **$VE/VCO_2$ slope** | 27.0 (4.5) | 27.6 (4.8) | 0.37 | 27.3 (4.7) | 27.5 (3.7) | 0.84 |
| **Peak watts** | 181 (61) | 173 (63) | 0.38 | 177 (62) | 174 (61) | 0.80 |
| **RER** | 1.18 (0.13) | 1.17 (0.10) | 0.75 | 1.18 (0.12) | 1.17 (0.11) | 0.80 |

# Supplemental Table 1: Baseline participant characteristics by non-white vs white race

| Baseline participant characteristics | Non-white (n=5) | White (n=161) | p-value |
|---|---|---|---|
| Mean age, years | 26.4 (11.4) | 23.3 (10.1) | 0.50 |
| Pre-pubertal, n (%) | 1 (20.0) | 35 (21.7) | 1.00 |
| Female, n (%) | 2 (40.0) | 64 (39.8) | 1.00 |
| Hispanic, n (%) | 4 (80.0) | 32 (19.9) | 0.008 |
| Country of enrollment, n (%) | | | 0.40 |
| USA | 3 (60.0) | 127 (78.9) | |
| Brazil | 2 (40.0) | 25 (15.5) | |
| Denmark | 0 (0.0) | 9 (5.6) | |
| Thick filament mutation, n (%) | 5 (100.0) | 141 (87.6) | 0.27 |
| BMI | 28.0 (7.1) | 25.1 (5.6) | 0.96 |
| Systolic BP, mmHg | 118 (7) | 118 (11) | 1.00 |
| NYHA class I, n (%) | 5 (100.0) | 148 (91.9) | 1.00 |
| NYHA class II, n (%) | 0 (0.0) | 13 (8.1) | 0.67 |
| LVEF, % | 65.3 (2.9) | 66.5 (6.5) | 1.00 |
| Beta blocker use, n (%) | 1 (20.0) | 29 (18.0) | 0.14 |
| Calcium channel blocker use, n (%) | 1 (20.0) | 4 (2.5) | <0.001 |
| Composite z-score | -0.956 (0.683) | 0.023 (0.578) | 0.002 |
| NT-proBNP, pg/ml (median, IQR) | 668 (323, 795) | 92 (41, 265) | 0.002 |
| LV mass index, $g/m^2$ | 108 (34) | 73 (24) | <0.001 |
| LA volume index, $ml/m^2$ | 64 (30) | 38 (14) | 0.85 |
| LV end diastolic volume index, $ml/m^2$ | 76 (15) | 75 (17) | 0.81 |
| LV end systolic volume index, $ml/m^2$ | 26 (6) | 25 (8) | 0.003 |
| Maximum LV wall thickness, mm | 21.4 (4.3) | 15.8 (4.1) | 0.005 |
| Maximum LV wall thickness, BSA-adjusted z-score | 14.7 (4.1) | 8.7 (4.6) | 0.015 |
| E' velocity, cm/s | 6.0 (2.7) | 9.5 (3.2) | 0.07 |
| S' velocity, cm/s | 6.7 (1.8) | 7.9 (1.4) | 0.30 |
| Peak $VO_2$, ml/(kg min) | 27.7 (16.0) | 32.0 (8.8) | 0.17 |
| $VE/VCO_2$ slope | 30.1 (5.8) | 27.2 (4.6) | 0.20 |
| Peak watts | 142 (72) | 178 (62) | 0.39 |
| RER | 1.22 (0.11) | 1.18 (0.12) | 0.10 |
| Percent predicted peak $VO_2$, % | 60 (21) | 72 (16) | 0.27 |

# Supplemental Table 2: Baseline participant characteristics by non-Hispanic vs Hispanic ethnicity

| Baseline participant characteristics | Non-Hispanic (n=36) | Hispanic (n=130) | p-value |
|---|---|---|---|
| Mean age, years | 21.8 (9.3) | 29.1 (11.1) | <0.001 |
| Pre-pubertal, n (%) | 29 (22.3) | 7 (19.4) | 0.82 |
| Female, n (%) | 52 (40.0) | 14 (38.9) | 1.00 |
| White, n (%) | 129 (99.2) | 32 (88.9) | 0.008 |
| Country of enrollment, n (%) | | | <0.001 |
| USA | 121 (93.1) | 9 (25.0) | |
| Brazil | 0 (0.0) | 27 (75.0) | |
| Denmark | 9 (6.9) | 0 (0.0) | |
| Thick filament mutation, n (%) | 110 (84.6) | 36 (100.0) | 0.008 |
| BMI | 25.0 (5.8) | 26.0 (5.0) | 0.33 |
| Systolic BP, mmHg | 119 (11) | 115 (10) | 0.14 |
| NYHA class I, n (%) | 124 (95.4) | 29 (80.6) | 0.008 |
| NYHA class II, n (%) | 6 (4.6) | 7 (19.4) | 0.008 |
| LVEF, % | 66.7 (6.8) | 65.6 (4.8) | 0.34 |
| Beta blocker use, n (%) | 18 (13.9) | 12 (33.3) | 0.013 |
| Calcium channel blocker use, n (%) | 3 (2.3) | 2 (5.6) | 0.30 |
| Composite z-score | 0.091 (0.546) | -0.360 (0.670) | <0.001 |
| NT-proBNP, pg/ml (median, IQR) | 78 (37, 208) | 245 (104, 496) | <0.001 |
| LV mass index, $g/m^2$ | 73 (25) | 77 (24) | 0.36 |
| LA volume index, $ml/m^2$ | 36 (13) | 50 (20) | <0.001 |
| LV end diastolic volume index, $ml/m^2$ | 74 (17) | 78 (17) | 0.14 |
| LV end systolic volume index, $ml/m^2$ | 25 (8) | 26 (10) | 0.41 |
| Maximum LV wall thickness, mm | 15.3 (4.0) | 18.4 (4.3) | <0.001 |
| Maximum LV wall thickness, BSA-adjusted z-score | 8.2 (4.6) | 11.4 (4.5) | <0.001 |
| E' velocity, cm/s | 10.0 (3.0) | 7.3 (3.1) | <0.001 |
| S' velocity, cm/s | 8.0 (1.4) | 7.3 (1.5) | 0.007 |
| Peak $VO_2$, ml/(kg min) | 32.5 (9.1) | 29.4 (8.4) | 0.07 |
| $VE/VCO_2$ slope | 27.0 (4.8) | 28.3 (3.8) | 0.13 |
| Peak watts | 180 (65) | 167 (51) | 0.27 |
| RER | 1.17 (0.12) | 1.21 (0.09) | 0.05 |
| Percent predicted peak $VO_2$, % | 72 (17) | 69 (14) | 0.27 |

# Supplemental Table 3: Baseline QOL in white vs non-white race, univariate adjustment

| | Composite QOL | | Physical QOL | | Psychosocial QOL | |
|---|---|---|---|---|---|---|
| | Estimate (95% CI) | p-value | Estimate (95% CI) | p-value | Estimate (95% CI) | p-value |
| **Unadjusted** | 13.9 (4.6, 23.2) | 0.004 | 20.3 (8.9, 31.7) | 0.001 | 10.6 (0.1, 21.0) | 0.048 |
| **Age** | 13.9 (4.5, 23.2) | 0.004 | 19.3 (8.2, 30.3) | 0.001 | 11.0 (0.6, 21.4) | 0.039 |
| **Country of origin** | 12.6 (3.4, 21.8) | 0.008 | 18.0 (6.8, 29.2) | 0.002 | 9.7 (-0.7, 20.1) | 0.066 |
| **Hispanic vs non-Hispanic ethnicity** | 11.0 (1.5, 20.5) | 0.023 | 16.3 (4.7, 27.9) | 0.006 | 8.2 (-2.5, 18.9) | 0.132 |
| **Thick filament mutation** | 13.5 (4.2, 22.8) | 0.005 | 19.8 (8.4, 31.2) | 0.001 | 10.2 (-0.3, 20.7) | 0.056 |
| **NYHA class** | 14.6 (5.5, 23.7) | 0.002 | 21.6 (10.8, 32.4) | <0.001 | 11.0 (0.5, 21.4) | 0.04 |
| **Beta blocker use** | 13.9 (4.6, 23.1) | 0.004 | 20.2 (8.9, 31.5) | 0.001 | 10.5 (0.1, 21.0) | 0.049 |
| **Log NT-proBNP** | 13.5 (4.0, 3.0) | 0.006 | 18.3 (6.6, 30.0) | 0.002 | 10.9 (0.2, 21.6) | 0.045 |
| **Maximum LV wall thickness, BSA-adjusted z-score** | 14.2 (4.6, 3.8) | 0.004 | 17.9 (6.3, 29.6) | 0.003 | 12.2 (1.5, 22.9) | 0.025 |

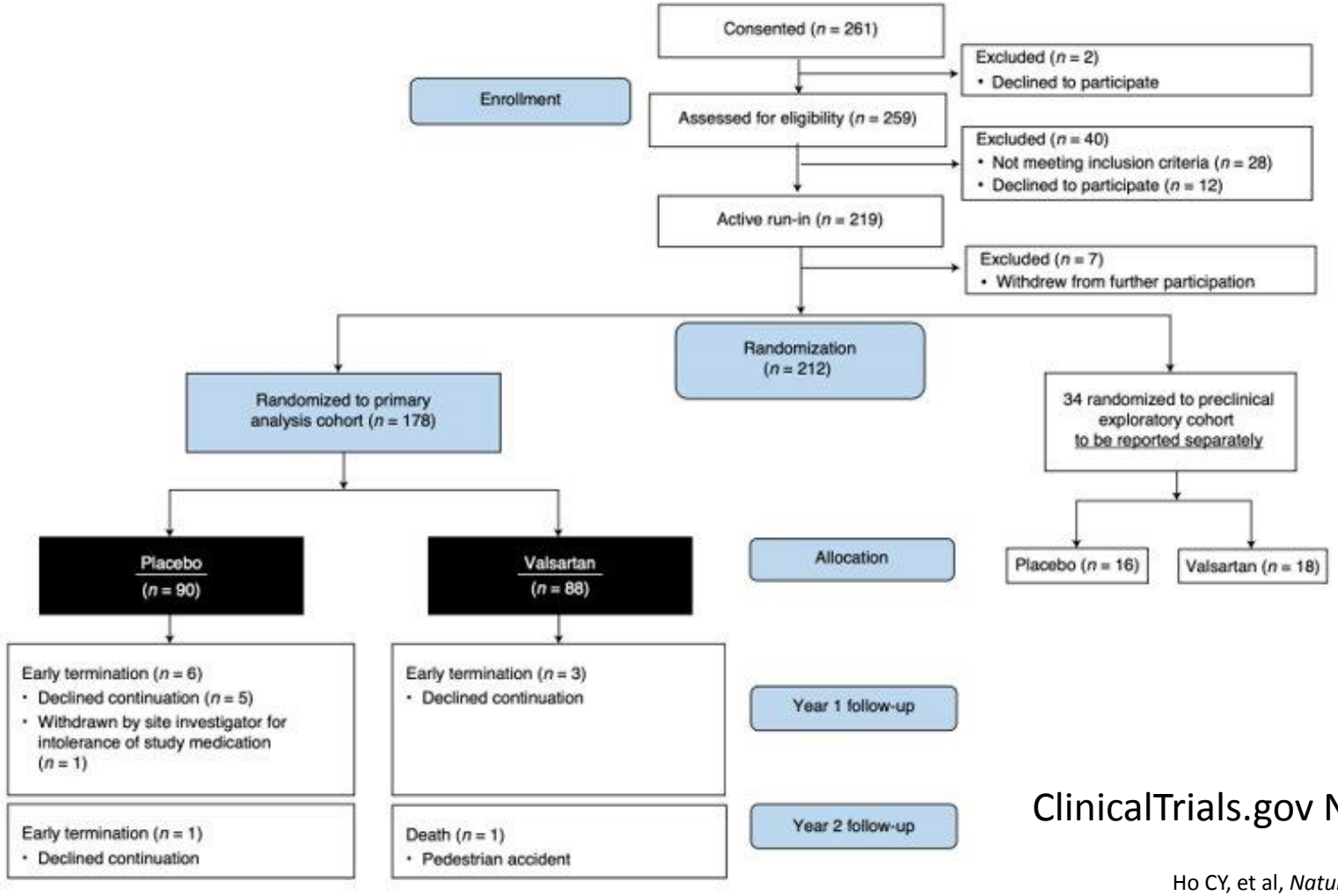
# Supplemental Table 4: Baseline QOL in Hispanic vs non-Hispanic ethnicity, univariate adjustment

| | Composite QOL | | Physical QOL | | Psychosocial QOL | |
|---|---|---|---|---|---|---|
| | Estimate (95% CI) | p-value | Estimate (95% CI) | p-value | Estimate (95% CI) | p-value |
| **Unadjusted** | -6.0 (-9.8, -2.1) | 0.003 | -8.3 (-13.1, -3.6) | 0.001 | -4.7 (-9.1, -0.4) | 0.032 |
| **Unadjusted, Hispanic vs non-Hispanic in American participants*** | -7.3 (-14.2, -0.4) | 0.037 | -3.6 (-11.6, 4.3) | 0.369 | -9.3 (-17.3, -1.4) | 0.022 |
| **Age** | -6.3 (-10.3, -2.2) | 0.003 | -6.4 (-11.2, -1.5) | 0.011 | -6.2 (-10.7, -1.8) | 0.007 |
| **Country of origin** | -7.3 (-14.3, -0.3) | 0.041 | -3.6 (-12.3, 5.0) | 0.41 | -9.3 (-17.1, -1.5) | 0.019 |
| **White vs non-white race** | -4.8 (-8.8, -0.9) | 0.017 | -6.6 (-11.4, -1.8) | 0.007 | -3.9 (-8.3, 0.6) | 0.086 |
| **Thick filament mutation** | -5.6 (-9.5, -1.7) | 0.006 | -7.9 (-12.7, -3.1) | 0.002 | -4.4 (-8.8, 0.0) | 0.051 |
| **NYHA class** | -5.0 (-8.9, -1.1) | 0.013 | -6.4 (-11.1, -1.7) | 0.008 | -4.3 (-8.7, 0.2) | 0.059 |
| **Beta blocker use** | -5.6 (-9.5, -1.6) | 0.006 | -7.6 (-12.4, -2.7) | 0.002 | -4.5 (-9.0, -0.1) | 0.045 |
| **Log NT-proBNP** | -5.7 (-9.7, -1.7) | 0.005 | -7.3 (-12.2, -2.4) | 0.004 | -4.9 (-9.4, -0.4) | 0.034 |
| **Maximum LV wall thickness, BSA-adjusted z-score** | -6.2 (-10.3, -2.2) | 0.003 | -7.2 (-12.1, -2.3) | 0.004 | -5.8 (-10.2, -1.3) | 0.012 |

# Supplemental Table 5: Quality of life score changes with valsartan

| Composite QOL | n | Mean difference | Confidence interval | p-value |
|---|---|---|---|---|
| Overall | 166 | 2.6 | (-0.4, 5.7) | 0.09 |
| Pre-pubertal | 36 | -1.7 | (-8.1, 4.8) | 0.61 |
| Post-pubertal | 130 | 3.8 | (0.3, 7.3) | 0.031 |
| Male | 100 | 3.6 | (-0.1, 7.3) | 0.06 |
| Female | 66 | 0.7 | (-4.7, 6.1) | 0.80 |
| LV wall thickness < median | 83 | 4.4 | (-0.7, 9.6) | 0.09 |
| LV wall thickness > median | 83 | 0.8 | (-2.7, 4.2) | 0.66 |
| Thin filament variant | 20 | 1.5 | (-7.9, 11.0) | 0.73 |
| Thick filament variant | 146 | 2.7 | (-0.6, 6.0) | 0.11 |
| MYH7 variant | 59 | 2.3 | (-3.1, 7.7) | 0.40 |
| MYBPC3 variant | 82 | 2.8 | (-1.6, 7.2) | 0.21 |
| Physical QOL | n | Mean difference | Confidence interval | p-value |
| Overall | 166 | 4.1 | (0.9, 7.3) | 0.012 |
| Pre-pubertal | 36 | 3.1 | (-3.9, 10.0) | 0.38 |
| Post-pubertal | 130 | 4.3 | (0.8, 7.9) | 0.018 |
| Male | 100 | 4.3 | (0.5, 8.1) | 0.028 |
| Female | 66 | 3.6 | (-2.1, 9.3) | 0.21 |
| LV wall thickness < median | 83 | 6.3 | (1.6, 11.0) | 0.009 |
| LV wall thickness > median | 83 | 2.0 | (-2.4, 6.3) | 0.38 |
| Thin filament variant | 20 | -4.3 | (-13.7, 5.1) | 0.35 |
| Thick filament variant | 146 | 5.0 | (1.5, 8.4) | 0.005 |
| MYH7 variant | 59 | 5.9 | (0.1, 11.7) | 0.046 |
| MYBPC3 variant | 82 | 3.6 | (-0.8, 8.0) | 0.11 |
| Psychosocial QOL | n | Mean difference | Confidence interval | p-value |
| Overall | 166 | 1.7 | (-2.0, 5.3) | 0.37 |
| Pre-pubertal | 36 | -4.2 | (-11.6, 3.2) | 0.26 |
| Post-pubertal | 130 | 3.4 | (-0.8, 7.6) | 0.12 |
| Male | 100 | 2.9 | (-1.4, 7.3) | 0.19 |
| Female | 66 | -0.7 | (-7.2, 5.8) | 0.83 |
| LV wall thickness < median | 83 | 3.2 | (-3.0, 9.4) | 0.31 |
| LV wall thickness > median | 83 | 0.0 | (-4.0, 4.1) | 0.98 |
| Thin filament variant | 20 | 4.9 | (-8.3, 18.2) | 0.44 |
| Thick filament variant | 146 | 1.3 | (-2.6, 5.2) | 0.51 |
| MYH7 variant | 59 | 0.4 | (-5.7, 6.5) | 0.89 |
| MYBPC3 variant | 82 | 2.2 | (-3.1, 7.5) | 0.41 |

# VANISH: A Phase II Randomized, Placebo-controlled, Double-Blind Clinical Trial of Valsartan for Attenuating Disease Evolution in Early Sarcomeric HCM




ClinicalTrials.gov NCT01912534

Ho CY, et al, *Nature Medicine,* 2021