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Increased Quality of Life with Immediate ART Initiation: Results from the START Trial

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Background

- Health-related quality of life (QOL) reflects a person's subjective assessment of his or her physical, emotional, and functional health status.
- HIV-related illnesses or medication side effects can both affect QOL. QOL is therefore an important outcome in assessing HIV treatment strategies. 1,2

OSTART

- Strategic Timing of Antiretroviral Therapy (START) is a multi-country study which randomized antiretroviral therapy (ART) naive participants with CD4+ >500 cells/mm³ to immediate ART vs. deferral of ART to either CD4 \leq 350 cells or clinical disease requiring ART.
- In START, immediate ART reduced the risk of AIDS-related events, serious non–AIDS events, or death by 57%, after a mean follow-up of 3 years ³.

Methods

QOL Measures

- QOL measures were obtained at baseline, month 4, 12 and then annually.
- We compared immediate vs. deferred ART groups for changes in four QOL measures:
 - (1) Current health visual analogue scale (VAS, 0-100): patient self-assessment of overall current health
 - (2) General health perception (single item) from the Short-Form 12-Item Health Survey version 2 (SF-12v2)⁴, 4-week recall, scaled to 0-100.
 - (3) Physical component summary (PCS) score from the SF-12v2
 - (4) Mental component summary (MCS) score from the SF-12v2
- PCS and MCS scores are standardized to mean=50, SD=10 in a U.S. reference population.

For all 4 measures, higher scores denote better QOL.

Current Health (VAS)

Using the line as a guide, mark on the line below your current state of health: 0 is worst possible health and 100 is perfect health:

General Health Perception (SF-12v2)

In general, would you say your health is:

|Excellent Very good

Other Items from the SF-12v2, examples

During the past 4 weeks, how much did pain interfere with your normal work (including both work outside and the home and housework?

□ Not at all □ A little bit □ Moderately □ Quite a bit □ Extremely

These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks.

A little of None of the time the time Have you felt calm and peaceful?

Statistical Methods:

- For each of the 4 QOL outcomes, the immediate and deferred ART groups were compared for changes from baseline, by intent-to-treat, using longitudinal mixed models adjusted for visit and baseline QOL.
- As a sensitivity analysis, follow-up in the deferred ART group was censored at ART start.

Study Participants

- 4561 of 4685 randomized participants had baseline and at least one follow-up QOL measure (4540 for the VAS and 4021 reported all items on the SF-12v2). Participants enrolled in 35 countries; in some countries, only VAS was collected.
- Baseline characteristics of participants are summarized in Table 1.

Table 1. Baseline Characteristics

	Median [IQR] or %	
Age	36	[29, 44]
Sex (% female)	26.8	
Race/Ethnicity (%)		
Asian	8.4	
Black	30.2	
Latino/Hispanic	13.6	
White/Other	47.8	
Likely mode of HIV infection (%)		
Sexual contact, same sex	55.2	
Sexual contact, opposite sex	38.2	
Injection drug use	1.4	
Other/unknown	5.2	
Geographic region: high-income countries (%)	45.8	
CD4+ (cells/mm ³)	651	[583, 763]
HIV RNA (log ₁₀ copies/mL)	4.1	[3.5, 4.6]
Smoking (%)	31.9	
Framingham 10-year risk of CHD	3.7	[0.5, 5.2]
Psychiatric diagnoses (%)	5.7	

Table 2. Baseline QOL Scores

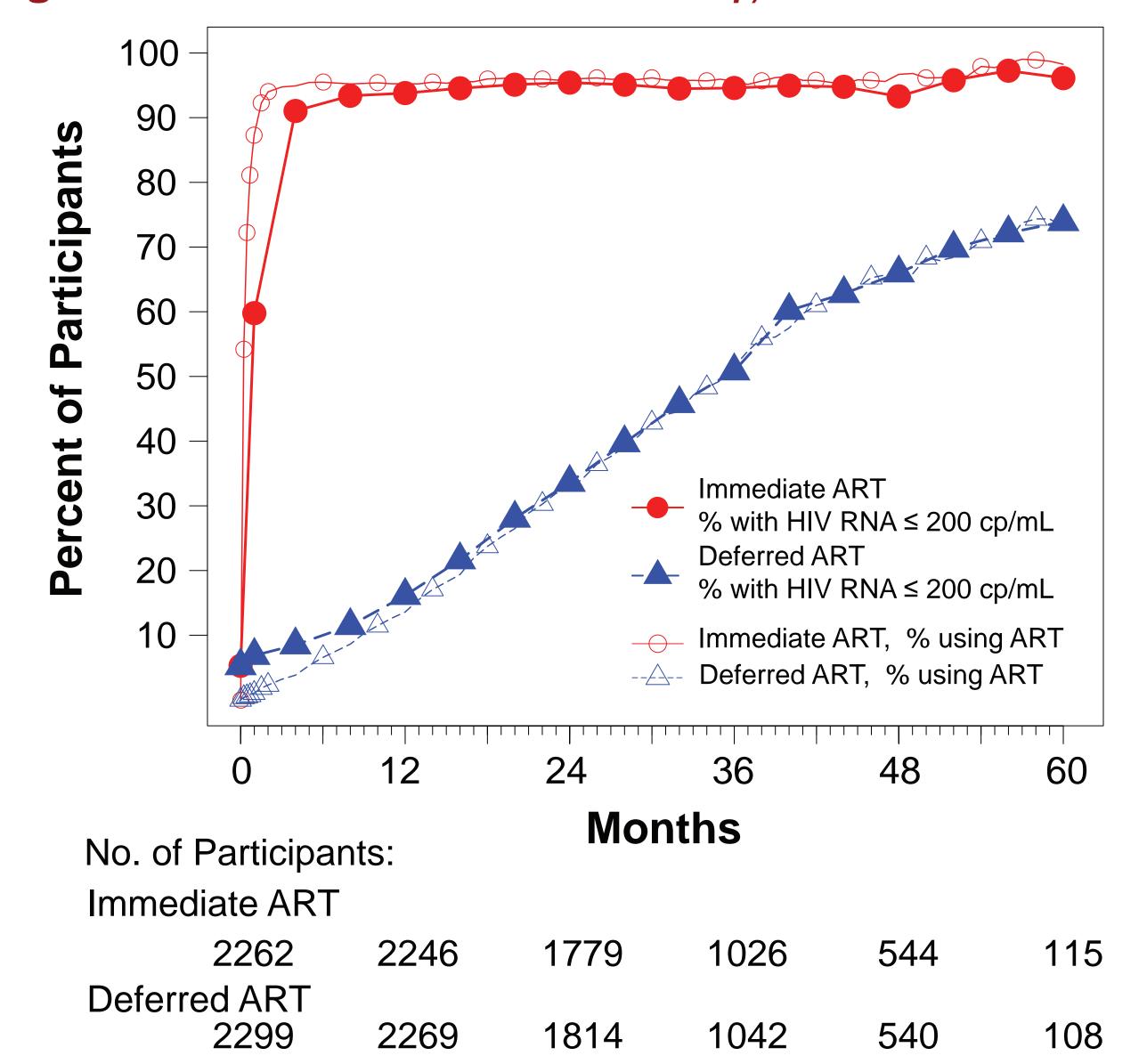
Current Health (Visual Analog Scale)	80.9	(15.7)
SF-12 v2		
General Health	72.5	(21.5)
Physical Component Summary (PCS)	53.7	(7.2)
Mental Component Summary (MCS)	48.2	(10.5)

ART Use

- Median follow-up time=2.6 years
- Percent of follow-up time on ART: 95% for the immediate group vs. 28% for the deferred group (Figure 1). In the immediate ART group, the first ART regimen contained EFV for 73% of participants, any NNRTIs for 77%, protease inhibitors for 19%, and integrase inhibitors for 4% of participants.

Mean (SD)

Figure 1: ART Use and HIV RNA ≤ 200 cp/mL

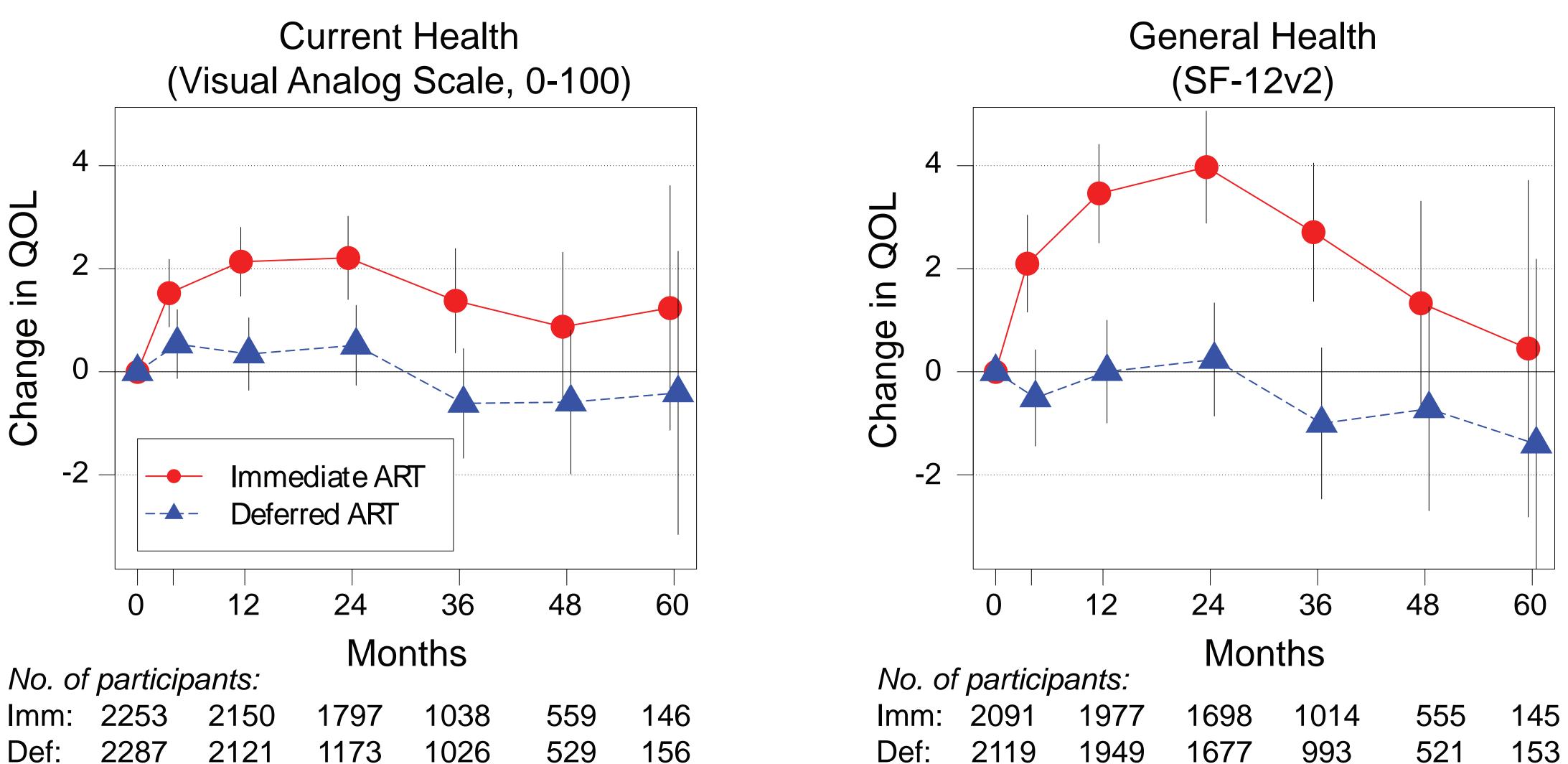


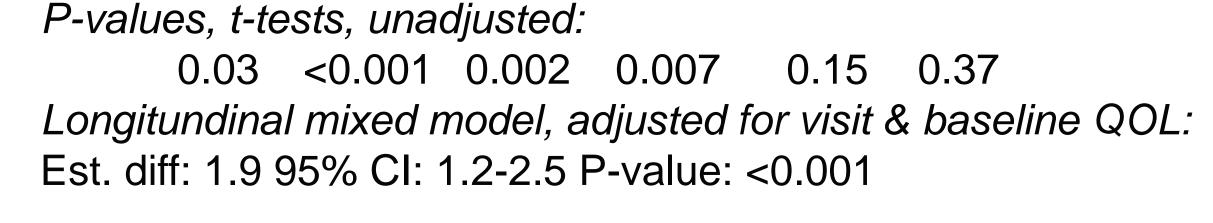
Results

Immediate vs. Deferred Group

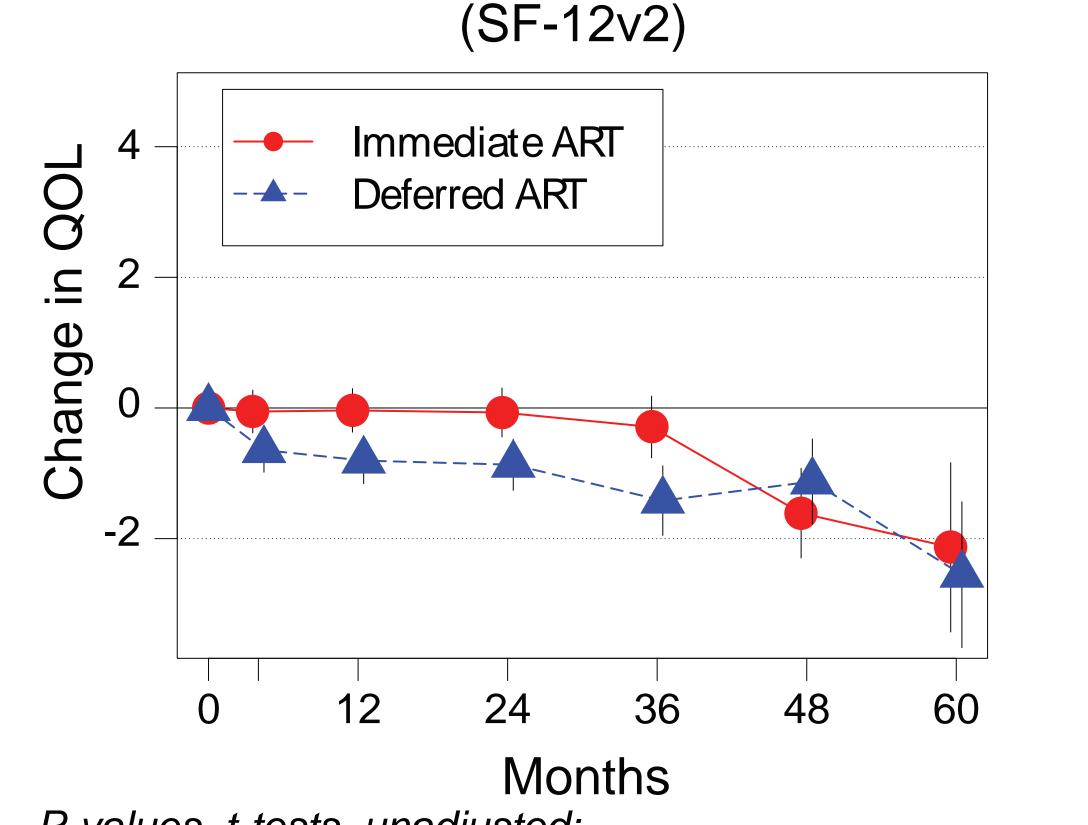
- Throughout follow-up, change in QOL favored the immediate group, in all 4 measures of QOL (p<0.001 for each measure) (Figure 2).
- Modest but significant differences were seen as early as 4 months, with increases in the immediate ART group through 24 months in the general health and MCS scales, and through 12 months in the current health visual analogue scale.
- Sensitivity analysis: Differences between groups were similar or slightly larger when follow-up for participants in the deferred group was censored at ART start and immediate group participants who never used ART were excluded (p<0.001 for difference for each measure).

Figure 2. Change in QOL (Mean +/- 2 SE), Immediate vs. Deferred Group

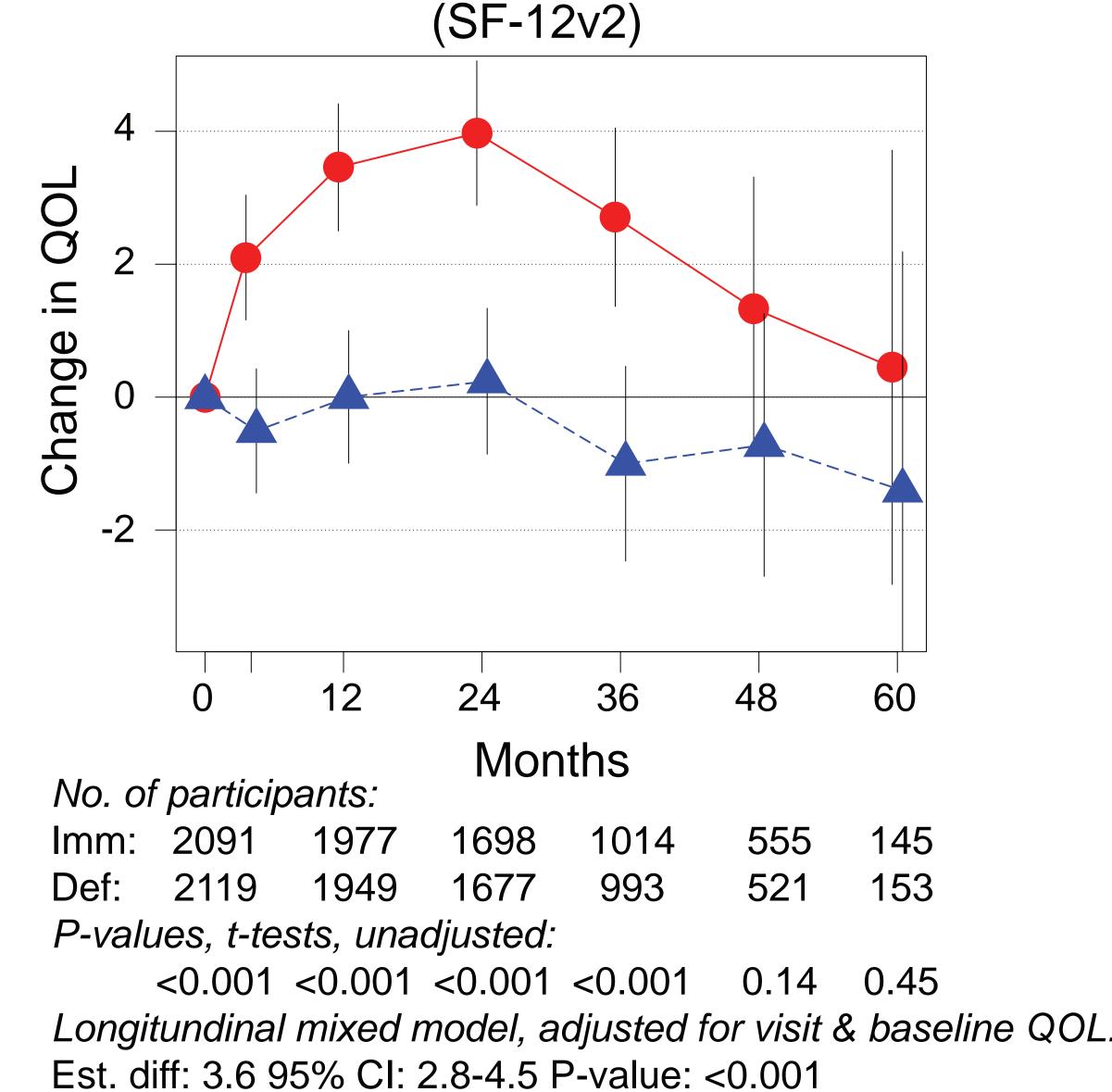


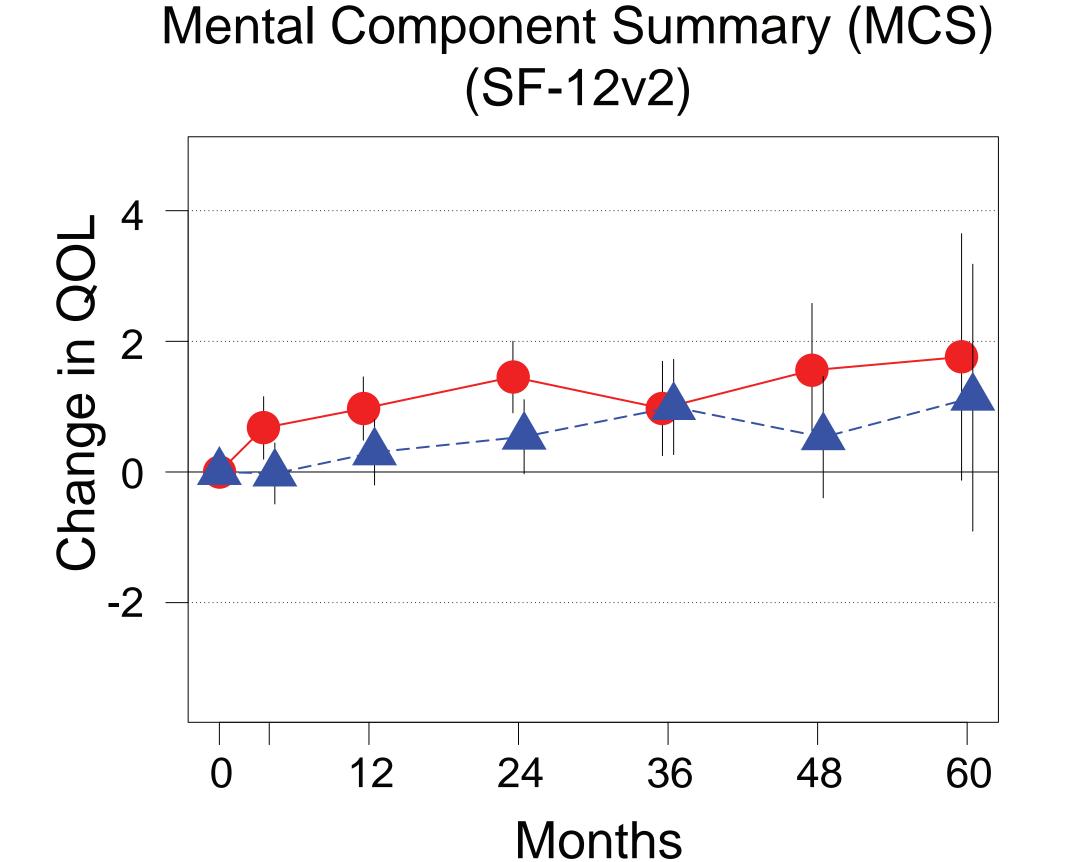


Physical Component Summary (PCS)



P-values, t-tests, unadjusted: 0.01 0.002 0.003 0.002 0.31 0.62 Longitundinal mixed model, adjusted for visit & baseline QOL: Est. diff: 0.8 95% CI: 0.5-1.1 P-value: <0.001





P-values, t-tests, unadjusted: 0.04 0.05 0.02 0.97 0.14 0.65 Longitundinal mixed model, adjusted visit & baseline QOL: Est. diff: 0.9 95% CI: 0.4-1.3 P-value: <0.001

Discussions and Limitations

- QOL differences between immediate and deferred groups were significant but generally modest.
- Change in QOL favored the immediate ART group in about equal measure in both the physical and mental health components of the SF-12v2.
- In the immediate ART group, the general health perception and current health improved relative to baseline, while remaining stable or decreasing slightly in the deferred ART group. Increases in QOL relative to baseline in the immediate group were primarily reflected by increases in MCS.
- START enrolled a specific population of people with HIV who were generally healthy and ART naive, with relatively high QOL scores. Maintenance of high quality of life is an important goal for those on ART.
- Limitations:
- o Treatment assignments were not blinded. Knowledge of ART treatment status may have affected QOL responses.
- o QOL measures reflect a subjective assessment of health status; participants from diverse cultures may attach different significance to symptoms/limitations. Because of randomization, such differences should minimally affect our primary results of treatment group differences.
- o PCS and MCS scores were standardized based upon U.S. populations, and the significance of a specific numerical QOL score may vary across countries.
- o Many biologic and socioeconomic factors not included in this analysis may also impact QOL, and are important for clinical care and psychosocial support of persons with HIV.

Conclusions

In this HIV-positive population with CD4 >500 cells/mm³ that was generally in good health, QOL improved in the immediate compared to the deferred ART group. These findings provide further support to the superiority of early ART as reported for major clinical outcomes in the START study.

Acknowledgements

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