

Supplemental Online Content

Temel JS, Jackson VA, El-Jawahri A, et al. Stepped palliative care for patients with advanced lung cancer. *JAMA*. Published online June 2, 2024.
doi:10.1001/jama.2024.10398

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This supplemental material has been provided by the authors to give readers additional information about their work.

eAppendix 1. Self-Report Assessments

Socio-demographic questionnaire: Patients reported age, gender, race/ethnicity, marital status, religion, education level, employment status, income, and tobacco use.

Self-Administered Comorbidity Questionnaire (SCQ): A 13-item questionnaire that assigns a comorbidity score ranging from 0-36, with higher scores indicating greater comorbidity.

Functional Assessment of Cancer Therapy-Lung (FACT-L): A 34-item tool that assesses physical, social/family, emotional, and functional well-being and lung cancer-specific symptoms over the past seven days with a 0 (not at all) to 4 (very much) point scale with scores ranging from 0-136 to assess QOL. Higher scores indicate a better QOL.

Patient Health Questionnaire-9 (PHQ-9): A nine-item measure with a 0 (not at all) to 3 (nearly every day) point scale that evaluates symptoms of major depressive disorder according to the criteria of the *Diagnostic and Statistical Manual of Mental Disorders*. Scores range from 0-27, with higher scores indicating more significant depression symptoms.

Brief-COPE: A 16-item modified version of the Brief COPE, with a 1 (not at all) to 4 (a lot) point scale, generating two factors assessing approach-oriented (score range: 6-24) and avoidant (score range: 4-16) coping. Higher scores indicate greater use of each strategy.

Prognosis and Treatment Perceptions Questionnaire (PTPQ): A 24-item measure to assess patients' self-reported prognostic understanding, including items inquiring about the primary goal of cancer treatment ("to cure my cancer" vs. other), perception of whether the cancer is curable (yes/no), and whether the patient discussed their end-of-life care wishes with their clinician (yes/no).

eAppendix 2. Sensitivity Analysis Methods for Primary FACT-L 24-Week Outcome Measure

In this eAppendix, we summarize the statistical methods used to conduct sensitivity analyses to evaluate the potential impact of missing data on the primary QOL outcome, FACT-L at week 24. Results from these sensitivity analyses are reported in eTable 4.

Our primary analysis of FACT-L at week 24 used a linear regression model with main effects for randomized intervention group, randomization stratification factors (study site and type of lung cancer) and baseline FACT-L score. The primary analysis excluded participants with missing FACT-L scores (e.g., due to nonresponse, loss to follow-up, or death).

Three sensitivity analyses were conducted to evaluate the impact of missing data on results for the primary outcome:

1. Sensitivity analysis using linear mixed effects model to incorporate longitudinal data.

We used a linear mixed effects regression model to estimate the difference in week 24 FACT-L means between intervention groups. This approach incorporates additional longitudinal data from participants into the analysis. This model utilized FACT-L scores at baseline, week 12, and week 24, with estimation via maximum likelihood. We included fixed effects for randomized intervention group, time from baseline (in weeks), group-by-time interaction, and randomization stratification factors, as well as random intercepts for each patient. A contrast was used to estimate the difference in means at week 24 with the lower one-sided 95% confidence limit, in line with how non-inferiority was evaluated for the primary analysis.

2. Sensitivity analysis using GEE model to incorporate longitudinal data and relax longitudinal modeling assumptions.

We used a generalized estimating equation (GEE) model to estimate the difference in week 24 FACT-L means between intervention groups. This approach incorporates additional longitudinal data from participants into the analysis. This model utilized FACT-L scores at baseline, week 12, and week 24, with estimation via GEE with unstructured correlation and robust standard errors. We included fixed effects for randomized intervention group, time from baseline (now as a categorical variable, to permit a non-linear trend in means), group-by-time interaction, and randomization stratification factors. A contrast was used to estimate the difference in means at week 24 with the lower one-sided 95% confidence limit, in line with how non-inferiority was evaluated for the primary analysis.

3. Sensitivity analysis using multiple imputation, excluding truncation due to death.

We used multiple imputation by chained equations (a.k.a., fully conditional specification) to impute FACT-L scores at week 24 that were missing for any reason other than death. Participants with missing FACT-L at week 24 who died before the week 24 survey window

closed (i.e., participants truncated due to death) were excluded prior to imputation and subsequent analysis. Variables considered for imputation included the following:

1. Randomized intervention group
2. Study site
3. Type of lung cancer
4. QOL (i.e., FACT-L) scores at baseline, week 12, and week 24
5. Depression (i.e., PHQ-9) scores at baseline, week 12, and week 24
6. ECOG performance status at baseline
7. Comorbidity (i.e., SCQ) score at baseline
8. Cancer mutation status (any mutation versus none)

We used the *mice* package in R (van Buuren and Groothuis-Oudshorn, 2011) to impute missing outcome data, fit the primary linear regression model on imputed data sets, and pool results. Based on the pooled results, we estimated the difference in means at week 24 with the lower one-sided 95% confidence limit, in line with how non-inferiority was evaluated for the primary analysis.

Supporting references:

- van Buuren S, Groothuis-Oudshoorn K (2011). “mice: Multivariate Imputation by Chained Equations in R.” *Journal of Statistical Software*, 45(3), 1-67.
[doi:10.18637/jss.v045.i03](https://doi.org/10.18637/jss.v045.i03).

eAppendix 3. Participant Race Selected as Other

Patients completed demographic questions in the baseline questionnaire which included questions about their self-reported race, ethnicity, gender, and relationship status. Patients could select as many of the provided options as needed when answering the question about their self-identified race. Five patients in the early PC arm and 3 patients in the stepped PC arm identified as a racial category that was not provided as one of the options for race.

In the early PC arm, 5 patients reported their race as: Hispanic/ispano (n = 2), Brazilian (n = 1), Greek (n = 1), Arab/Middle Eastern (n = 1).

In the stepped PC arm, 3 patients reported their race as: Hispanic/Hispano/Latina (n = 2), annoying [expletive] question (n = 1).

eTable 1. FACT-L Completion by Study Group at Weeks 36 and 48

Early Palliative Care N=257	Stepped PC N=250
179 Eligible to complete FACT-L at 36 weeks 115 Completed within time window 64 Not completed within time window 36 Incomplete/declined 8 Hospitalized/hospice 10 Transferred care/lost to follow up 10 Other 69 Died 9 Withdrew	176 Eligible to complete FACT-L at 36 weeks 122 Completed within time window 54 Not completed within time window 30 Incomplete/declined 8 Hospitalized/hospice 7 Transferred care/lost to follow up 9 Other 67 Died 7 Withdrew
162 Eligible to complete FACT-L at 48 weeks 104 Completed within time window 58 Not completed within time window 30 Incomplete/declined 9 Hospitalized/hospice 12 Transferred care/lost to follow up 7 Other 86 Died 9 Withdrew	151 Eligible to complete FACT-L at 48 weeks 103 Completed within time window 48 Not completed within time window 25 Incomplete/declined 5 Hospitalized/hospice 10 Transferred care/lost to follow up 8 Other 91 Died 8 Withdrew

eTable 2. Baseline Characteristics by Week 24 FACT-L Completion

Characteristic	N (%) ^a		p-value ^b
	Completed Week 24 FACT-L (n=291)	Did not complete Week 24 FACT-L (n=216)	
Age (years)			
Mean (SD)	65.5 (9.6)	67.7 (10.9)	0.018
>75 years	48 (16.5)	53 (24.5)	0.032
Gender, Woman	158 (54.3) [n=291]	102 (47.4) [n=215]	0.150
Race^c	[n=291]	[n=214]	
African American or Black	33 (11.3)	24 (11.2)	>0.99
American Indian or Alaskan Native	1 (0.3)	3 (1.4)	0.316
Asian	11 (3.8)	3 (1.4)	0.169
Native Hawaiian or Pacific Islander	0 (0)	0 (0)	>0.99
Other	4 (1.4)	4 (1.9)	0.727
White	245 (84.2)	182 (85.0)	0.805
Hispanic or Latino Ethnicity	4 (1.4) [n=286]	4 (1.9) [n=207]	0.726
Religion	[n=288]	[n=207]	0.456
Other Christian (e.g., Protestant)	124 (43.1)	79 (38.2)	
Catholic	104 (36.1)	85 (41.1)	
None	31 (10.8)	21 (10.1)	
Jewish	13 (4.5)	15 (7.2)	
Other	12 (4.2)	6 (2.9)	
Atheist	3 (1.0)	0 (0)	
Muslim	1 (0.3)	1 (0.5)	
Relationship Status	[n=286]	[n=213]	0.097
Married/partner	200 (69.9)	128 (60.1)	
Divorced/separated	39 (13.6)	34 (16.0)	
Widowed/loss of partner	29 (10.1)	35 (16.4)	
Single	18 (6.3)	16 (7.5)	

Education	[n=286]	[n=206]	0.063
High school graduate or less	81 (28.3)	77 (37.4)	
Associate degree/technical school	71 (24.8)	54 (26.2)	
College graduate	65 (22.7)	42 (20.4)	
Master's, professional, or doctoral level degree	69 (24.1)	33 (16.0)	
Annual Income	[n=267]	[n=179]	0.120
Less than \$25,000	47 (17.6)	33 (18.4)	
\$25,000-\$49,999	55 (20.6)	46 (25.7)	
\$50,000-\$99,999	65 (24.3)	54 (30.2)	
\$100,000-\$149,999	40 (15.0)	20 (11.2)	
\$150,000 or more	60 (22.5)	26 (14.5)	
Smoking Status	[n=266]	[n=194]	<0.001
Current or former smoker	165 (62.0)	149 (76.8)	
Never smoker or <10 pack-years	101 (38.0)	45 (23.2)	
Cancer Type			0.854
Non-small Cell Lung Cancer	227 (78.0)	170 (78.7)	
Small Cell Lung Cancer	59 (20.3)	41 (19.0)	
Mesothelioma	5 (1.7)	5 (2.3)	
Cancer Treatment			0.001
Platinum-based doublet chemo	129 (44.3)	115 (53.2)	
Radiation	47 (16.2)	45 (20.8)	
Oral targeted chemotherapy	66 (22.7)	24 (11.1)	
Immunotherapy	42 (14.4)	19 (8.8)	
Single agent IV chemo	5 (1.7)	7 (3.2)	
No treatment	1 (0.3)	5 (2.3)	
Combined radiation and chemo	1 (0.3)	0 (0)	
Other treatment	0 (0)	1 (0.5)	
Cancer Mutation Status			<0.001
Other or no mutation	214 (73.5)	188 (87.0)	
EGFR	56 (19.2)	20 (9.3)	

ALK	16 (5.5)	5 (2.3)	
ROS	2 (0.7)	3 (1.4)	
RET	3 (1.0)	0 (0)	
ECOG Performance Status			0.003
0 (Fully active with no restrictions)	88 (30.2)	37 (17.1)	
1 (Able to do light work)	163 (56.0)	143 (66.2)	
2 (Unable to work and in bed < 50% of the day)	40 (13.7)	36 (16.7)	
Medical Comorbidity by SCQ^d, mean (SD)	7.8 (4.2) [n=286]	8.7 (4.3) [n=201]	0.032
Quality of Life by FACT-L^e, mean (SD)	97.0 (19.3) [n=291]	91.5 (19.6) [n=215]	0.002
Depression Symptoms by PHQ-9^f, mean (SD)	6.0 (5.0) [n=285]	6.8 (4.9) [n=201]	0.066
Coping Skills by Brief-COPE			
Approach-Oriented Coping ^g , mean (SD)	18.1 (3.8) [n=259]	17.7 (3.8) [n=177]	0.270
Avoidant Coping ^h , mean (SD)	6.2 (2.5) [n=268]	6.1 (2.4) [n=185]	0.429
Perceptions of Prognosis			
Goal of therapy “To cure my cancer”	88 (31.8) [n=277]	66 (33.8) [n=195]	0.690
“Yes” My cancer is curable	59 (23.0) [n=256]	54 (29.0) [n=186]	0.185
End-of-Life Care Communication	30 (10.8) [n=278]	30 (15.5) [n=193]	0.160

Abbreviations: PC, palliative care; SD, standard deviation; EGFR, epidermal growth factor receptor; ALK, anaplastic lymphoma kinase; ROS, ros oncogene; RET, ret proto-oncogene; ECOG, Eastern Cooperative Oncology Group; SCQ, Self-Administered Comorbidity Questionnaire; FACT-L, Functional Assessment of Cancer Therapy-Lung Scale; PHQ-9, Patient Health Questionnaire-9; Brief-COPE, Brief-Coping Orientation to Problems Experienced Inventory

^a Data are N (%) unless otherwise reported.

^b P-values are calculated using t-tests (continuous variables) and chi-square or Fisher’s exact test (categorical variables).

^c Participants could check all applicable categories. Sum of percentages may exceed 100%.

^d Score range, 0-36, with higher scores indicating greater comorbidity

^e Score range, 0-136, with higher scores indicating better quality of life

^f Score range, 0-27, with higher scores indicating more significant depression symptoms

^g Score range, 6-24, with higher scores indicating greater use of approach-oriented coping strategies

^h Score range: 4-16, with higher scores indicating greater use of avoidant coping strategies

eTable 3. FACT-L Completion Among Stepped PC Patients on Step 1 at All Study Timepoints

Timepoint	Frequency (%) completed among patients on step 1 eligible to complete FACT-L
Week 6	202/236 (85.6%)
Week 12	150/186 (80.7%)
Week 18	119/161 (73.9%)
Week 24	117/143 (81.8%)
Week 30	98/131 (74.8%)
Week 36	86/111 (77.5%)
Week 42	66/95 (69.5%)
Week 48	66/85 (77.7%)

eTable 4 Sensitivity Analysis Model Estimates of Study Group Effects on Primary FACT-L 24-Week Outcome Measure

Sensitivity Analysis ^a	N ^b	Difference (lower one-sided 95% confidence limit) ^c Stepped PC minus Early Integrated PC
<i>Primary analysis (for reference)</i>	291	2.9 (-0.1)
1. Longitudinal mixed model	507	1.6 (-1.7)
2. Longitudinal GEE model	507	0.8 (-2.6)
3. Multiple imputation	409	2.8 (-0.1)

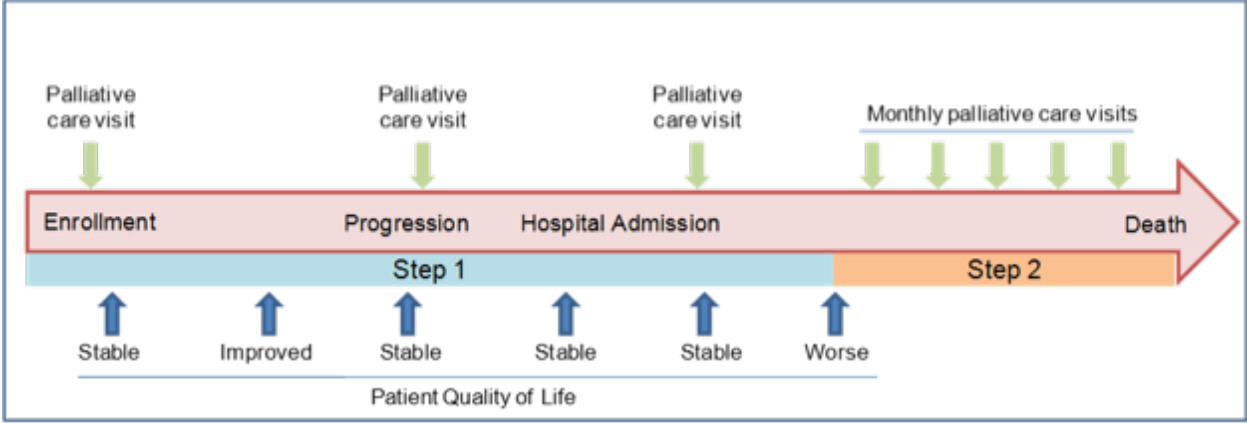
Abbreviations: CI=confidence interval; PC=palliative care; FACT-L=Functional Assessment of Cancer Therapy-Lung Scale; GEE=generalized estimating equation.

^a Sensitivity analysis methods are described in eAppendix 2.

^b N reflects the number of participants whose data were included in the model.

^c Pre-specified non-inferiority margin was -4.5 (FACT-L). Comparing the lower one-sided 95% confidence limit with the non-inferiority margin corresponds to the primary one-sided 5% significance level test for non-inferiority.

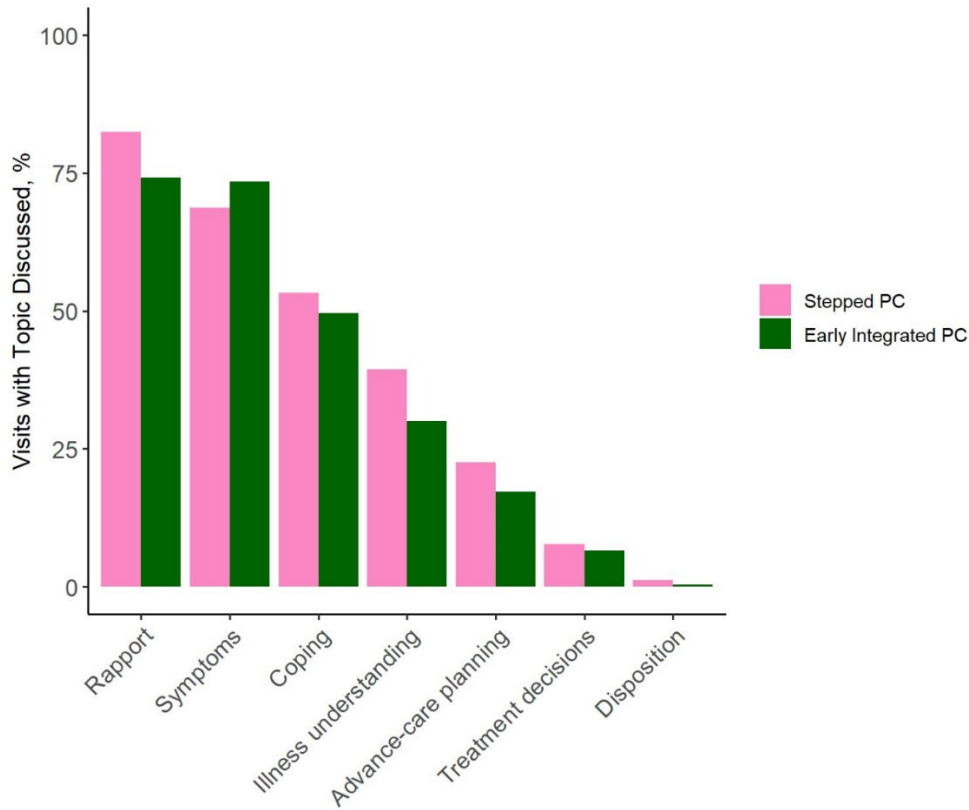
eFigure 1. Stepped PC Study Procedures Example



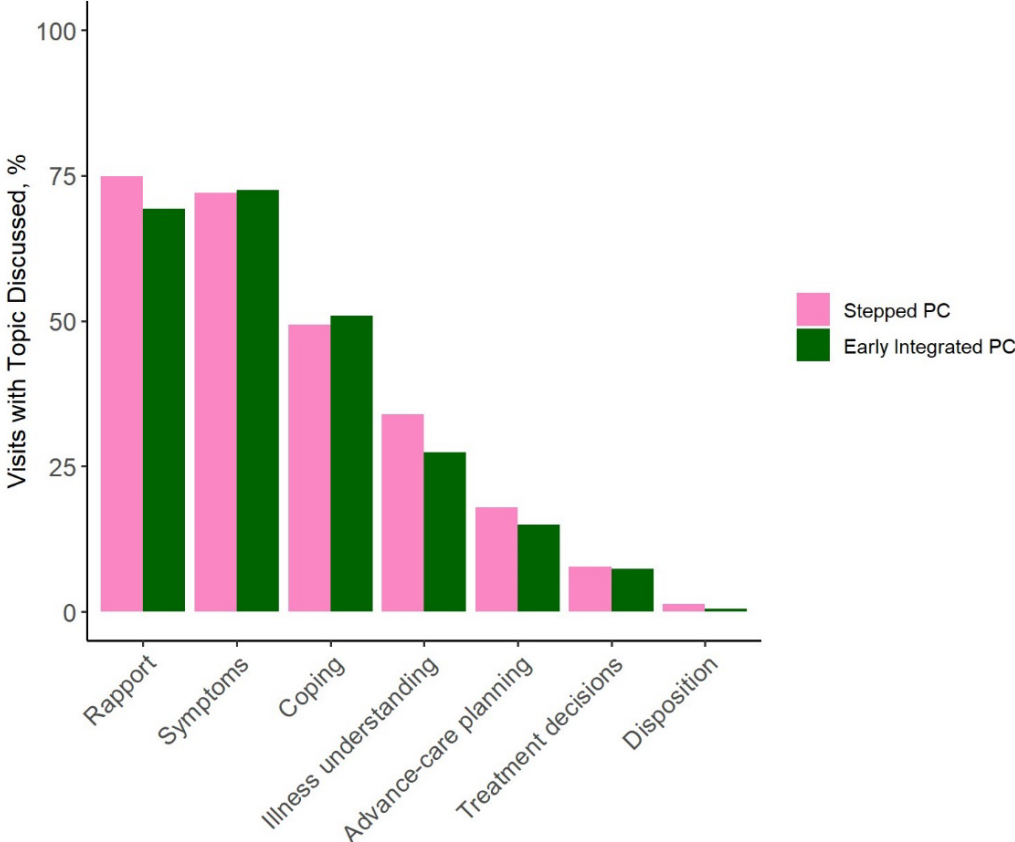
eFigure 2. Intervention Delivery Up to 24 and 48 Weeks

Legend: Bar heights represent (A) the proportion of documented visits (n=1583) with each topic discussed through week 24 (clinicians completed this documentation for 1180/1251 (94.3%) of face-to-face visits and 403 telephone calls), and (B) the proportion of documented visits (n=2549) with each topic discussed through week 48 (clinicians completed this documentation for 1812/1927 (94.0%) of face-to-face visits and 728 telephone calls). PC=palliative care

Panel A: Intervention Delivery Up to 24 Weeks

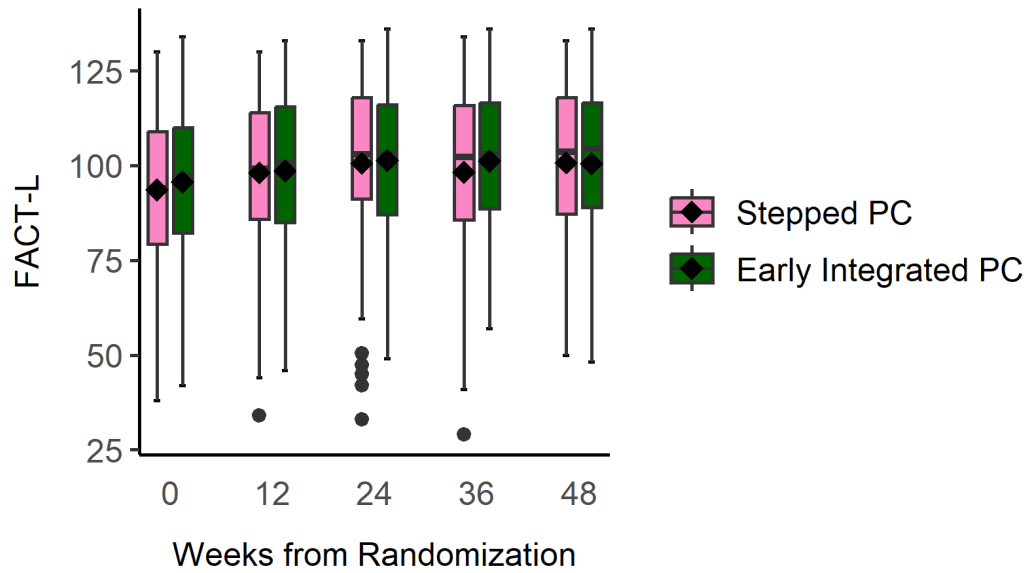


Panel B: Intervention Delivery Up to 48 Weeks



eFigure 3: Patient-Reported Quality of Life Over 48 weeks

Legend: On box plots, the ends of the boxes are located at the first and third quartiles. The horizontal line in the middle illustrates the median, and diamonds represent the mean. Whiskers extend to the highest and lowest values within 1.5 times the interquartile range, and dots beyond the whiskers reflect outlying data. Beneath the box plots, N reflects the number of patients in each group who completed the patient-reported assessment. FACT-L=Functional Assessment of Cancer Therapy-Lung Scale; PC=palliative care



	N				
Stepped PC	250	171	146	122	103
Early Integrated PC	256	178	145	115	104