Supplemental Materials

Supplemental Table 1. Baseline characteristics for providers of HCC patients (n=13,714)

Variable	Consistent screening* (%)	Inconsistent screening** (%)	No screening (%)	P-value
Provider specialty				<.001
Gastroenterology	840 (89.7)	3,895 (67.5)	2,295 (32.7)	
Internal medicine	97 (10.4)	1,792 (31.1)	4,075 (58.1)	
Other ‡	0 (0)	81 (1.4)	639 (9.1)	
Practice setting				<.001
Solo practice	347 (37.0)	2,076 (36.0)	2,284 (32.6)	
Group practice	400 (42.7)	2,720 (47.2)	3,468 (49.5)	
Hospital-based	76 (8.1)	394 (6.8)	530 (7.6)	
University-based	17 (1.8)	52 (.9)	58 (.8)	
Other	97 (10.4)	526 (9.1)	669 (9.5)	
Medical school graduation				.058
Prior to 1968	84 (9.0)	534 (9.3)	727 (10.4)	
1969-1984	414 (44.2)	2,654 (46.0)	3,276 (46.7)	
1985-2000	405 (43.2)	2,416 (41.9)	2,794 (39.9)	
After 2001	34 (3.6)	164 (2.8)	212 (3.0)	
Training location				<.001
Within U.S.	601 (64.1)	3,750 (65.0)	4,923 (70.2)	
Outside U.S.	319 (34.0)	1,894 (32.8)	1,927 (27.5)	
Unknown	17 (1.8)	124 (2.2)	159 (2.3)	

*****Receipt of ≥1 abdominal ultrasound per calendar year

******Receipt of ≥1 abdominal ultrasound during study period but less than annually

‡ Providers other than gastroenterologist or primary care provider

Supplemental Table 2. Correlates of consistent and inconsistent HCC screening receipt (n=13,714)

	Consistent Screening*			Inconsistent Screening**		
Variable	Adjusted OR	95% CI	P-value	Adjusted OR	95% CI	P-value
Age at HCC diagnosis	1.00	1.00-1.01	.07	1.00	.99-1.00	.07
Sex						
Male	Ref	Ref	Ref	Ref	Ref	Ref
Female	1.29	1.09-1.53	.003	1.21	1.11-1.32	<.001
Race/ethnicity						
Non-Hispanic White	Ref	Ref	Ref	Ref	Ref	Ref
Black	.98	.74-1.29	.87	1.01	.88-1.16	.87
Hispanic	1.51	1.20-1.89	<.001	1.24	1.09-1.41	.001
Asian	3.24	2.52-4.16	<.001	1.33	1.15-1.55	<.001
Other	2.11	1.54-2.91	<.001	1.12	.93-1.34	.23
Year of HCC diagnosis						
2003	Ref	Ref	Ref	Ref	Ref	Ref
2004	.91	.57-1.47	.71	.98	.78-1.22	.83
2005	.70	.44-1.13	.15	1.04	.84-1.29	.72
2006	.65	.41-1.02	.06	.86	.69-1.06	.16
2007	.77	.50-1.19	.25	.89	.72-1.10	.27
2008	.54	.35-.85	.007	.81	.66-.99	.04
2009	.43	.28-.67	<.001	.74	.60-.90	.003
2010	.82	.54-1.24	.34	.78	.64-.96	.02
2011	.64	.42-.97	.04	.74	.60-.90	.003
2012	.72	.48-1.10	.13	.79	.65-.97	.02
2013	.94	.563-1.41	.77	.67	.55-.82	<.001
Cirrhosis duration						
No prior diagnosis	Ref	Ref	Ref	Ref	Ref	Ref
<3 years prior to HCC	3.31	2.53-4.34	<.001	2.12	1.88-2.40	<.001
>3 years prior to HCC	3.13	2.38-4.12	<.001	1.14	.99-1.31	.07
Liver disease etiology						
No known liver disease	Ref	Ref	Ref	Ref	Ref	Ref
Hepatitis B	12.36	7.26-20.7	<.001	2.47	1.90-3.22	<.001
Hepatitis C	7.43	5.07-10.91	<.001	1.91	1.68-2.16	<.001
Alcohol-related	2.40	1.35-4.27	.003	1.35	1.08-1.68	.008
Other liver disease	6.66	4.37-10.16	<.001	2.18	1.88-2.54	<.001
>1 liver disease	18.98	13.11-27.50	<.001	3.62	3.14-4.16	<.001
Presence of ascites	1.63	1.29-2.05	<.001	1.67	1.43-1.96	<.001
Hepatic encephalopathy	1.70	1.35-2.15	<.001	1.20	1.01-1.43	.04
NCI comorbidity index						
None	Ref	Ref	Ref	Ref	Ref	Ref
Low (1-2)	1.96	.19-1.21	.16	1.22	1.01-1.48	.04

Moderate (3-4)	2.21	.19-1.17	.10	1.45	1.20-1.76	<.001
High (5+)	3.72	.14-.87	.005	1.99	1.65-2.41	<.001
Provider specialty						
Other ‡	Ref	Ref	Ref	Ref	Ref	Ref
Gastroenterology	>999.99	>999.99	<.001	6.47	5.04-8.30	<.001
Internal medicine	>999.99	>999.99	<.001	2.89	2.25-3.70	<.001
Practice setting						
Solo practice	Ref	Ref	Ref	Ref	Ref	Ref
Group practice	.89	.74-1.06	.19	.94	.86-1.03	.19
Hospital-based	.94	.69-1.27	.67	.81	.69-96	.02
University-based	1.40	.72-2.72	.32	.79	.51-1.24	.31
Other	.99	.75-1.31	.93	.91	.78-1.05	.20
Training location						
Outside U.S.	Ref	Ref	Ref	Ref	Ref	Ref
Within U.S.	.95	.80-1.13	.59	.91	.83-.99	.03
Unknown	1.12	.63-2.02	.70	1.01	.76-1.33	.96

*****Receipt of ≥1 abdominal ultrasound per calendar year

******Receipt of ≥1 abdominal ultrasound during study period but less than annually

†Reference screening category were HCC patients who did not receive screening

‡ Providers other than gastroenterologist or primary care provider

Lead and Length Time Bias Sensitivity Analysis

Following the parametric model by Duffy and colleagues, correction for lead time bias involves estimation of the additional follow-up time due to lead time in the case of screen-detected cancer.[28] The expected additional follow-up time, s, is $E(s) = \frac{1-e^{-\lambda t}-\lambda t e^{-\lambda t}}{\lambda(1-e^{-\lambda t})}$ for a patient with screen-detected cancer known to be dead at time t after diagnosis and $E(s) = \frac{1-e^{-\lambda t}}{\lambda}$ for a patient with screen-detected cancer known to be alive at time t after diagnosis. To correct for lead time bias, $E(s)$ was subtracted from observed survival time of screen-detected patients, which were defined as those who received screening ultrasound within 6 months prior to HCC diagnosis.[28]

After the lead-time was adjusted among screen-detected patients, we further adjusted for length time bias following the method proposed by Duffy and colleagues. The relative risk of death from screen-detected versus symptomatic tumors, φ, was estimated by the observed probability of death from screen-detected, p_1, and symptomatic tumors, p_2, and the observed probability of screen-detected tumors, p_3, by giving plausible values for a proportion of patients with slow-growing tumors, $1-q$, and the relative risk of death from slow-growing tumors versus aggressive tumors, θ, that is: $\hat{\varphi} = \frac{p_2\{(\theta q+1-q)(\theta+q(1-\theta))-p_3\theta\}}{p_1\theta(1-p_3)}$. By multiplying $\hat{\varphi}$ and the survival rate for patients with symptomatic tumors, in this section, we estimate the survival rate for screen-detected tumors correcting for length time bias under various plausible data inputs.[28]

Supplemental Table 3. Kaplan-Meier survival estimates by receipt of HCC screening for all patients, unadjusted and adjusted for lead and length time biases (n=13,714)

Screening group	Median survival, months (95% CI)	1-year survival(%) (95% CI)†	3-year survival(%) (95% CI)†	5-year survival(%) (95% CI)†	log-rank test
Unadjusted					
Consistent screening*	17.00 (15.00-19.00)	58 (55-61)	25 (22-28)	15 (12-18)	<.001
Inconsistent screening**	10.00 (10.00-11.00)	45 (44-46)	20 (19-21)	10 (9-11)	
No screening	5.00 (5.00-6.00)	34 (33-35)	13 (12-14)	6 (6-7)	
Adjusted for lead time bias					
Mean sojourn time = 3 months					
Consistent screening*	16.00 (13.09-18.00)	56 (53-59)	24 (22-27)	14 (12-17)	<.001
Inconsistent screening**	10.00 (9.00-10.00)	45 (43-46)	19 (18-21)	10 (9-11)	
Mean sojourn time = 6 months					
Consistent screening*	14.05 (13.00-16.72)	54 (51-57)	24 (21-27)	13 (11-16)	<.001
Inconsistent screening**	9.94 (9.00-10.00)	44 (43-45)	19 (18-20)	10 (9-11)	
Mean sojourn time = 9 months					
Consistent screening*	14.00 (12.65-16.00)	54 (51-57)	22 (19-25)	13 (11-16)	<.001
Inconsistent screening**	9.86 (9.00-10.00)	44 (43-45)	19 (18-20)	10 (9-11)	
Adjusted for lead and length time biases					
Mean sojourn time = 3 months					
Consistent screening*		55 (53-58)	24 (22-26)	14 (13-16)	
Inconsistent screening**		44 (44-45)	19 (19-20)	10 (10-10)	
Mean sojourn time = 6 months					
Consistent screening*		54 (52-56)	23 (21-25)	13 (11-15)	
Inconsistent screening**		44 (44-45)	19 (19-20)	10 (10-10)	
Mean sojourn time = 9 months					
Consistent screening*		54 (52-56)	22 (20-24)	13 (11-15)	
Inconsistent screening**		44 (44-44)	19 (19-19)	10 (10-10)	

*Receipt of ≥1 abdominal ultrasound per calendar year

**Receipt of ≥1 abdominal ultrasound during study period but less than annually

†For lead and length time bias adjustment, weighted average of screen-detected and symptomatic cancer was calculated with the results of Supplemental Table 4, that is, we assumed $1 - q = 20\%$ and $\theta = 0.9$

Supplemental Table 4. Survival estimates by receipt of HCC screening for patients with screen-detected and symptomatic tumors, unadjusted (n=13,714) and adjusted for lead and length time biases for only the screen-detected patients (n=1,136)

Screening group		N (%)	1-year survival(%) (95% CI)†	3-year survival(%) (95% CI)†	5-year survival(%) (95% CI)†
Unadjusted for lead time bias					
Consistent screening*	Screen-detected	390 (2.8)	63 (58-68)	31 (26-36)	19 (15-24)
	Symptomatic	547 (4.0)	54 (50-59)	21 (17-25)	12 (9-15)
Inconsistent screening**	Screen-detected	746 (5.4)	59 (55-62)	29 (26-33)	17 (14-20)
	Symptomatic	5,022 (36.6)	43 (42-44)	18 (17-20)	9 (8-10)
No screening	Symptomatic	7,009 (51.1)	34 (33-35)	13 (12-14)	6 (6-7)
Adjusted for lead time bias					
Mean sojourn time = 3 months					
Consistent screening*	Screen-detected	390 (2.8)	57 (52-62)	29 (24-34)	18 (14-22)
Inconsistent screening**	Screen-detected	746 (5.4)	54 (50-57)	26 (23-30)	16 (13-19)
Mean sojourn time = 6 months					
Consistent screening*	Screen-detected	390 (2.8)	54 (49-59)	26 (21-31)	15 (11-20)
Inconsistent screening**	Screen-detected	746 (5.4)	51 (47-55)	24 (21-27)	15 (13-18)
Mean sojourn time = 9 months					
Consistent screening*	Screen-detected	390 (2.8)	54 (48-58)	24 (19-29)	15 (11-19)
Inconsistent screening**	Screen-detected	746 (5.4)	51 (47-54)	23 (20-26)	14 (12-17)
Adjusted for lead and length time biases					
Mean sojourn time = 3 months					
Consistent screening*	Screen-detected	390 (2.8)	57 (56-57)	28 (28-29)	17 (16-18)
Inconsistent screening**	Screen-detected	746 (5.4)	53 (53-53)	26 (25-26)	16 (15-16)
Mean sojourn time = 6 months					
Consistent screening*	Screen-detected	390 (2.8)	54 (53-54)	25 (25-26)	15 (14-15)
Inconsistent screening**	Screen-detected	746 (5.4)	51 (50-51)	24 (23-24)	15 (14-15)
Mean sojourn time = 9 months					
Consistent	Screen-	390	54 (53-54)	23 (22-23)	14 (13-15)

screening*	detected	(2.8)			
Inconsistent screening**	Screen-detected	746 (5.4)	50 (50-50)	22 (22-23)	13 (13-14)

*****Receipt of ≥1 abdominal ultrasound per calendar year

******Receipt of ≥1 abdominal ultrasound during study period but less than annually

†For length time bias adjustment, the survival rates are estimated by $1 - q = 20\%$ and $\theta = 0.9$