The University of Texas MD Anderson Cancer Center Tobacco Treatment Program

A Comprehensive

Tobacco Cessation Program for Cancer Patients

Presented June 9, 2014
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Mission Statement

The mission of the Tobacco Treatment Program is to implement a comprehensive tobacco-cessation and relapse prevention program for all M. D. Anderson Cancer Center patients and employees.

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Tobacco Treatment Program
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Need For Intervention is Great

- Nearly 70% of smokers say they want to quit
  - 42% of all smokers report a quit attempt in the past 12 months
  - Annually less than 6% of all smokers quit using any means
- Nicotine dependence should be considered a chronic relapsing disorder
  - It may take up to 14 attempts for some smokers to achieve success
  - One of the most important psychosocial predictors of smoking prevalence and relapse are related to affect: particularly symptoms of depression or negative mood.

Evidence Based Treatment Recommendations

- Recommendation: Both counseling and Medications (except where contraindicated) should be provided to all patients*
  - Combination Counseling & Medication More Effective vs. Brief Advice or Less Intense Support (i.e.<30 min; < 4 sessions)**
- Increasing counseling intensity provides small but significant benefit to the combination (i.e. > 4 sessions; 30-300 minutes)
  - More intense follow-up needed for smokers with significant medial comorbidities
  - None of these meta-analyses examine counseling approach/content
    - For example, affect focused counseling, mindfulness, ACT

- **Clinical Practice Guideline: Treating Tobacco Use and Dependence U.S. Department of Health and Human Services** Public Health Service, June 2008
- ** Stead LF, Lancaster T. Combined pharmacotherapy and behavioural interventions for smoking cessation (Review). Cochrane Database of Systematic Reviews 2012, Issue 12.

Behavioral Interventions and Pharmacotherapy vs. Brief Advice, Usual Care or Less Intensive Support

Combined pharmacotherapy and behavioural interventions for smoking cessation

Patient or population: People who smoke
Settings: Community and healthcare settings
Intervention: Combined pharmacotherapy and behavioural interventions

Protective-ND

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Combined pharmacotherapy and behavioural interventions				
Cessation at longest follow-up (all but Lung Health Study)	83 per 1000[1]	151 per 1000 (138 to 166)	RR 1.82 (1.66 to 2)	15021 (40 studies)	⊕⊕⊕⊕ high[2]	Based on 4-8 sessions; >30 but <300 minutes; most used NRT. Without Lung Health Study
Cessation at longest follow-up (Lung Health Study only) Follow-up: mean 12 months	90 per 1000	350 per 1000 (302 to 406)	RR 3.88 (3.35 to 4.5)	5887 (1 study)	⊕⊕⊕○ moderate[3]	Substantially larger treatment effect than seen in other studies. Particularly intensive intervention, hence not included in main analysis

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio;

CC on Varenicline >CC on Bupropion. B=V for CC/TT

With Lung Health: Extended NRT, recycling, multiple group sessions, long term maintenance

Stead LF, Lancaster T. Combined pharmacotherapy and behavioural interventions for smoking cessation (Review). Cochrane Database of Systematic Reviews 2012, Issue 12.

Behavioral Interventions of Increasing Intensity as Adjuncts to Pharmacotherapy

Behavioural interventions as adjuncts to pharmacotherapy for smoking cessation

Patient or population: People using smoking cessation pharmacotherapy
Settings: Health care and community settings
Intervention: Behavioural interventions as adjuncts to pharmacotherapy

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Behavioural interventions as adjuncts to pharmacotherapy				
Smoking cessation at longest follow-up Follow-up: 6 - 24 months	**Study population**		**RR 1.16** (1.09 to 1.24)	15506 (38 studies)	⊕⊕⊕⊕ **high**[1,2]	**Small but significant benefit from more intensive behavioral support when above**
	183 per 1000	**213 per 1000** (200 to 227)				
	Median quit rate		**Response Rate=21%**			**4-8 sessions; >30 but <300 minutes; most used NRT**
	210 per 1000	**244 per 1000** (229 to 260)				

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio;

Stead LF, Lancaster T. Behavioural interventions as adjuncts to pharmacotherapy for smoking cessation. Cochrane Database of Systematic Reviews 2012, Issue 12. Art. No.: CD009670. DOI: 10.1002/14651858.CD009670.pub2

Pharmacotherapies for Nicotine Dependence

- First-Line Medications
  - Nicotine replacement therapies (NRTs)*
  - Bupropion-SR*
  - *Varenicline**
- Second-Line Medications
  - Nortriptyline* (TCA, Norepinephrine blocker)
  - Clonidine* (Antihypertensive, presynaptic alpha-2 agonist)

* **Clinical Practice Guideline: Treating Tobacco Use and Dependence U.S. Department of Health and Human Services** Public Health Service, June 2008

RTC of 5 Pharmacotherapies

Table 3. Logistic Regressions Predicting Initial Cessation and Point-Prevalent Abstinence

Treatment	Initial Cessation			1 wk Postquit		
	Wald	*P* Value	OR (95% CI)	Wald	*P* Value	OR (95% CI)
Relative to placebo						
Bupropion	9.25	.002[a]	2.04 (1.29-3.22)	6.52	.01	1.73 (1.14-2.64)
Lozenge	7.60	.006	1.91 (1.21-3.03)	1.97	.16	1.36 (.89-2.09)
Patch	20.32	<.001[a]	3.14 (1.91-5.17)	14.29	<.001[a]	2.24 (1.47-3.40)
Bupropion + lozenge	13.14	<.001[a]	2.40 (1.50-3.84)	10.00	.002[a]	1.97 (1.29-3.00)
Patch + lozenge	31.18	<.001[a]	4.73 (2.74-8.16)	19.23	<.001[a]	2.53 (1.67-3.83)
Relative to monotherapies						
Bupropion + lozenge	0.07	.79	1.05 (0.71-1.56)	0.61	.43	1.12 (0.84-1.50)
Patch + lozenge	9.01	.003[a]	2.08 (1.29-3.36)	6.46	.01	1.44 (1.09-1.92)
Monotherapies relative to each other[b]						
Patch vs lozenge	3.86	.049	0.61 (0.37-0.999)	7.20	.007	0.61 (0.42-0.88)
Bupropion vs lozenge	0.07	.78	0.94 (0.59-1.48)	1.65	.20	0.79 (0.54-1.14)
Patch vs bupropion	2.94	.09	0.65 (0.40-1.06)	2.01	.16	0.77 (0.54-1.10)
Patch + lozenge vs bupropion + lozenge	5.77	.02	0.51 (0.29-0.88)	2.00	.16	0.78 (0.55-1.10)

Treatment	End of Treatment, 8 wk Postquit			6 mo Postquit		
	Wald	*P* Value	OR (95% CI)	Wald	*P* Value	OR (95% CI)
Relative to placebo						
Bupropion	4.75	.03	1.55 (1.05-2.31)	5.01	.03	1.63 (1.06-2.51)
Lozenge	4.93	.03	1.57 (1.05-2.33)	6.68	.01	1.76 (1.15-2.70)
Patch	9.64	.002[a]	1.87 (1.26-2.77)	7.70	.006	1.83 (1.20-2.81)
Bupropion + lozenge	18.10	<.001[a]	2.35 (1.59-3.49)	6.42	.01	1.74 (1.13-2.67)
Patch + lozenge	24.02	<.001[a]	2.67 (1.80-3.96)	15.65	<.001[a]	2.34 (1.54-3.57)
Relative to monotherapies						
Bupropion + lozenge	5.95	.02	1.42 (1.07-1.88)	0.00	>.99	1.00 (0.74-1.35)
Patch + lozenge	11.19	.001[a]	1.61 (1.22-2.13)	4.12	.04	1.35 (1.01-1.79)
Monotherapies relative to each other[b]						
Patch vs lozenge	0.97	.32	0.84 (0.59-1.19)	0.05	.83	0.96 (0.67-1.38)
Bupropion vs lozenge	0.003	.96	1.01 (0.71-1.43)	0.38	.54	.89 (0.62-1.28)
Patch vs bupropion	1.09	.30	0.83 (0.59-1.18)	0.38	.54	.89 (0.62-1.28)
Patch + lozenge vs bupropion + lozenge	0.53	.47	0.88 (0.63-1.24)	2.68	.10	0.74 (0.52-1.06)

Remains After Correction for MC

Abbreviations: CI, confidence interval; OR, odds ratio.
[a] $P < .005$, Bonferroni-corrected for 11 comparisons with $\alpha = .05$.
[b] First condition listed is the reference condition.

Piper et. al Arch Gen Psychiatry. 2009;66(11):1253-12627

MTC Meta-analysis Pharmacotherapies

Protective-ND

Table III. Probability of each treatment being best, derived on the basis of the random-effects multiple treatment comparison (MTC) model for smoking cessation.

Treatment	Short term	3 months	6 months	12 months
Control	0.0000	0.0000	0.0000	0.0000
Standard-dose NRT	0.0000	0.0000	0.0000	0.0000
High-dose NRT	0.0005	0.0112	0.3572	0.0099
Combination NRT	0.0181	0.0075	0.0287	0.0005
Bupropion	0.0005	0.0000	0.0000	0.0000
Varenicline	0.9809	0.9813	0.6141	0.9896

Patch + Acute

- Varenicline was associated with statistically significant improvements in smoking abstinence compared to all interventions at all time points except at 6 months compared to high-dose (>22 mg) nicotine patch therapy and combination NRT.

Mills et. al . Annals of Medicine, 2012; 44: 588–597

Decisions for Pharmacotherapies

Patch + Lozenge or Gum

Effectiveness Risk-Benefit Cost

Varenicline

Cost Analysis: Varenicline & NRT: More Quitters, More Life (QALY) Gained, Higher Savings

Table 2. *Input data: quit rates and 12-week intervention costs of the smoking cessation interventions considered in the model*

	OR versus placebo, 12 months abstinence (95% CI)	12-months abstinence rates	Intervention costs (Euro)**
Varenicline	2.80 (2.05–3.83) [19,45]	22.4% [19,45]	383.10
Bupropion	2.00 (1.72–2.31) [8]	17.0%*	327.10
Nortriptyline	1.77 (1.08–2.91) [8,46]	15.4%*	155.55
Nicotine replacement therapy	1.69 (1.55–1.85) [7]	14.8%*	323.34
Placebo	–	9.3% [19,45]	97.20
Unaided cessation	–	5.0% [47]	0

*Calculated versus the efficacy rate of placebo using the formula: $P_{drugA} = (OR_{drugA\text{-}placebo} * P_{placebo})/(1-P_{placebo} + [OR_{drugA\text{-}placebo} * P_{placebo}])$, where P_{drugA} is the probability of abstinence at one year for Drug A and $P_{placebo}$ is the probability of abstinence at 1 year on placebo

**Based on a 12-week treatment period and including: counseling time (120 min × 0.81 Euro/min[48]), consultation time general practitioner prescribing the medication (5 min × 2.04 Euro/min[48]) and medication costs[49] (varenicline: 3.28 Euro/day, bupropion: 2.62 Euro/day, nortriptyline: 0.57 Euro/day and NRT: 2.57 Euro/day). The mean costs for NRT were calculated based on the costs of NRT gum and NRT patches weighted by the percentage of use

Table 3. *Costs per (quality-adjusted) life year gained for all interventions compared to unaided cessation and for varenicline compared to all other interventions*

	Additional number of quitters	Life years gained	QALYs gained	Additional intervention costs (million Euro)	Costs per additional quitter (Euro)*	Savings from prevented diseases (million Euro)	Costs per life year gained†	Costs per QALY gained‡
Each intervention versus unaided cessation								
Varenicline	117 100	79 900	121 900	338.7	2890	299.2	490	320
Bupropion	80 800	55 100	84 100	289.8	3590	206.4	1510	990
Nortriptyline	70 000	47 800	72 900	137.5	1960	178.8	Cost saving	Cost saving
NRT	65 800	44 900	68 400	285.8	4350	168.0	2630	1720
Varenicline versus								
Bupropion	36 400	24 800	37 800	48.9	1350	92.9	Cost saving	Cost saving
Nortriptyline	47 100	32 100	49 000	201.2	4270	120.4	2510	1650
NRT	51 400	35 000	53 500	52.8	1030	131.2	Cost saving	Cost saving

*Costs per additional quitter = additional intervention costs/additional number of quitters

†Costs per life year gained = (additional intervention costs–savings from prevented diseases)/life years gained

‡Costs per QALY gained = (additional intervention costs–savings from prevented disease)/QALYs gained

Hoogendoorn, et.al. Current Medical Research & Opinion, 24, 2008, 51–61

The Tobacco Treatment Program provides progressively more intensive treatment options suitable for every patient

- To accommodate the needs of **all patients** the Tobacco Treatment Program includes multiple options for service delivery. These include:
  - Educational Packet (Self-help) & Follow-Up Call
    - Benefits of quitting smoking
    - Preparing to quit
    - Additional resources
    - 3-month motivational follow-up call
  - Motivational Intervention, Education Packet & Follow-Up Call
    - Assess motivation and explore all treatment options on phone
    - Provide motivational interaction to determine patient choice
    - Conduct Follow-up calls

The Tobacco Treatment Program provides progressively more intensive treatment options suitable for every patient

- Telephone Counseling Only (Phone only option)
  - Behavioral counseling for smoking cessation by phone only
  - Outside physician consultation for pharmacotherapy
  - Outside referral for treatment of psychiatric co-morbidity
- Comprehensive In-Person Counseling & Pharmacotherapy
  - Individualized Counseling and Pharmacological Intervention 10-12 weeks
    - both in-person and telephone follow-up
    - Addresses Psychiatric Co-Morbidity
    - Pharmacological treatment combinations for recycling/relapse

To Implement the Program We use a Proactive Treatment Model Operating System Wide within MD Anderson

- Referral to the TTP is automatic and not provider dependent
- Automatic identification of smokers and recent quitters (with12 months) on the EHR triggers action from the TTP staff
- The response/triage is made within 3 business days
- Proactive vs provider referral is much more effective for reaching all patients

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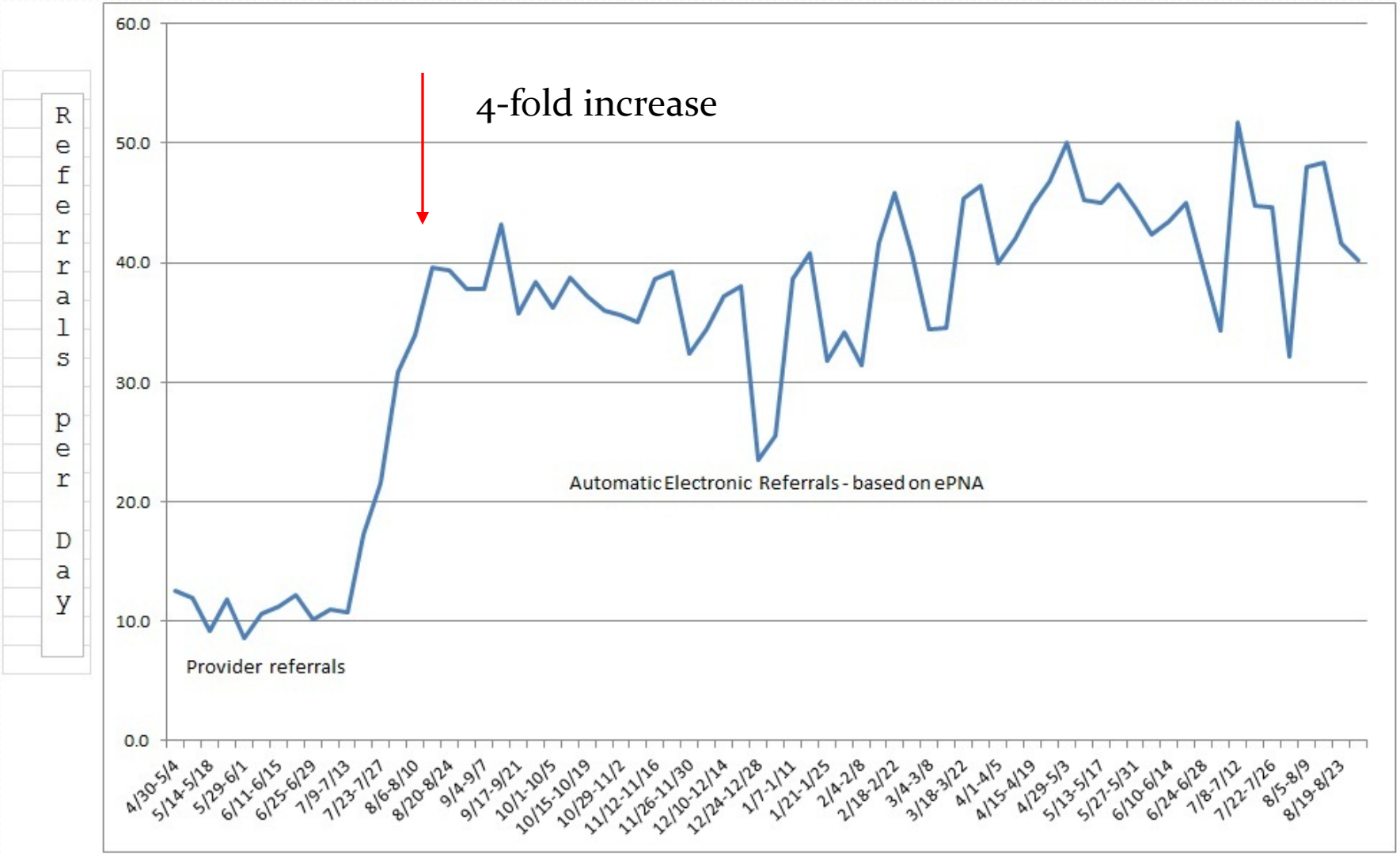
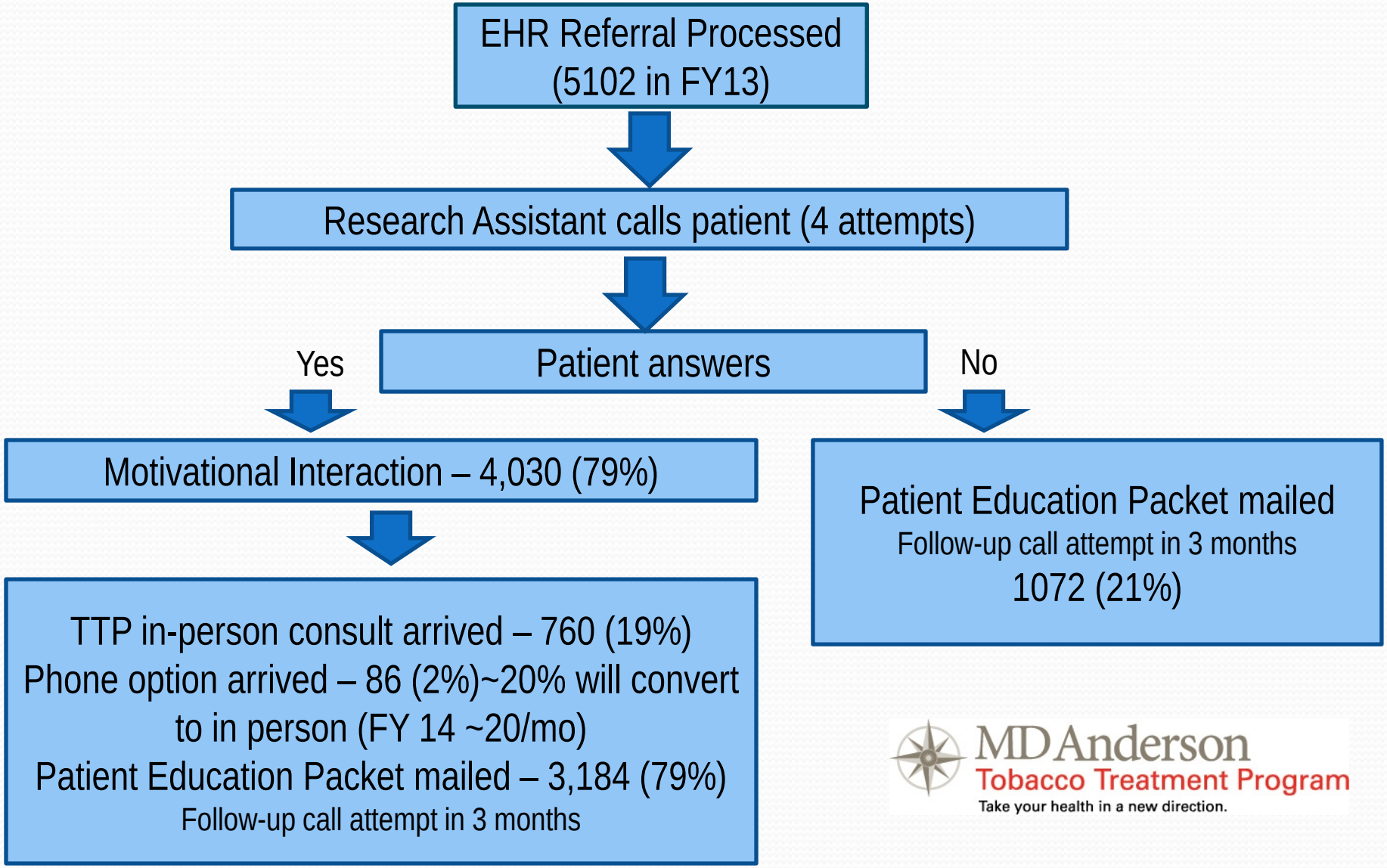
Referral Tracking – Average Number of Referrals per Day by Week
April 30, 2012 through August 31, 2013



TTP Patients Served: Sep 2013 – Aug 2014



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Abstinence Over Time

for Cancer vs No Cancer

Patient Demographic Information

N = 1820 - Cancer vs No Cancer Cohort

Date Range: 1/1/2006 - 10/15/2010

	Cancer		No Cancer	
Sample	Total	Percent	Total	Percent
No	1577	86.7%	243	13.4%

Gender	Total	Percent	Total	Percent
Female	790	50.1%	132	54.3%
Male	787	49.9%	111	45.7%

Ethnicity	Total	Percent	Total	Percent
Black	161	10.3%	33	16.4%
Hispanic	75	4.8%	11	5.5%
Other	20	1.3%	15	7.5%
White	1302	83.6%	142	70.6%
		missing = 19		missing = 42

Psychiatric Comorbidity	Total	Percent	Total	Percent
No	802	58.9%	132	62.0%
Yes	559	41.1%	81	38.0%
		missing = 216		missing = 30

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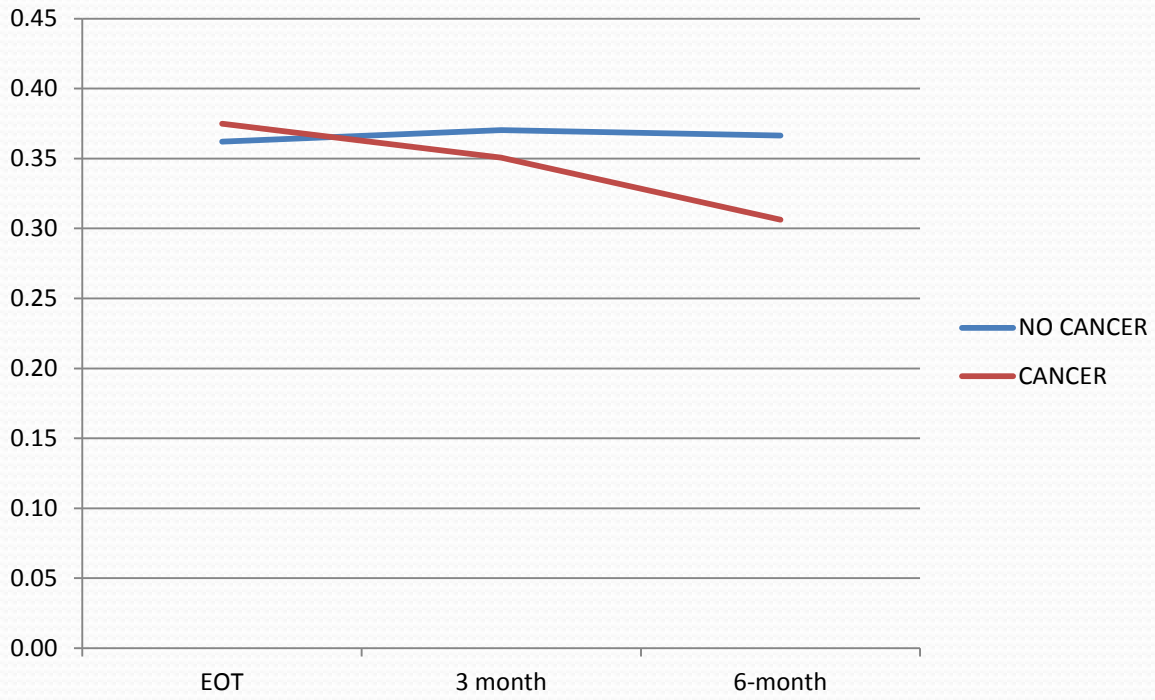
Cancer vs No Cancer - Quit Rates

Controlling for number of sessions, medication, age, sex, psychiatric disorder, cigarette use, FTND



Cancer vs No Cancer
at 6 months
Odds ratio: 1.31 (NS)
95% CL: 0.95 – 0.1.80

	EOT	3 month	6 month	N
No Cancer	**0.36**	**0.37**	**0.37**	243
Cancer	**0.37**	**0.35**	**0.31**	1577
			Total	1820

Abstinence Over Time

for Smoking-Related Cancer

Smoking-Related Cancers - Frequencies

Cancer Site	Frequency	Percent
Not Smoking-Related	685	40
Smoking-Related	774	46
No Cancer	243	14
Total	1702	100

Frequency Missing = 118

Cancer site unknown = 20

Survivors = 98 (no active cancer site)

Smoking vs. non-smoking cancer related patients were more likely to be male, older, more nicotine dependent, have smoked longer and attended fewer sessions

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Smoking-Related Cancers[1]

Frequencies by Cancer Site

Cancer Site	Frequency	Percent
Lung	241	31.1
Head & Neck	258	33.3
Colorectal	48	6.2
Bladder	45	5.8
Leukemia (acute myeloid)	13	1.7
Cervical	19	2.5
Kidney	39	5.0
Pancreas	18	2.3
Esophagus	29	3.7
Stomach	17	2.2
Vulva	12	1.6
Other*	35	4.5
Total	774	100.0

1-ACS and literature based evidence for smoking as a risk factor

* Other = cancer sites with frequency < 1%

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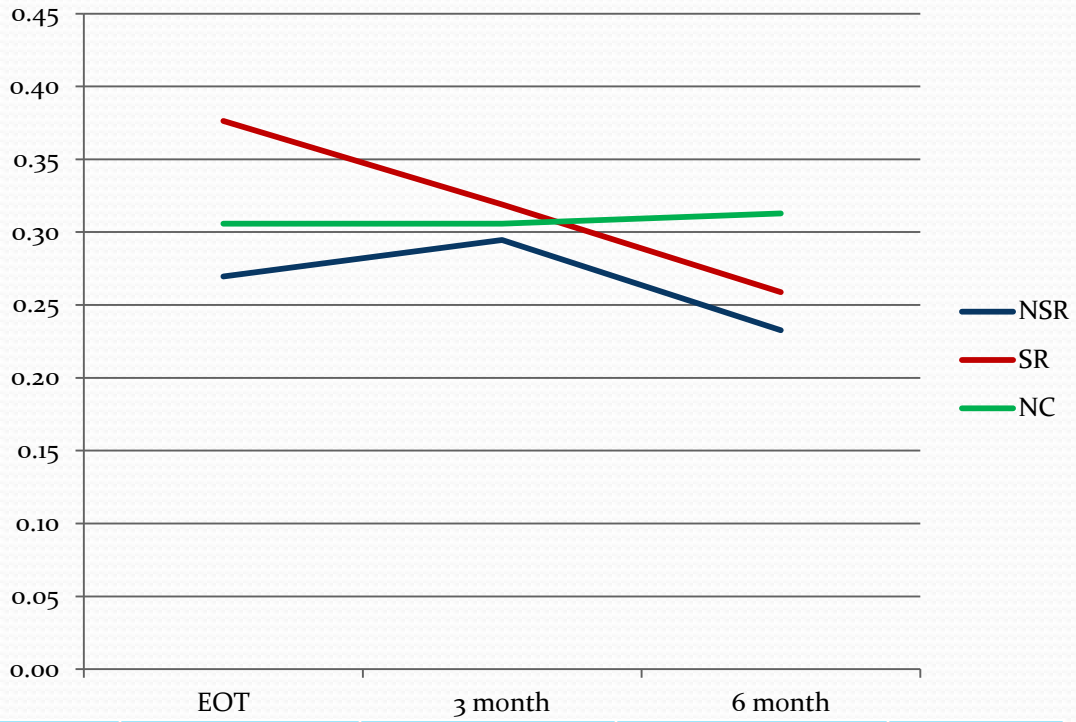
Smoking Related Cancers - Estimated Quit Rates

Controlling for number of sessions, medication, age, sex, psychiatric disorder, cigarette use, FTND



Non-smoking-related vs smoking-related at EOT
Odds ratio: 0.694
95% CL: 0.534 – 0.901

	EOT	3 month	6 month	N
Not smoking-related	0.27	0.29	0.23	685
Smoking-related	0.38	0.32	0.26	774
No cancer	0.31	0.31	0.31	243
			Total	1702

Abstinence Over Time by Cancer Site vs No Cancer

Cancer Site - Frequencies

Cancer Site	Frequency	Percent
Breast	255	15
Lung	242	14
Head & Neck	258	15
Colorectal & Other GI	145	8
Prostate	57	3
Other GU	151	9
Lymphoma & Other Hema	158	9
Melanoma & Other Skin	115	7
Other	100	6
No Cancer	241	14
Total	1722	100

Frequency Missing = 98

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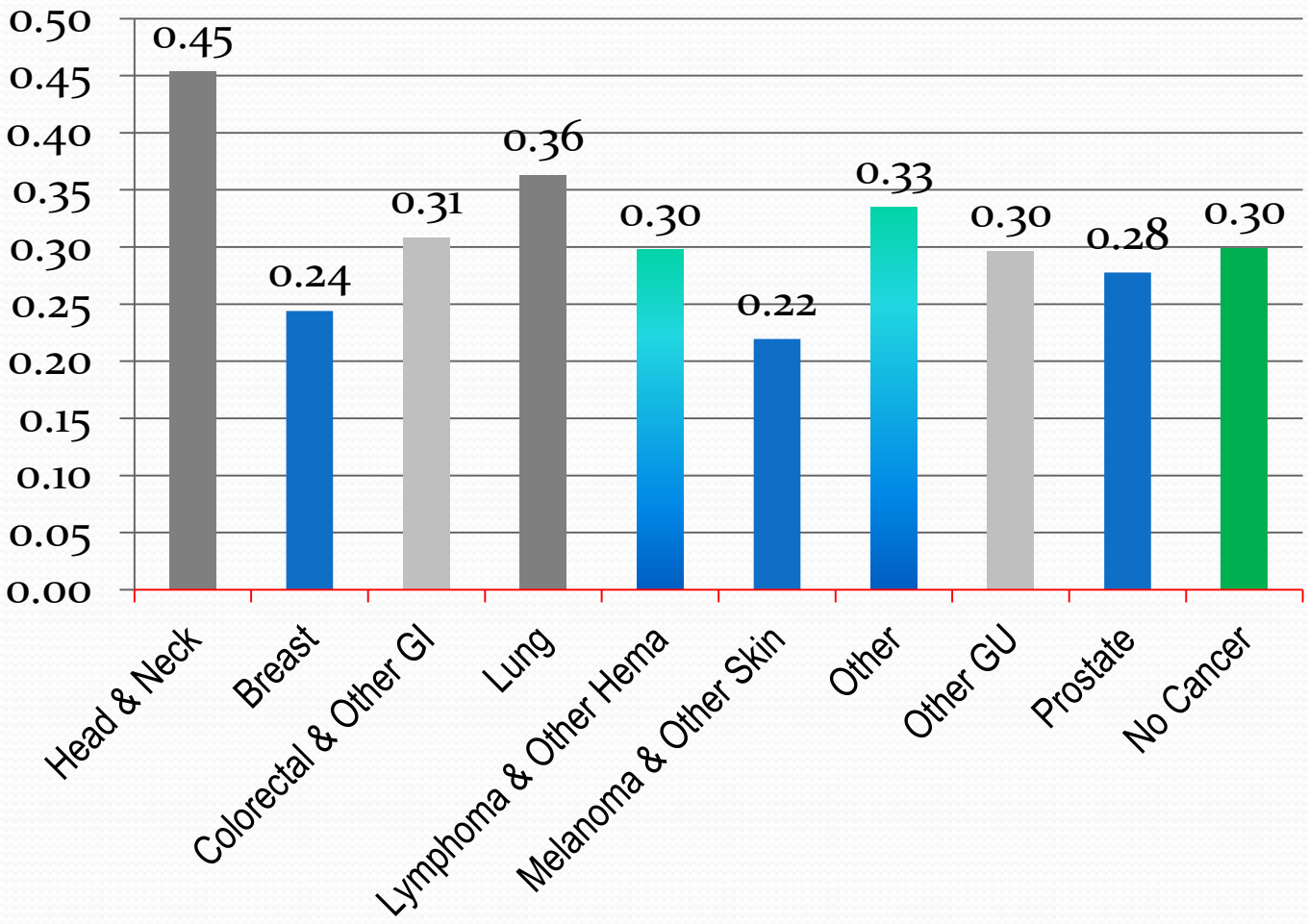
Cancer Site - Estimated Abstinence Rates at EOT

Controlling for number of sessions, medication, age, sex, psychiatric disorder, cigarette use, FTND



Head & Neck vs
No Cancer
at EOT
Odds ratio: 1.68
95% CL: 1.09 – 2.57

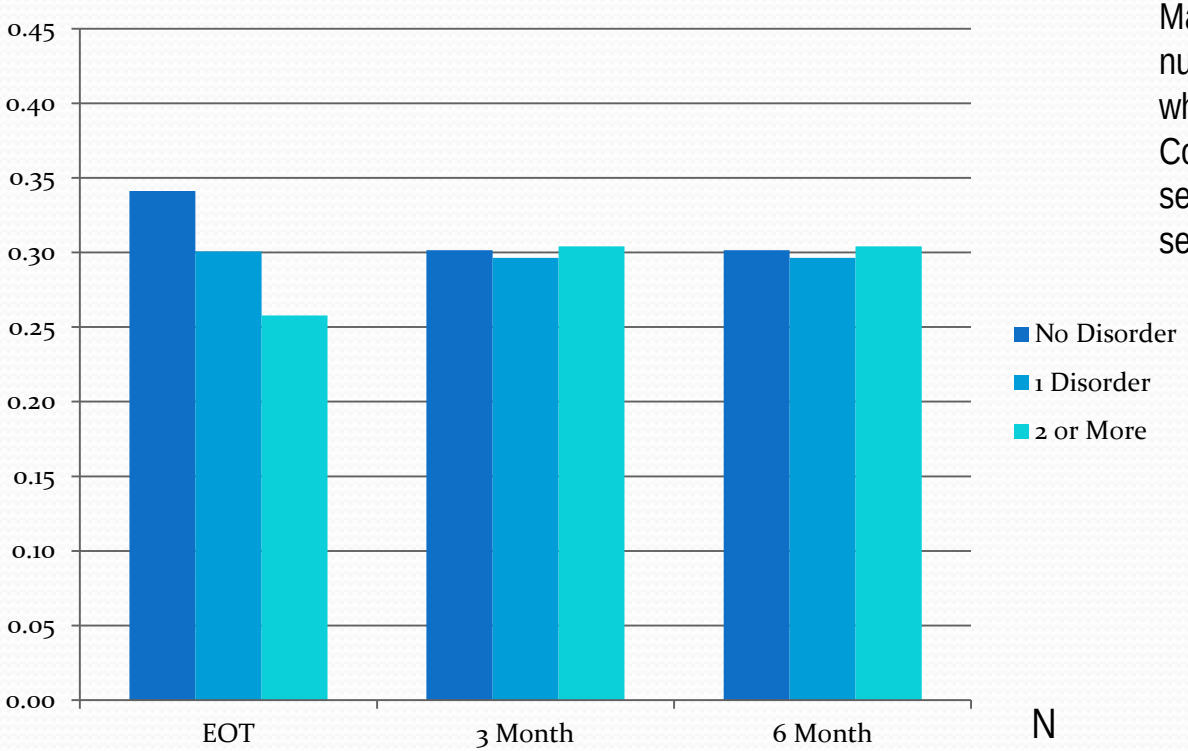
There were no
other significant
or marginal effects
for a specific
cancer site vs no cancer
at any of the 3 time points.

Abstinence Over Time

for Psychiatric Disorders

Abstinence Rate by Number of Psychiatric Disorders

2006 – 2010 (N = 1361)



Main effect of disorder number not significant at EOT when controlling for Controlling for number of sessions, medication, age, sex, cigarette use, FTND

				N
No Disorder	0.34	0.30	0.30	802
1 Disorder	0.30	0.30	0.30	316
2 or More	0.26	0.30	0.30	243

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Conclusions

MDACC Tobacco Treatment Program (TTP) is a comprehensive program that offers cessation assistance to cancer patients tailored to their individual needs.

TTP offers behavioral counseling for smoking cessation, psychological and psychiatric counseling for related issues with aggressively monitored and managed cessation medication plans, all free of charge to MDACC cancer patients.

The content, number, and length of counseling sessions are tailored to each individual patient's needs, as are medications. Progress is regularly monitored and if a treatment plan isn't working, we change it.

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Conclusions

- Logistic regressions controlling for treatment variables (medication use and number of sessions) and patient characteristics (age, gender, psychiatric disorder, cigarettes per day, years smoked, FTND.) were performed at 3 time points – EOT, 3, & 6 months after initial patient consult.

  - Patients with cancer displayed a non-significant trend ($p = .10$) toward lower abstinence rates at 6 months than patients with no cancer. No significant or marginal relationships between cancer and quit rates were observed at EOT or 3 months.

  - Patients with smoking-related cancers had significantly higher abstinence rates at EOT than patients with non smoking-related cancers. No significant relationships between smoking-related cancers and quit rates were observed at 3 or 6 months.

  - Patients with head and neck cancers had significantly higher abstinence rates at EOT than patients with no cancer. No significant relationships among cancer sites vs no cancer on abstinence rates were observed at 3 or 6 months.

  - Patients with psychiatric disorders had lower abstinence rates at EOT than patients with no disorders however these differences were not significant when analyses controlled for treatment variables and patient characteristics.

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Tobacco Treatment Program Leadership

Paul M. Cinciripini, PhD – Program Director
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Janice A. Blalock, PhD – Assistant Director
Associate Professor, Department of Behavioral Science

Questions

Psychiatric Adverse Events*

- **Post marketing reports of psychiatric adverse events with varenicline. Concern that smokers with psychiatric illness were excluded from clinical trials.**
- **Prospective trials have not demonstrated an association between varenicline and psychiatric adverse events in smokers in the general population of ‘real world smokers’ or in smokers with depressive disorders or schizophrenia**
- **Controlled trials have not demonstrated an association between varenicline and psychiatric adverse events in smokers with schizophrenia**
- **Smoking Cessation alone may result in increased irritability and depressed mood**

* Psych AE slides compiled by Dr. Eden Evins and used with permission

Nicotine Dependence Strongly, Independently Assoc with Suicide

- Nicotine dependence independently assoc with suicidal ideation, attempts and completed suicide in large studies controlling for psychiatric illness and alcohol use. Beratis 1997; Miller 2000; Breslau 05; Bronisch 08; Donald 06; Hawton 02; Hintikka 09; Kessler 09; Martinez-Ortega 08; Tanskanen 2000
- the 3rd highest Population Attributable Fraction for suicide attempts of any Axis I or II disorder, after MDD and BPD, higher than PTSD Bolton and Robinson 2010

No Signal in Large Observational Studies

- 80,660 smokers from UK Gen. Practice Research Database (Gunnel 2009)
- No evidence of increased risk of depression, suicidal thoughts, or self harm during smoking cessation attempt with varenicline vs. NRT or bupropion

Relative Risk Varenicline vs. NRT or Buproprion

Study Endpoint	**Varenicline vs. NRT**	**Varenicline vs. Bupropion**
Fatal/non-fatal self-harm	1.12 (0.67-1.88)	1.17 (0.59-2.32)
Suicidal Thoughts	1.43 (0.53-3.85)	1.20 (0.28-5.12)
Start of Antidepressant Therapy	0.88 (0.77-1.00)	0.91 (0.77-1.07)