

OBJECTIVES:

Many conditions exhibit strong diurnal variations and phenotypes which may influence work productivity. These relationships have not been well understood.

Gastroesophageal Reflux Disease (GERD) places a substantial burden on the working age population

- Of the 18.7 million suspected GERD cases in the U.S., 75% are working-age individuals
- GERD is by far the most costly digestive disorder in the U.S. with an estimated \$10 billion in direct and \$15 billion in indirect costs per year¹
- These estimates, along with other recent research,² suggest that indirect costs due to GERD-related work loss may exceed direct medical costs by a substantial margin^{1,2}
- Among GERD patients, nocturnal symptoms are common (80% report nighttime heartburn) and can lead to problems sleeping and with functioning the next day³
- No prior research has assessed the productivity impact of nighttime GERD (NTG) among full-time working adults living in the U.S.

Aim:

We develop a model to evaluate the relationship between sleep impairment and work productivity loss due to nighttime symptoms using the example of symptomatic daytime vs. nighttime gastro-esophageal reflux disease (GERD).

METHODS:

An Internet-based survey (September, 2004) recruited individuals by email invitation. Included respondents completed the questionnaire and met key inclusion criteria (a least 18 years of age, employed full-time, and living in U.S.) and exclusion criteria (at least 1 nighttime shift during the past 7 days, sampling quota filled [GERD target, n = 1000; control target, n = 500]). The questionnaire consisted of 4 primary components:

1) The GERD Symptom and Medication Questionnaire (GERD-SMQ).⁵ GERD-SMQ is a valid and reliable GERD screening tool designed to assess frequency and severity of heartburn and acid regurgitation during the past 12 months, and GERD medication use during the past 6 months⁵;

2) Nighttime & daytime symptoms of GERD during the past 7 days. Questions were developed to assess the presence (yes/no scale), frequency (8-point scale ranging from "0 nights/days" to "7 nights/days" with symptoms) and severity (10point scale ranging from "1-very mild symptoms" to "10-very severe symptoms") of nighttime and/or daytime symptoms of GERD;

3) Work Productivity and Activity Impairment Questionnaire (WPAI).⁶ General health problem and GERD-specific versions of the validated WPAI instrument were used to assess work impairment due to absenteeism and reduced productivity while at work ("presenteeism").⁶ The Work Productivity Score (WPS) is a scale that combines absenteeism and presenteeism to produce a measure of total work productivity loss. WPAI scales (presenteeism, absenteeism, and WPS) are all reported in terms of percent productivity loss.

4) Sleep impairment (SI) was assessed by a panel of 6 questions concerning problems with sleep. Questions assessed the frequency (8-point scale ranging from "0 nights/days" to "7 nights/days" with symptoms) GERD-related sleep impairment such as: getting a good night's sleep; feeling tired from lack of sleep; waking during the night; and the ability to fall back to sleep. A simple summative score was created from the 6 items (Cronbach's $\alpha = 89\%$).

Symptomatic GERD Cases were defined as follows: GERD Cases = GERD-SMQ >9 +heartburn and/or acid regurgitation during the past 7 days; Nighttime GERD = GERD Case + Nighttime heartburn or acid regurgitation ≥ 2 nights during the past 7 days; Daytime GERD = GERD Case + NOT nighttime GERD.

ANALYSIS:

Our conceptual framework modeled the impact of nighttime symptoms as causing Sleep Impairment (SI) which, in turn, influences daytime work productivity loss (PL). Thus, 2-equations – 1) SI as a function of GERD status (and covariates) and 2) WPAI as a function of SI (and covariates) – were simultaneously estimated using 3stage least squares (3SLS) regression. Results were compared to those of an alternative instrumental variables specification.

Briefly, the model consists of 2 equations:

residence + e_1

Equation 1 reflects the influence of GERD status on Sleep Impairment. Equation 2 accounts for SI influence on Productivity Loss - thus allowing GERD status to affect PL through this indirect mechanism – as well as the direct effects of GERD status on PL. Three-stage Least Squares (3SLS) was used to estimate the structural system defined by equations 1 and 2; respondents' state of residence was used to identify equation 1. All analyses were conducted in STATA version 8.7

RESULTS:

Table 1. Characteristics of Respondents with GERD

13,231 (21.4%) of 65,001 invited to participate responded

	GERD Type					
Characteristic	Daytime		Nighttime		p-value	
Ν	525		475			
Age, mean (sd)	44.7	(11.4)	44.6	(11.3)	0.835	
Male, %	40.1		42.2		0.497	
Spousal, %	69.4		70.8		0.627	
White, %	92.0		90.8		0.477	
Any College, %	59.9		53.2		0.032	
GERD Severity, %						
Mild	10.1		3.6			
Moderate	77.2		72.3		<0.001	
Severe	12.7		24.2			
Depression, %	25.1		23.7		0.618	
Other Chronic Conditions, %	14.4		20.8		0.008	
SF-36: PCS, mean (sd)	48.5	(8.0)	46.5	(8.5)	<0.001	
SF-36: MCS, mean (sd)	45.9	(8.8)	43.3	(9.9)	< 0.001	
Dependent Variables						
Sleep Impairment, mean (sd)	-0.207	(1.0)	0.229	(1.0)	< 0.001	
Productivity Loss (WPS), mean (sd)	0.054	(0.1)	0.122	(0.2)	<0.001	

1,515 respondents completed the questionnaire, 1000 were identified as GERD cases, 47.5% of these met the criteria for NTG.

Linking Symptoms Diurnality to Productivity Loss – **A New Conceptual Approach**

Robert J. Nordyke, PhD¹, Daniel Aguilar, MPH¹, Albert Lee, PhD¹, Amitabh Singh, PhD², Michael Tedeschi, RPh, MBA², Robert W. Dubois, MD, PhD¹ ¹Cerner Health Insights, Beverly Hills, CA, USA, ²Wyeth Research, Collegeville, PA

1) $SI = \beta_{10} + \beta_{11}NTG + \beta_{11}GERD$ Severity $+ \beta_{13}$ patient characteristics $+ \alpha_{11}$ state of

2) $PL = \beta_{20} + \alpha_{21}SI + \beta_{21}NTG + \beta_{22}GERD$ Severity $+ \beta_{23}$ patient characteristics $+ \alpha_{22}QOL + e_{23}$

NTG Impairs Sleep / NTG and Sleep Impairment Reduces Daytime Productivity

 Table 2.
 Three-stage Least Squares Regression Results

-	Std.			Std.				
	β	Err.	P>(z)		β	Err.	P>(z)	
				Sleep Impairment	0.043	(0.022)	0.049	
Nighttime GERD	0.394	(0.060)	<0.001	Nighttime GERD	0.029	(0.012)	0.012	
GERD Severity				GERD Severity				
Mild	Ref			Mild	Ref			
Mod	0.164	(0.117)	0.162	Mod	0.007	(0.019)	0.731	
Severe	0.289	(0.135)	0.035	Severe	0.089	(0.022)	<0.001	
Age	-0.004	(0.003)	0.069	Age	-0.001	(0.000)	0.006	
Male	-0.179	(0.061)	0.003	Male	0.004	(0.010)	0.694	
Other Chronic Conditions	-0.325	(0.072)	< 0.001	Other Chronic Conditions	0.009	(0.012)	0.480	
Depression	0.279	(0.081)	0.001	Depression	-0.043	(0.014)	0.002	
Spousal	-0.048	(0.065)	0.460	Spousal	-0.008	(0.010)	0.425	
White	-0.186	(0.106)	0.081	White	-0.009	(0.017)	0.616	
Any College	-0.095	(0.060)	0.116	Any College	0.025	(0.010)	0.010	
State *	Nr							
				SF-36: PCS	-0.004	(0.001)	<0.001	
				SF-36: MCS	-0.003	(0.001)	0.010	
Constant	2.498	(0.328)	<0.001	Constant	0.422	(0.073)	<0.001	
	n = 1000			1	n = 1000			
2	$\chi^2 = 206.6$			χ^2	² = 308.6			

*Individual state coefficient estimates not reported; test for joint significance: Wald $\chi^2(49) = 72.8$, (p=0.019)

NOTE: For both Sleep Impairment and Productivity Loss variables, higher values reflect higher levels of impairment or loss.

Sleep Impairment Results

- Nighttime GERD has a strong association with Sleep Impairment
- Jointly, the estimates on Moderate and Severe GERD are significant at the 10% level (p=0.092)

Productivity Loss Results

- Both Sleep Impairment and Nighttime GERD have strong associations with Sleep Impairment
- Those with severe GERD experience greater PL than those with Mild or Moderate disease
- Gender has no independent impact of PL
- Results of the IV regression estimation of Equation 2 were consistent with those of 3SLS.

NTG Affects Productivity both Indirectly and Directly Figure 1. Adjusted Outcomes by GERD Status



Note: All within-severity differences are significant at p<0.001

Figure 1 further demonstrates the effect of GERD status on Sleep Impairment and Productivity Loss by presenting adjusted outcomes by Nighttime vs. Daytime GERD and by severity.

- For all severity levels, those with Nighttime GERD experienced greater Sleep Impairment than those with Daytime GERD.
- At any given severity, those with Nighttime GERD experienced greater Productivity Loss.

CONCLUSIONS:

- Our analytic approach shows clearly that Nighttime GERD has a greater negative impact in Productivity than Daytime GERD
- Our framework also highlights the 2 separate effects of NTG on daytime productivity:
- An indirect effect working through the mechanism of greater sleep impairment
- A direct effect likely due to the impact of NTG on overall health status
- These distinct effects suggest that to mitigate the negative effects of NTG symptoms on productivity the specific impact of NTG on sleep impairment must be addressed
- The impact of the distinct daytime vs. nighttime nature of many chronic conditions is little understood. This framework should prove useful in evaluating similar chronic health conditions (eg, asthma) and related adverse events due to medication use.

REFERENCES:

- 1. American Gastroenterology Association. The Burden of Gastrointestinal Disease. 2001.
- 2. Dean BB, et al. J Managed Care Med. 2003; 7:6-13.
- 3. Shaker R, et al. Am J Gastroenterol 2003;98: 1487-93.
- 4. Farup C, et al. Arch Intern Med 2001;16:45-52.
- 5. Ofman JJ, et al. Dig Dis Sci. 2002;47(8):1863-9
- 6. Reilly MC, et al. *Pharmacoeconomics.* 1993; 4:353-365.
- 7. StataCorp. STATA statistical software: release 8.0. College Station, TX, 2003.