

Work productivity improvement after acid suppression in patients with uninvestigated dyspepsia

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ABSTRACT

INTRODUCTION: Lost productivity account for a significant part of the costs caused by gastro-intestinal symptoms. We aimed to describe self-reported productivity in patients presenting with dyspepsia.

MATERIAL AND METHODS: Data were sourced from a randomized, double-blinded study of two weeks of esomeprazole 40 mg or placebo in 805 primary-care patients with uninvestigated dyspepsia. Work productivity was tested using the Work Productivity and Activity Impairment questionnaire. Treatment effect on work productivity loss was tested according to the likelihood of treatment response.

RESULTS: A total of 401/805 employed patients were included in the analysis. The average work productivity loss in the past seven days was 10.5 working hours/week. The productivity loss grew with increasing severity of symptoms at baseline. Following two weeks of treatment, the mean improvement in work productivity was significantly higher for both absenteeism (1 hour versus 0.1 hour, $p < 0.05$) and presenteeism (5.3 hours versus 4.3 hours, $p < 0.05$) in patients treated with esomeprazole versus placebo. The most substantial improvement was seen in patients who, based on baseline symptoms, were assessed to be likely treatment responders.

CONCLUSION: Dyspepsia symptoms represent a significant economic burden in terms of lost productivity. The RESPONSE algorithm is successful in determining which patients will benefit from acid suppression in terms of enhanced productivity.

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TRIAL REGISTRATION: ClinicalTrials.gov NCT00318968.

Upper gastrointestinal symptoms (UGIS) are prevalent in the general Danish population [1] and among patients consulting a primary care physician [2]. A few studies have found a negative impact of gastroesophageal reflux disease (GERD) on health-related quality of life when compared with a healthy population [3]. The marked effects of UGIS on health and well-being can have consequences for the performance of the affected individuals, particularly at work [3, 4].

Impaired performance at work in the form of lost work productivity is also of interest when considering the economic burden of a disease, as it is a major element in indirect costs. The indirect costs of a disease are

those that are not directly related to health care. For patients with UGIS, the indirect costs related to absence (absenteeism) from work and reduced productivity (presenteeism) while at work can exceed any health-care costs [5, 6].

Agréus & Borgquist reported on a study of the total cost of gastro-oesophageal reflux disease, dyspepsia and peptic ulcer disease in Sweden. They estimated the indirect costs to 39% of the total cost (at the same magnitude as cost of medication, which was 37% of total cost) [5]. In a study conducted by the Swedish health authorities, the societal cost of dyspepsia in Sweden was estimated to be in the range of 434-507 million € of which 51-59% were indirect costs [7]. In both studies the indirect costs were calculated on the basis of absence from work and early retirement and did not include lower productivity while at work.

As a consequence, improved work productivity and reduced indirect costs are important economic elements in the treatment of patients with gastro-intestinal symptoms. In the primary care environment where unselected patients present with diffuse and overlapping symptoms with different aetiology, empirical therapy with a proton-pump inhibitor (PPI) has been adopted by many clinicians because it is considered practical, safe and cost-effective. Epidemiological surveys have suggested that the majority of patients are managed initially with a short course of PPI before decisions are made about invasive testing or long-term therapy [8-10].

The purpose of this study is to describe the work productivity impairment in patients with un-investigated dyspepsia in Danish primary care and the responsiveness to two weeks of proton-pump inhibition treatment.

MATERIAL AND METHODS

Data were sourced from the RESPONSE study which is a double-blinded, randomized, placebo-controlled primary-care study focusing on treatment of uninvestigated dyspepsia [11]. Cases of uninvestigated dyspepsia were defined as patients presenting with UGIS that the primary-care physician considered acid-related.

RESPONSE main study

The study was conducted at 59 primary-care centres in Denmark, and a total of 807 patients were recruited.

ORIGINAL ARTICLE

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TABLE 1

Patient characteristics of working population in RESPONSE.

	Esome- prazole	Placebo
n	197	204
Age, years, mean (SD)	44 (11)	46 (11)
Weight, kg, mean (SD)	79.1 (15.7)	79.2 (16.8)
Height, cm, mean (SD)	172.8 (9.47)	172.9 (9.59)
Male, %	48.7	46.6
Caucasian origin, %	98.5	96.6
Nicotine use, %	31.0	30.4
Alcohol use, ^a %	4.1	3.5
<i>Duration of gastrointestinal symptoms, %</i>		
≤ 3 months	52.8	49.0
> 3 and ≤ 12 months	16.2	15.2
> 12 months	31.0	35.8
<i>Key complaint, severity during last 24 hours, %</i>		
Mild	19.9	27.6
Moderate	59.2	54.7
Severe	20.9	17.7
<i>Duration of key complaint, %</i>		
< 1 week	13.7	13.2
1 week-1 month	42.6	34.8
> 1 month	43.7	52.0

SD = standard deviation.

a) Alcohol use above recommended limits: > 21 units/week in males; > 14 units/week in females.

The study population consisted of Caucasian males (45%) and females with a median age of 52 years. 42% reported having suffered from their symptoms for less than one month, while 40% reported a long duration (> 1 year). Based on data from 805 patients who completed the trial, an algorithm was established which estimates the likelihood of response to a two-week course of esomeprazole (40 mg once daily). The findings from the main study and the properties of the algorithm – here referred to as the RESPONSE therapeutic index (TI) – have been presented elsewhere [11].

RESPONSE work productivity sub-study

For this analysis of work productivity loss, we used data from the sub-group of patients who reported being employed both on the date of the first visit and at follow-up (two weeks after).

Work productivity loss due to dyspepsia was measured using the validated Work Productivity and Activity Impairment questionnaire [12, 13] specific for patients with UGI symptoms (WPAI:UGIS). The WPAI instrument is a disease-specific, patient administered questionnaire adapted from the general WPAI instrument specifically for the RESPONSE study. A related adaptation of WPAI to symptoms of reflux disease, WPAI:GERD, has been used in several studies [4] and has shown good cross-sectional construct validity and responsiveness to change [13].

The WPAI:UGIS instrument provides information on the respondents' normal working hours, hours absent from work due to UGI symptoms and a rating of reduced productivity while at work due to UGI symptoms. A one-week recall period was used for productivity data.

From WPAI:UGIS data, the number of hours absent from work (absenteeism) and reduced productivity while at work in hours (presenteeism) were calculated at study inclusion and at end of therapy. Absenteeism was defined as the number of work hours lost per week because of UGIS-related absence from work. Presenteeism was defined as the self-rated UGIS-related reduction in effectiveness while present at work, and expressed in work-hour equivalents (reduced effectiveness per hour × hours at work).

Overall work productivity losses (absenteeism + presenteeism) were converted into a monetary cost by multiplying the total number of hours lost with the average hourly employment cost of a Danish employee (228 DKK, where 1 € = 7.45 DKK; calculated from official national employment statistics available in 2007 [14]).

The treatment effect on work productivity loss (mean change in work productivity between baseline and end of study in the esomeprazole arm compared with the placebo arm) was tested in the sub-group of employed patients using the Kolmogorov-Smirnov test.

Furthermore, we studied the relationship between the RESPONSE therapeutic index and work productivity. The TI was calculated for each individual patient, and the likelihood of treatment response was categorised as low, intermediate or high according to the algorithm developed as the primary objective of the RESPONSE study [11]. The TI is constructed to be predictive of treatment response to proton-pump inhibition based on the patient's presenting symptoms; therefore it is of interest to know whether work productivity differs between patients with a different likelihood of treatment response, and whether the index is predictive of changes in work productivity.

Trial registration: ClinicalTrial.gov NCT00318968.

RESULTS

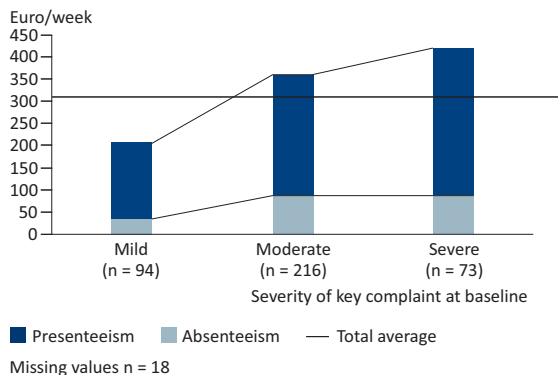
Out of the 805 patients in the primary analysis, 401 patients reported being employed at both baseline and follow-up, and they were included in the analysis. **Table 1** gives the baseline characteristics of the sub-group.

Overall, the average productivity loss at baseline was 10.5 working hours/week per patient (absenteeism 2.2 hours (95% confidence interval (CI): 1.6-2.8 hours) and presenteeism 8.3 hours (95% CI: 7.3-9.3)). This equated to an average monetary loss of € 316 per patient (95% CI: € 277-355).

The value of the estimated overall work productiv-

FIGURE 1

Average work productivity loss in the seven days preceding contact with the physician in monetary value by severity of key upper gastrointestinal symptom at baseline (n = 401).



ity loss for the seven days preceding contact with the physician rose with increasing severity of the key UGI complaint (pain, heartburn, regurgitation, nausea or other) at baseline (Figure 1).

Compared with placebo, improvement in work productivity per week was significantly increased for both absenteeism (1 hour versus 0.1 hour, $p < 0.05$) and presenteeism (5.3 hours versus 4.3 hours, $p < 0.05$) in patients treated with esomeprazole 40 mg once daily for two weeks. The economic value of the incremental gain in overall work productivity was € 45/week per patient.

Figure 2 presents the work productivity loss for the seven days preceding enrollment by likelihood of treatment response according to the RESPONSE therapeutic index at baseline. The highest number of hours lost was seen in patients with a high likelihood of response to esomeprazole (12.6 hours (95% CI: 9.8-15.4 hours)) as compared with patients with low (9.6 hours (95% CI: 7.7-11.5 hours)) and intermediate scores (8.9 hours (95% CI: 7.1-10.7 hours)).

Figure 3 presents the change in work productivity after therapy by likelihood of treatment response at baseline. The highest improvement was seen in patients (n = 126) with a high likelihood of treatment response (change esomeprazole versus placebo: 8.7 versus 5.5 hours/week; $p = 0.025$). The improvements in work productivity in patients with a lower score were smaller and not significantly different between treatment arms.

DISCUSSION

This study adds to the growing knowledge on the work productivity impairment associated with gastrointestinal disease. The strength of the study lies in that it is the first large study of work productivity in Danish patients with UGI symptoms using the validated WPAI instrument, and it is the first to include patients as they

FIGURE 2

Total hours lost productivity (absenteeism and presenteeism) due to upper gastrointestinal symptoms during seven days preceding consultation with physician by likelihood of treatment response assessed at first visit.

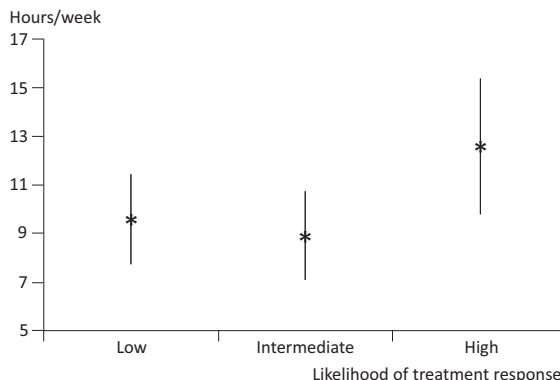
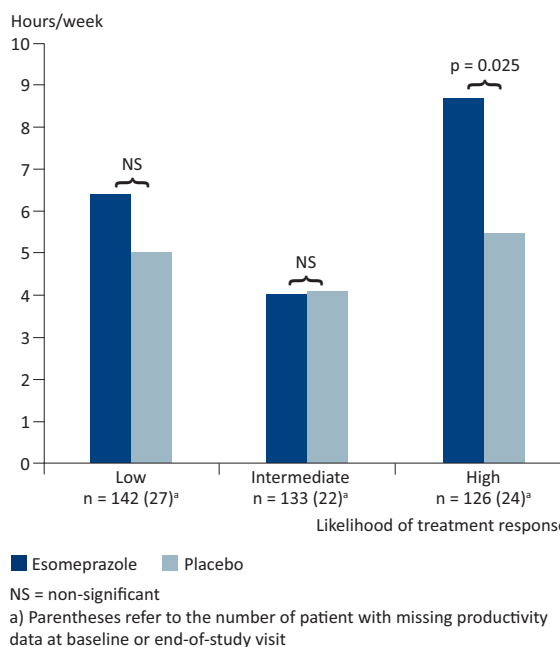


FIGURE 3

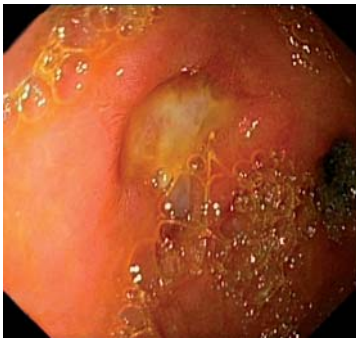
Change in work productivity after two weeks of therapy (40 mg esomeprazole or placebo) by likelihood of treatment response at baseline (n = 401). For 73 patients Work Productivity and Activity Impairment questionnaire data at baseline or end-of-study were missing.



present in primary care with diffuse and overlapping symptoms with different aetiology.

We found work productivity impairment at a level similar to that previously reported for patients with reflux disease [15] and, hence, uninvestigated dyspepsia in primary care is associated with considerable costs to society in the form of reduced ability to work and to work effectively. The level of impairment is clearly related to

Endoscopic photo of gastric ulcer.



the severity of the patient's key complaint, but fairly similar across the therapeutic index for predicted treatment response. This indicates that work productivity loss is related to the symptom as such and not to whether the disease is acid-related or not.

Two weeks proton-pump inhibition using esomeprazole 40 mg entails a significant improvement in work productivity compared with placebo. The largest numeric difference is seen in patients who were categorised as having a high likelihood of treatment response on the basis of their baseline characteristics.

There are a couple of limitations to this study. First of all, this study did not estimate the full societal costs because impairment in daily activities outside work was not included. Furthermore, the WPAI is a subjective measure and could be accused of being just another expression of symptom severity or bother and not predictive of actual productivity. For many modern job roles, objective measures of productivity cannot be established. However, studies of patients engaged in activity where production can be measured in units have reported levels of productivity loss in the same range as those captured by the subjective WPAI instrument [15].

Finally, the study does not provide a definite answer to whether use of the TI index will identify the patients with the highest benefit in terms of work productivity. To do this, a confirmatory study of such use of the tool would be needed. Still, the results strongly suggest that the RESPONSE algorithm will support primary-care physicians in targeting esomeprazole use to those dyspepsia patients who will benefit the most in terms of treatment response as well as work productivity.

In conclusion, our results indicate that acid-related UGI symptoms in Danish primary-care patients represent a significant economic burden in terms of lost productivity. The RESPONSE algorithm is successful in determining which patients will benefit from acid suppression in terms of enhanced productivity.

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