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ADHERENCE IN PHARMACEUTICAL UTILISATION

– A demand for health analysis based on the Swedish Survey of Living Conditions and the Pharmaceutical Registry.

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SUMMARY
The World Health Organization rapports general low adherence to medical treatments in long term therapies among developed countries. The aim of this study was to analyse the individual variation in drug adherence to long term use. A set of individual data with people interviewed in year 2004/2005 was created from the Swedish Survey of Living Conditions and the Pharmaceutical Registry. The data set included 909 individuals that had been dispensed selective-beta-receptor inhibitors for long term use for cardiovascular treatment. Drug adherence was approximated as dispensed daily doses divided with the total number of days in the study period. Drug Adherence was regarded as a health-investment. We found that adherence was positively correlated with (1) wage, (2) having been dispensed other types of prescribed drugs for cardiovascular diseases, and (3) being overweight or obese. Moreover, a net of crosseffects were found significant, smokers among those with low education have higher adherence compare to non smokers or smokers with higher education. Furthermore, wage was found to be negatively correlated to wage among women. Adherence behaviour can be analysed within the demand-for-health framework. Further research need to be done in order to understand the mechanisms behind decision making concerning adherence.

KEY WORDS: Adherence; Drug utilisation; Human capital; Grossman model;

Sweden

CONTENTS

1. INTRODUCTION

According to Victor Fuchs the utilisation of various pharmaceuticals is responsible for the bulk part of the improvements in health, measured as, for instance, reduced morality, that have taken place in the industrialised world during the second half of the 20th century (Fuchs 1998). Thus, the utilisation of pharmaceuticals, and how it is related to individual characteristics, is a question of immense policy importance (Murphy and Topel, 2006). Individual utilisation of prescribed pharmaceuticals comprises at least two decisions made by the individual: the decision to seek out a physician, and, assuming that a prescription results from that visit, the degree to which the prescribed utilisation is followed – adherence. In this paper we will address the issue of adherence.

In what follows we will use WHO's (2003) definition of adherence in long-term therapy, which is based on Haynes (1979*)* and Rand (1993) definitions of adherence: *the extent to which a person's behaviour taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider.*

The degree of adherence varies among therapies and between individuals within the same therapy group (Andersson *et al*., 2005; Rizzo and Simons, 1997). The decision to follow or not to follow treatments as prescribed is made by the patient. Therefore, adherence behaviour reveals information about the individual's subjective view about the treatment. For example, the behaviour of an individual that do not collect the prescribed drug at all from the pharmacy, reveals that his or her subjective value is less than the cost (monetary and time) of initiating the treatment. Analogously, long-

term adherence behaviour reflects the individual's subjective net value of following the treatment plan.

Cardiovascular diseases are in a global perspective, the most common cause for death among individuals below 65 years of age. Apart from individual suffering, cardiovascular events affect many people in the working force, leading to substantial losses of production. (WHO, 2003) For instance, the value of production losses associated with cardiovascular events was calculated to 9 866 EUR per patient in the Swedish workforce during the first 12 month after the event (Lindgren *et al.*, 2006). Hypertension is a well known risk factor for coronary heart diseases, stroke and other cardiovascular diseases. An estimated 1.8 million individuals in Sweden suffer from hypertension, which corresponds to 27 percent of the adult population in the age group 20 years of age and older (SBU, 2004). The prevalence is roughly the same among men and women, and increases with age. The main treatment for hypertension involves pharmaceuticals (and, of course, lifestyle changes). Adherence to medical treatment or lifestyle changes in general, is determinant for the economic impact of cardiovascular diseases.

Drug treatment using selective beta receptor inhibitors is a cost-efficient way of reducing hypertension and the incidence of cardiovascular events (Johannesson *et al.*, 2003; Dias da Costa *et al.*, 2003). In spite of this, the majority of the population with hypertension in the U.S. is not optimally treated (Ostchega *et al.*, 2007). A similar scenario is seen in Sweden, approximately 20-30 percent of all individuals treated for hypertension reach their target blood pressure although effective drugs are available (Läkemedelsboken, 2007/2008).

The most important explanation for pharmaceutical-treatment failure is low adherence and the World Health Organisation (2003) estimate that adherence in developed countries is on average 50 percent, meaning that every second drug dose is not taken as prescribed. Drug adherence is even lower in developing countries, presumably due to non-affordability. For most drugs, long-term treatment effect is often strongly dependent on adherence over time, where insufficient adherence results in reduced or non pharmaceutical effect.

The purpose of this study is to examine the degree of medical adherence in the utilisation of selective beta-receptor-inhibitors among individuals with long-term treatment for cardiovascular diseases, using the "demand-for-health" framework. Fundamentally, this framework regards health-related behavior as *derived* from the underlying demand for good health. The demand for health model can be modified and used to explain differences in drug adherence in long-term treatment, both between individuals and between different treatments. Knowledge about the relationship between adherence and individual characteristics is essential to improve real-life effectiveness of drug therapy.

2. THEORETICAL FRAMEWORK

The theoretical framework for analysing investments in human capital was originally developed by Gary Becker (1964) and is still today the foundation for both theoretical and empirical analyses for health related behaviour.

Our theoretical basis is the “demand-for-health” model, a central economic model for analysing individual health behaviour developed by Grossman (1972a,b) and extended, inter alia, by Bolin *et al*., (2001, 2002a,b), Jacobson (2000), Liljas (1998), Muurinen (1982), and Wagstaff (1993); for a survey and review, see Grossman (2000). According to this model, the individual is the producer of his or her own health. Naturally, the notion of ”producer of health” does not mean that the individual fully determines his or her state of health - heredity, environment, and chance are three factors, which interfere - but rather that the individual does *influence* his or her health. Thus, the individual provides efforts for health improvements and, hence, may be regarded as investing in his or her health. Health investments are in this context produced by choosing lifestyle, making better and worse health states more or less probable, and by using medical advice, pharmaceuticals, hospital treatment etc.

Thus, individual health behaviour might be regarded as a process in which the individual simultaneously both demands and supplies his or her own health. Many different factors have an impact on the individual’s demand for health and supply of investments in health. These demand and supply aspects of the individual’s health-related behaviour are used below to discuss the effects of various variables on the demand for health and the efforts to improve health. Grossman’s initial formulation of the model incorporated the utilisation of medical care goods as inputs into production of investments in health. In this paper, we are interested in a very specific kind of health investment: the adherence to a prescribed pharmaceutical regimen. We will assume that deviations from that regimen result in diminished health improvements.

Next, we will develop a modified version of the demand-for-health model, in which the degree of adherence and the deviation from a prescribed pharmaceutical-utilisation regime are incorporated.

2.1. A modified demand-for-health model

We consider an individual who derives utility from consumption of a market commodity, *Z*, and from the stock of health, *H*. We assume that the utility function is time additive, increasing in consumption and the stock of health, and jointly concave in consumption and health. Thus, preferences are:

$$U(Z, H_t); U_i' > 0; U_{i,j}'' < 0. \ (i, j = Z, H) \qquad (1)$$

The individual invests in the stock of health capital. These investments are partially offset by natural depreciation – at rate δ_t – of the existing stock of health capital. Following Grossman (1972), Muurinen (1982), Wagstaff (1986), Liljas (1998), Jacobson (2000), and Bolin *et al*., (2001), we examine a model in which the rates of depreciation are time dependent. Further, we distinguish between the ability to produce gross investments in health, and the rate at which this utilisation is transformed into health capital. Gross health investments, *I*, is comprised of adherence to a prescribed pharmaceutical-utilisation scheme and, hence, the ability to produce gross health investments is the ability to be adherent. Any deviation from the prescribed scheme is costly in the sense that the adherence produced is diminished.

More specifically, letting I^* denote the optimal level of adherence, and assuming that the diminishing effect of deviating from perfect adherence is proportionate to the difference $(I - I^*)$, we get the following equation for the motion of the stock of health capital over time:

$$\dot{H}_t = I_t + \varphi \cdot (I_t - I^*) - \delta_t \cdot H_t, \qquad (2)$$

where φ is a parameter reflecting the rate at which any deviation diminishes the effect of the actual adherence on health. Notice, that the individual cannot be more than perfectly adherent, i.e., $I \le I^*$. Further, we assume that these consequences may vary between being insignificant, in which case φ is close to zero, and being important, in which case $0 << \varphi \le 1$. The size of φ depends on (1) drug characteristics, for example; drug formula, half-life i.e., the period of time required for the amount of drug in the body to be reduced by one-half, therapeutic window, i.e., the dose range where the drug has a desired efficacy and at the same time has an acceptable safety profile and, (2) specific health related conditions. In general, drugs with a narrow therapeutic window and a short half-life have a large φ, hence, a large marginal investment-benefit of adherence. The relationship between, on the one hand, the amount of adherence that is transformed into health capital (net health investment) and on the other hand, the level of adherence (I), is dependent on both the gap between adherence and the optimal adherence $(I - I^*)$ and the parameter φ, see illustration in Figure 1.

Figure 1

We assume that the production technology used for producing adherence is homogenous of degree zero, results in a cost-of-gross-investment function of the following shape:

$$C(I_t) = \pi(p, w; E) \cdot I_t , \tag{3}$$

where $\pi_t(p, w; E)$ is the one-unit cost of gross health investment, p is the composite price of market goods and services used in the production of adherence, and w is the wage rate. We also assume that the level of education influences the ability to produce adherence: the more education the lower one-unit cost, i.e, $\frac{\partial \pi}{\partial E} < 0$.

2.2. Constraints

The sum of the return on financial capital, the market income, and the cost of investments in health capital must equal the rate of growth of the stock of financial capital. Hence, the cost of the gross investments in health, and earned income, denoted y_t, must follow the asset accumulation constraint:

$$\dot{W}_t = rW_t + y_t(H_t) - \pi_t \cdot I_t - p^Z \cdot Z_t, \tag{4}$$

where W denotes total assets, r the rate of interest, and p^Z the price of the market commodity. Sick time is a function of health capital, $\tau_t^s(H_t)$ and, hence, the individuals full income is:

$$y_t = w_t(\Omega - \tau_t^s(H_t)), \tag{5}$$

where Ω denotes total time. Time available for market work increases as the stock of health capital increases. This is manifested through the amount of time spent at being sick being inversely related to the stock of health capital, i.e., $\partial\tau_t^s / \partial H_t^i < 0$. We assume that $(\partial^2\tau_t^s / \partial H_t^{\,2}) > 0$. The connection between the health stock and earned income is $\partial y / \partial H_t = -\omega_t(\partial\tau_t^s / \partial H) > 0$.

2.3. The individual's control problem

The intertemporal problem that faces the individual is to choose the time path of the health capital so that his or her lifecycle utility is maximised. We are now ready to formally state the maximisation problem that faces the individual. Assume that the individual chooses the time path of health capital and the planning horizon T. Future utility is discounted at the rate ρ and, hence, the individual acts as to solve the following:

$$max \int_0^T e^{-\rho t} U(Z_{t,} H_t)\, dt$$

subject to:

$$\dot{H}_t = I_t + \varphi \cdot (I_t - I^*) - \delta_t \cdot H_t \qquad \dot{W}_t = rW_t + y(H_t) - \pi_t \cdot I_t - p^Z \cdot Z_t$$

$H_0 = \hat{H}$; $W_0 = W$; $H_T \leq H_{\min}$, and $W_T \geq 0$.

Our model distinguishes itself from previous extensions of the demand-for-health model in recognising that investments in health may not only be impeded by diminishing returns to scale, as assumed by Ehrlich and Chuma (1990), but also since the net health benefits from a certain level of investments may diminish in proportion to the investments divergence from a specific "target" level.

2.4. Optimality conditions

The solution to the maximisation problem is achieved by applying optimal control theory (see appendix A).

$$\frac{e^{-(\rho-r)t}}{\lambda_0^W}\frac{\partial U}{\partial H_t} - w_t(E)\cdot\frac{\partial \tau_t^s}{\partial H_t} = (r+\delta_t^H)\cdot\frac{\pi}{(1+\varphi)}. \qquad (6)$$

The interpretation of equation (6) is as follows; the left-hand side is the net benefit of health capital and the right-hand side is the net marginal cost of health capital. The first term on the left-hand side is the discounted consumption benefit of health; the second term is the gain accruing from health capital as less time is spent being sick. Similarly, the right-hand side constitutes the marginal cost of an additional unit of health capital: the term r reflects the opportunity cost of investing in health rather than in the capital market; the depreciation term reflects the fact that each unit of health capital depreciates by a certain amount at each point in time, making it more expensive to add an additional unit of health capital to the stock. The last term on the right-hand side reflects that for each unit of adherence produced the individual enjoys an additional φ units of health capital.

2.5. Predictions

The predictions regarding age, wage and education on the demand for health and health investments (adherence) are the same as the ones derived by Bolin *et al*. (2002). The additional prediction obtained from the extended model presented in this

paper relates to the rate at which deviations from the optimal level of adherence diminish the health effect of adherence, φ.

The therapeutic results depends both on adherence and on φ. The level of φ, as stated previously, depends on drug characteristics. For example, antibiotic treatments have a relatively large φ and, hence, treatment of infectious diseases is strongly dependent on adherence. This is so since early interruption of the treatment may result in no positive treatment effect but instead, a negative health investment due to side effects. On the other hand, treatments with, for instance, paracetamol and ibuprofen for pain relief have a smaller φ. This means that the degree of pain relief corresponds closely to the level of adherence. Further, we assume that the size of φ, depends also on specific health related conditions (which are considered exogenous in this paper). In our case, the prevalence of overweight, obesity, diabetes, depression and/or smoking are all risk factors that make adherence to the cardiovascular treatment more important. Moreover, the use of other hypertension lowering drugs may also influence φ. The impact on φ may go in both directions. This is because hypertension lowering drugs both can be a complement or a substitute to selective-beta-receptor-inhibitor treatment depending on the individual's treatment plan from the physician. The size of φ, and hence, the impact on adherence is (1) negative if BT is a substitute and (2) positive if BT is a complement to selective beta receptor inhibitors. See table I for predictions.

Figure 2 and Table I