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## Jose L Turabian\*

Family Doctor, Regional Health Service of Castilla La Mancha (SESCAM), Centro de Salud Benquerencia, Gadarrama s/n, Toledo, Spain

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\*Corresponding author: Jose L Turabian, Family Doctor, Regional Health Service of Castilla La Mancha (SESCAM), Centro de Salud Benquerencia, Gadarrama s/n, Toledo, Spain, E-mail: [jturabianf@hotmail.com](mailto:jturabianf@hotmail.com)

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## Case Report

# A Narrative Review of Natural History of Diseases and Continuity of Care in Family Medicine

## Abstract

Natural history of disease refers to the progression of a disease process in an individual over time. Family medicine has important epidemiological connotations, presenting a unique opportunity to study natural history of a disease. We present an example case of the natural history of the disease: the continued care of a patient with thromboangiitis obliterans for 37 years, who was continuously attended over many years in family medicine level, with the aim of reflecting and conceptualizing the importance that, for epidemiological knowledge of natural history of diseases have the data provide by family medicine, which can be classified as biopsychosocial typologies of the natural history of diseases, according to their pattern of natural history, and through an epidemiological classification directed by medical intervention. So, there are two complementary perspectives to characterize the natural history of the disease: that of the general practitioner, who through the medical records the entire process of each patient, and can determine both that there is a new health problem and its peculiarities; is an individualized vision. And the epidemiologist, who through the multiple health records he handles, and the support of biostatistics can discover a new disease and its evolution; is a population view. Future epidemiological strategies that use longitudinal study designs or "continuing care", using homogeneous definitions of diseases, could play a pivotal role in better elucidating the controversies in natural history and the pathophysiology of subtypes of many common diseases, leading to improved clinical care. Cohort studies on the natural history of diseases should be enhanced in order to provide a basis for the development of health strategies and prevention and treatment measures. The ordinary general practitioners can make a significant contribution to research on the basis of patients seen in routine practice.

*"There was a time of adolescence when the green light dyed the walls dry and covered with plaster; then in the city it seemed that the cool vegetation froze the smoke of the houses in fog. Then it paled, lost all the colors ...: a dye of dry opal a little eclipsed by the centuries".*

## Introduction

Natural history of disease refers to the progression of a disease process in an individual over time, in the absence of treatment. Although at present, the natural history of disease is affected by the medical or surgical treatment, and new drugs are going to change the natural history and epidemiology of many diseases worldwide. However, the global consequences will depend on treatment accessibility, and of medication adherence [1-5].

Natural history of disease represents the course of biological events between the sequential action of component causes (etiology) until the disease develops and the outcome occurs (healing, passing to chronicity or death). For example, untreated infection with HIV causes a spectrum of clinical problems beginning at the time of seroconversion (primary

HIV) and terminating with AIDS and eventually death. In this example, it is now recognized that it may take 10 years or more for AIDS to develop after seroconversion [6]. Many, if not most, diseases have a characteristic natural history, although the time frame and specific manifestations of disease may vary from individual to individual and are influenced by preventive and therapeutic measures.

The interest of medicine to know the natural evolution of each disease is to discover the different stages and components of the pathological process, to can intervene as early as possible and change the course of the disease, in order to avoid the deterioration of health. There are two complementary perspectives to characterize the natural history of the disease: that of the general practitioner, who through the medical record records the entire process of each patient, and can determine both that there is a new health problem and its peculiarities;



is an individualized vision. The epidemiologist, who through the multiple health records he handles, and the support of biostatistics can discover a new disease and its evolution; is a population view.

The person is the center of interest for the family doctor; but the importance of epidemiological research at the family physician level is often forgotten. This epidemiological level today is downplayed or underestimated; however, there have been family physician pioneers who studied the epidemiologic problems of their community with scientific rigor. Some of them have been recognized for their seminal work in the last 125 years [7-11].

In this context, we present an example-case of the natural history of the disease: the continued care of a patient with thromboangiitis obliterans for 37 years, including selected co-pathologies. The patient was continuously attended over many years in family medicine level, and it is presented with the aim of reflecting and conceptualizing the importance that, for epidemiological knowledge of natural history of diseases, have the data provide by family medicine.

### Case Example

#### Thromboangiitis obliterans: a natural history for 37 years

**1974:** JRM was diagnosed of thromboangiitis obliterans, at 24 years of age, being a smoker of 20 cigarettes / day for 8 years. The onset symptomatology consisted of hypersensitivity to cold, with pain and coldness in both hands and feet. From its diagnosis, the disease followed a progressive course, with ulcerations in the right hand and both feet that forced the amputation of six fingers.

**1981:** In spite of the indication to suppress the tobacco, the patient did not stop smoking until 7 years after the diagnosis.

**1986:** The patient continued medical treatment with antiplatelet agents, peripheral circulation stimulants and calcium antagonists, and a sympathectomy was performed.

**1995:** The patient quit smoking.

**2001:** Six years after quitting smoking, the patient began to experience improvement in his symptoms but still needed medical attention and cures for his skin lesions.

**2004:** Certain hematological alterations (hemoglobin increase and thrombocytosis) that are related to thromboangiitis obliterans are maintained.

**2007:** After 12 years of quitting smoking, the symptoms had practically disappeared and there was no recurrence of ulcerations, reducing the requirement for analgesics.

**2008:** It is diagnosed of type 2 diabetes mellitus.

**2009:** From 1986 to this date has maintained the treatment of nifedipine and analgesics.

**2010:** Ureteral carcinoma (bladder tumor) grade II-III is diagnosed and transurethral resection and percutaneous nephrectomy are performed, as well as chemotherapeutic treatment. There is a left common femoral vein thrombosis.

**2011:** The patient presents venous thrombosis in lower right limb. There is sepsis of urinary origin. Pulmonary, bony, thoracic, hepatic, and splenic metastases are found. The patient dies at 60 years of age.

### Discussion

#### The relationship between continuity of care in family medicine and the epidemiological knowledge of the natural history of diseases

Family medicine is a major source of information about health problems and their evolution. For most illnesses the general practitioner is the first point of contact in the health care system and he looks after a population whose age and sex composition is known. He is therefore in an ideal position to conduct inquiries about natural history of disease (the factors predisposing, precipitating and perpetuating the disease). The essence of family medicine is to assist individuals in families and communities, and this implies, on the one hand a good continuity of care, and moreover a knowledge of the nature of diseases in the community.

The continuity of care is considered as a defining characteristic of family medicine and primary health care [12-18], although it can be seen from different perspectives, suggesting a hierarchy of dimensions from less to more complexity (Table 1) [19-23].

In medicine a priority objective of the studies must be the knowledge of the natural history of the disease [24]. Family

**Table 1:** Hierarchy of Continuity Dimensions of Attention.

Continuity dimensions of attention according to degree of complexity	Concept
1) Continuity of information	Is the availability of clinical information to any health care provider who treats the patient
2) Geographical continuity	It refers to care provided with continuity, regardless of the location of the patient - consultation, home, hospital, etc.
3) Interdisciplinary or team continuity	It involves the care that allows the prior knowledge of the patient even when it requires a wide range of specialized services
4) Longitudinal or chronological continuity	It refers to the fact that health care is produced in the same place, with the same medical record, and with the same professionals, but does not directly address the nature of the relationship between the patient and the provider
5) Interpersonal continuity in the doctor-patient relationship	It refers to a special type of longitudinal continuity in which there is a continuous personal relationship between patient and care, and is characterized by personal trust and responsibility
6) Family Continuity	It refers to a special type of longitudinal continuity in which there is a continuous personal relationship between patient and care, and is characterized by personal trust and responsibility

medicine presents a unique opportunity to study the natural history of disease and allows the establishment of patient-physician-family-community relationships. Family doctor work includes the natural history of disease and the human life cycle, and so, no one is better able to observe, from family history, the ultimate consequences of any health problem (Figure 1) [25–28]. The simplest and most basic way to achieve effective care is by continuing care [25].

### A case example of thromboangiitis obliterans

Although our main interest in this article is not to communicate a clinical case, but to present it as an example of the ideal position of the family physician to observe the natural history of the diseases, thanks to his work of continuous care [25], this clinical observation agrees With other publications where patients were followed for several years, and those who stopped smoking responded better to treatment and evolved more favorably than those who did not [29,30]. Our patient needed 6 years of smoking cessation to begin to notice improvement in his symptoms, and throughout the 17 years that passed without smoking evolved towards the disappearance of ulcerations and improvement of pain. Finally, another disease possibly related also to tobacco and in the context of its vascular problem, causes the fatal outcome.

### The natural history of diseases

The process begins with the appropriate exposure to or accumulation of factors sufficient for the disease to begin in a susceptible host. For an infectious disease, the exposure is a microorganism. For cancer, the exposure may be a factor that initiates the process, such as asbestos fibers or components in tobacco smoke (for lung cancer), or one that promotes the process, such as estrogen (for endometrial cancer).

After the disease process has been triggered, pathological changes then occur without the individual being aware of them. This stage of subclinical disease, extending from the time of exposure to onset of disease symptoms, is usually called the incubation period for infectious diseases, and the latency period for chronic diseases. During this stage, disease is said to be asymptomatic (no symptoms) or unapparent. This period may be as brief as seconds for hypersensitivity and toxic reactions to as long as decades for certain chronic diseases. Even for a single disease, the characteristic incubation period has a range.

For example, the typical incubation period for hepatitis A is as long as 7 weeks. The latency period for leukemia to become evident among survivors of the atomic bomb blast in Hiroshima ranged from 2 to 12 years, peaking at 6–7 years [31].

Although disease is not apparent during the incubation period, some pathologic changes may be detectable with laboratory, radiographic, or other screening methods. Most screening programs attempt to identify the disease process during this phase of its natural history, since intervention at this early stage is likely to be more effective than treatment given after the disease has progressed and become symptomatic.

The onset of symptoms marks the transition from subclinical to clinical disease. Most diagnoses are made during the stage of clinical disease. In some people, however, the disease process may never progress to clinically apparent illness. In others, the disease process may result in illness that ranges from mild to severe or fatal. This range is called the spectrum of disease. Ultimately, the disease process ends either in recovery, disability or death.

Because the spectrum of disease can include asymptomatic and mild cases, the cases of illness diagnosed by clinicians in the community often represent only the tip of the iceberg. Many additional cases may be too early to diagnose or may never progress to the clinical stage. Unfortunately, persons with unapparent or undiagnosed infections may nonetheless be able to transmit infection to others. The challenge to public health workers is that these carriers, unaware that they are infected and infectious to others, are sometimes more likely to unwittingly spread infection than are people with obvious illness [32].

Man is subject to a great variety of diseases and it has always been one of the main functions of clinical research to provide accurate descriptions of these various pathologic entities. The characteristics of most acute diseases and of the acute phases of most chronic diseases have been reasonably well defined. With some notable exceptions, however, accurate descriptions of the entire courses of common, chronic conditions are woefully lacking.

### Some ways of classifying and systematizing the study of the natural history of diseases

A- Biopsychosocial typologies (classification biopsychosocial of etiologies) of the natural history of diseases:

A typology of the natural history of diseases can be established [33]:

- \* Beginning: acute / gradual
- \* Course: progressive, constant, recurrent
- \* Result: non-fatal, limiting life expectancy, fatal.
- \* Inability: no disability, moderate, severe
- \* Grade of uncertainty or predictability.

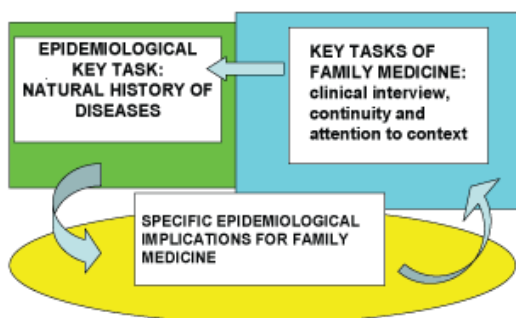


Figure 1: Relationship between the continuity of care in family medicine and the natural history of diseases.

- \* Other factors: Visibility of symptoms; Severity of crises; Genetic contribution; Treatment regime

With these variables a relationship matrix (Table 2) can be constructed. However, there are some diseases that can be located in different places, and these cannot be placed with some certainty in that matrix.

### B-A classification of diseases according to their pattern of natural history

Different diseases affect people at different ages and their course and results differ. Five patterns of the natural history of diseases can be described [34-60]:

1. The common disease pattern in children. For example: catarrhal syndrome, umbilical hernia, nevus "strawberry", growing pains, enuresis, etc. They have high incidence and prevalence during a plateau and a descent to a level of low incidence that is maintained.
2. Many diseases become more prevalent with age and some become serious. For example: osteoarthritis, coronary heart disease, stroke, peripheral arteriopathy, hypertension, COPD and cancers. There is a plateau of low incidence and prevalence, followed by an increase from the average age of life to a plateau of high prevalence and incidence.
3. Some diseases are "once and always". That is, once they arise they persist all their lives. Example: some congenital diseases such as Down syndrome and cystic fibrosis, and acquired diseases such as diabetes,

hypothyroidism, blindness and deafness. They present a constant plateau of prevalence and incidence.

4. Some diseases appear to follow a course and disappear: they tend to appear early in the middle of adulthood. There is a period of clinical activity, persistent or intermittent, that can last 10-20 years and then the symptoms decrease or disappear. Examples: asthma, migraine, allergic rhinitis, low back pain, duodenal ulcer, anxiety, depression, urinary tract infections in women, and various gynecological problems.
5. Some diseases with high prevalence and incidence in young and old. They include bronchial hyperreactivity, hydrocele, hernias and constipation.

### An epidemiological classification directed by medical intervention

The diseases can be grouped into three blocks, following an epidemiological classification directed by medical intervention [61]:

- a) Diseases whose etiology is understood sufficiently for prevention (for example: coronary heart disease, adverse drug reactions, pulmonary tuberculosis, stroke, traffic accidents).
- b) Diseases whose etiology is only partially known but for which there are proposed screening or prevention approaches (for example, breast cancer, bladder cancer, prostatic hypertrophy, hypertension and genetic diseases).

**Table 2:** Approach to a matrix of the natural psychosocial history of diseases.

		Incapacitant		Not disabled	
		Acute	Gradual	Acute	Gradual
Fatal	Progressive	-Acute leucemia	-Lung cancer -Heart failure	-Traffic accident -PE	-Cystic fibrosis
	Recurrent	-Incurable cancer in remission	-General multiorganic fragility of the elderly	-Adverse Drug Reaction	-Suicide attempt
Limited expectation of life	Progressive	-Myasthenia gravis	-COPD -Multiple sclerosis -Alzheimer disease	-Prostate cancer -thromboangiitis obliterans	-Diabetes mellitus 1 and 2
	Recurrent	-Coronary syndrome	-Angina pectoris	-Hemophilia	-SLE
	Constant	-Cerebrovascular accident	Chronic Renal Failure -Hodking disease	-Hyperthyroidism	-Drug's use
No fatal	Progressive	-Schizophrenia	-Parkinson's disease -Arthrosis -Rheumatoid arthritis	-Nephrolithiasis	-Hypertension -Osteoporosis
	Recurrent	-Hernia disc	-Depression -Anxiety	-Gout -Migraine -Epilepsy -Asthma -Seasonal allergy	-Ulcerative colitis -Irritable colon -Psoriasis
	Constant	-Cerebral palsy -Total deafness	-Congenital malformations	-Congenital heart disease -Gallstones	-Hypertension -Glaucoma -Distimia -Dental caries

PE: Pulmonary embolism  
 COPD: Chronic obstructive pulmonary disease  
 SLE: Systemic lupus erythematosus



- c) Diseases whose etiology is not well known and where it is not possible to implement prevention or screening (for example, senile dementia, hyperparathyroidism, ovarian cancer, Paget's disease and lymphoma).

## Conclusion

Family medicine has important epidemiological connotations, presenting a unique opportunity to study natural history of a disease. So, there are specific implications for epidemiology in family medicine which have not been sufficiently systematized conceptually [62,63]. There have been family physician pioneers who studied the epidemiologic problems of their community with scientific rigor. Some of them have been recognized for their seminal work in the last 125 years [7-10,64-68]. Because of their detailed reports, they were able to discover what was contained in their practice, improve their clinical tasks and improving the knowledge of the natural history of the diseases. These pioneers made much of this original work based on their observations of individuals for years; it is what we call "continuing care" [21]. For example, James Mackenzie [7,25] performed much of his original work based on observation of individuals for years. The accumulation of knowledge about the disease can be obtained in family medicine, but requires an effort of observation and good records.

Further studies are needed to better elucidate and overcome the present limitations represented by the lack of large prospective longitudinal investigations. Future epidemiological strategies that use longitudinal study designs or "continuing care", using homogeneous definitions of diseases, could play a pivotal role in better elucidating the controversies in natural history and the pathophysiology of subtypes of many common diseases, leading to improved clinical care. Cohort studies on the natural history of diseases should be enhanced in order to provide a basis for the development of health strategies and prevention and treatment measures.

As drug development and technology continues to improve, it will be important to design rationale longitudinal clinical studies enrolling patient populations that represent the overall population, including racial minorities, gender differences, the elderly, and with the presence of co-morbidities, so that studies results can be appropriately extrapolated. Future research should focus on elaborating the causal framework that leads to the development and persistence of severe common diseases, with an emphasis on identifying modifiable factors for intervention by policy makers or health professionals. Further, more research is needed on the natural history of diseases in low-income and middle-income countries, from the patient's perspective, and relating the natural history of diseases with the family life cycle and family transitions [69-71].

The ordinary general practitioners can make a significant contribution to research on the basis of patients seen in routine practice. It does not need the usual obsession for statistics, but an equivalent clinical mentality to that of Alexander Fleming -to realize the patchy shape in Petri disk which turns up in surgery: yeast floats through the windows, lands on a plate of

germs, and kills them; it is penicillin. The trick is to know what to notice, and what to ignore [72].

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