

# Health-Related Quality of Life in Inflammatory Bowel Disease

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## 1. Introduction

There is a generalized conviction that morbidity and mortality indexes commonly used to assess health outcomes are scarce in information. Furthermore, the accelerated rate at which new means of therapeutic intervention emerge has stressed the interest in other ways to assess the health status; namely the subjective health status while depicting the functional ability. Which, given the exponential growth of studies coming to light, became indexed in MEDLINE since 1977 under the keywords Quality-of-Life. But although much has been written on the use of this sort of questionnaires in several areas of research, and particularly in epidemiological studies and in clinical trials, it is also true that its infiltration in clinical practice is little more than shy.

## 2. Conceptualization

### 2.1 Model

In fact, clinicians have always kept some reserve towards adopting in daily practice aspects related with human characteristics that they somehow consider subjective and personal; especially when compared with laboratory data or endoscopic findings. They seem reluctant to adopt variables of this type in order to quantify their interventions' outcomes. That is, insofar as Quality of Life is considered a relatively vague concept and not in the least in accordance with medical requirements. However, in this sense it is meant to be stripped of all generic notions such as satisfaction with lifestyle, involving instead mostly aspects related with health and medical care related experiences.

This is why it is usually considered equivalent to health status in terms of symptoms and functional ability; further specifying **Health-related Quality of Life (HR-QoL)**, thus aiming at limiting the concept's scope and cleansing the acknowledged multidimensionality of its content from the refuse of aspects less related with medical intervention objectives, as is the case, for example, of aspects concerned with financial or housing situation.

### 2.2 Applications

As mentioned above, in recent years there has been a growing interest in evaluating Health-related Quality of Life [1, 2], particularly when it concerns chronic conditions which are not curable, but also have considerably remote prospects of death. This way one can assume that one of the main goals of the therapeutic intervention is somehow to improve patients'

Quality of Life; and this must be in a final analysis the touchstone by which to assess the outcomes of those interventions.

Therefore, the main goal is to achieve an accurate assessment of the health status, either at individual or population level, in order to consider the outcomes of care more positively or negatively. In fact, it has been observed that activity indexes used in chronic Inflammatory Bowel Disease (IBD) are no exception, turning out to be insufficiently sensitive and even differing from the patients' perception of their own status [3, 4]. Moreover, these Quality of Life indexes have been shown to be more heavily related with well-being and fewer requests of health services than the clinical evaluation of the disease's activity [5].

Hence some of the applications that one can infer for this type of assessment. For example, where **clinical trials** are concerned, they usually focus on physiological reactions; however the assessment of Quality of Life is by far a much better way to assess functional ability. Therefore, if functional ability is indeed an important outcome, then it must be evaluated directly. In other words, clinical trials should include more information of this type in order to properly assess the therapeutic effectiveness.

In fact, **patients in particular** and society in general care more about symptomatic complaints and functional ability than laboratorial findings and physiological responses. However, given that these complaints frequently take an emotional aspect, they are often ignored. Faced with increasingly incapacitated patients, the clinicians continually report "improvement" in their notes on patient status. This only stresses the importance of a standardized assessment of functional ability and the need to translate this added interest from the field of research to that of clinical practice. In other words, this will allow triages aimed at identifying patients who stand out in terms of need for special attention or certain differentiated healthcare; namely through the potential involvement of certain problems of psychosocial nature, liable to be identified or determined by these instruments. Furthermore, it may allow monitoring clinical assessment and suggesting alternative therapeutic solutions; thus contributing to a more adequate clinical intervention. As previously stated, Quality of Life may often collide with clinical assessment, but what has been observed is that this type of data, whether on grounds of mistrust, inadequacy, or the unavailability on the opportune moment, is often ignored in decision making at this level [6]. It all comes down, in the specific context of the therapeutic relationship, to meet patient's expectations; which this process somehow makes more explicit.

Systematic research at the **population level** may determine with some precision which areas of healthcare intervention, if untended by conventional epidemiological measures, may be considered especially problematic, as perceived by patients. Furthermore, the quality of services rendered can and should be assessed in terms of results attained in this domain, allowing the elaboration, and result comparison, of alternative strategies.

### 3. Methods

#### 3.1 Dimensions

The notion of Health-related Quality of Life (HR-QoL) is nonetheless an encompassing notion, as it includes patients' perceptions of their own health condition and their experience of the disease. From this **multidimensionality** stem the main obstacles in conceiving, analyzing and interpreting studies on Quality of Life. As such, although it integrates disease-related factors, it is also shaped by a psycho-affective dimension and influenced by aspects of socio-cultural nature. It is in this sense that disease activity is

understood in the context of a somatic dimension, of which Quality of Life is a part, but differs in two fundamental aspects; namely, the fact that the assessment must take into account factors not only disease-related but also psychosocial, and the consequent aspect that the assessment is necessarily subjective as it is based on the patients' account of those factors. However, just as in the disease assessment in the form of histopathological typification and determination of location and extent, the Quality of Life assessment aims at quantifying the multiple factors that contribute to the illness status. In other words, the goal is to assess not only the disease but also the patients' perception of the disease.

### 3.2 Requirements

The trustworthiness clinicians usually attribute to their data, as opposed to those based on elements given by patients, rests upon three types of factors: their quantifiable nature, their objectivity (observable by third parties), and their susceptibility to material storage (histopathology, radiology) for future consultation or verification. But above everything else, what is at stake is their coherence and repeatability; which to a great extent include all other aspects. However, the possibility of obtaining the same results in different observations, regardless of the observer, is precisely one of the criteria in the elaboration of the psychometric instruments, among which are those aimed at Quality of Life; and this lends them the same reliability as in the abovementioned laboratorial results [7].

In order to assess Quality of Life some aspects must be taken in consideration first [8]. The instrument must have **validity**, as well as coherence and reliability. In other words, it must be specific in the sense that it assesses what it is meant to assess, and thus allowing to separate the cases from the non-cases within the context of the model on which it is based. This issue may be addressed by the concurrency method, which consists in comparing the results with those obtained by other previously validated or commonly used methods, such as clinical and laboratorial results. These external criteria, although they may evaluate partial aspects of the problem, should not yield overlapping results; which would indicate the redundancy of the new method. In fact, the goal is a quantifiable means of approaching in a more significant manner the issue of patient's Quality of Life. Additionally, in the absence of a validation capable of providing standardized data from which to interpret the results, these should always be referred to the population from which they were drawn, in order to allow a careful weighing of all inferences, as population specificities and idiosyncrasies may be an important source of artifacts.

The instrument must have coherence, which may be tested by the split-half method, as well as **reliability**, in the sense that observations are repeatable; which may be tested by the test-retest method, somehow granting the basic postulate of all scientific processes that under the same circumstances the same results will be obtained regardless of the observer. As far as this aspect is concerned, that is, in order to ensure repeatability, stability is paramount. However, to provide for any **utility** regarding the abovementioned applications, an instrument such as this must have enough **sensitivity** to allow for discrimination. In other words, it must be able not only to differentiate among people with more or less Quality of Life, but also to detect Quality of Life variations in a given patient or group of patients. This type of sensitivity to change, crucial in clinical trials and cost/benefit analysis, is also known as reactivity.

Specificity may be seen, to a certain extent, as a characteristic varying reversely to sensitivity. That is to say that a greater sensitivity, which allows an identification of most cases, is useful mostly in studies of epidemiological triage. In clinical practice, however, it is

detrimental in the sense that a lower specificity leads to many false positives. High specificity, although it yields more false negatives, which is to say that many cases go undetected on account of insufficient sensitivity, is more useful in clinical practice in the sense that it provides a higher degree of certainty in a particular case. In this aspect as well, Quality of Life is not different from other assessment methods being used in other areas of biomedical intervention. Consider for instance the methods used to detect tuberculosis as compared to the tests used instead to corroborate the therapeutic intervention for the same disease. Additionally, an instrument well suited in a research context may prove impractical as an administrative routine or hard to read in the daily rush of clinical practice. Although patients usually enjoy answering to questionnaires whose contents they believe to be important for their clinician [9]. Still, although it is known that abridged versions are prone to be less valid, aspects such as time-consuming implementation or difficult interpretation of results must be taken into account, given that, added to their unfamiliarity, their significance is less intuitively grasped than clinical or laboratorial data obtained through more conventional means [10]. Therefore the **adequacy** of the instruments to their goal, that is, the rigorous construction and selection in terms of the aims to be achieved, is also a crucial requirement to meet.

Finally, there are issues remaining such as the assessment of illiterate patients, for whom self-assessment is not an option. It is known that interviewing, regardless of its degree of structure, deviates from the standard procedure required for repeatability; forcing the assessment of aspects such as inter-rater reliability.

### 3.3 Instruments

The scales for assessment of patient functional ability date back to the 1940s. Some noteworthy examples are the *American Rheumatism Association Function Scale* [11], the *Karnofsky Score* [12] created for cancer patients – from which has somehow derived the V axis of the Diagnostic and Statistical Manual of Mental Disorders (DSM) as used in present days –, or the *New York Heart Association Functional Classes*. These early instruments aimed at combining several dimensions into a single scale. In the 1950s appeared the *Daily Activities Scales* to assess the degree of incapacitation of patients interned in tertiary healthcare units. By their own nature they were less useful regarding psychosocial aspects; and the first instruments capable of assessing health status as we understand it today, appeared only in the 1970s. However, despite the studies of validation and reproducibility, they were still hard to implement; mainly due to questionnaire length, which came to be reduced only in the 1980s. A few examples of this trend are the *Nottingham Health Profile* [13], the *Dartmouth COOP Charts* [14], the *Medical Outcome Study Short Form* [15, 16] and the *Mini-Duke Health Profile* [17].

The trend throughout the 1990s was towards specificity, granting them more face value with clinicians and added on sensitivity to changes in patient status in terms of clinical progression. Furthermore, their multidimensionality allows for more detailed information on certain aspects. Ulterior psychometric refinement and improvements in adequacy progressively contributed to spread out the interest about its implementation in daily use.

#### 1. Global assessment

The simplest method consists in posing patients a single question; the patients themselves somehow include in the answer the various implicit dimensions. There lies also its main shortcoming: single point assessments do not give us any information whatsoever on the factors leading to this or that answer.

Such is the case, for example, of questions like “On a scale from 0 to 4, how would you describe your general health status and well-being?”; to which patients must reply either “good”, “reasonable”, “poor”, “bad” or “very bad”. The obtained answer has proven to be a clinically effective way of globally assessing health status. In patients with Inflammatory Bowel Disease (IBD) it was even shown to be a strong indicator of the number of consultations taken [18].

## 2. Generic assessment

Generic assessments [8, 19] are characterized by the fact that they do not take into account aspects pertaining to specific diseases. From the start this allows for obtained scores to be compared between different groups of patients and even different pathologies. Furthermore, as they represent the answers of a group of patients, they are especially useful in epidemiological studies or as a mean to analyze factors to be considered in decisions regarding healthcare policy and guidelines.

### i. Time Trade-off Technique (TTOT)

Defined as a utilitarian assessment, the *Time Trade-off Technique* [20] is an application issuing from the clinical decision model. It consists in assessing patients’ perception of their health status in relation to death. Ranging from 0 (death) to 1 (perfect health), the score is obtained by asking the patient to choose (hypothetically, of course) between living with their present health status, with all it may imply in terms of physical and psychosocial limitations, and living less time with perfect health. For example, let us consider two thirty-year-old patients with Crohn’s disease whose life expectancy is 75 years: the healthier one may be willing to give up on 5 years in order to live with perfect health to the age of 70, while the less healthy one may be willing to give up on 30 years to live with perfect health to the age of 45. The utilitarian score would then be 0.93 (70/75) for the former and 0.60 (45/75) for the latter.

Variation in this type of score may be used, for example, to assess how a patient deals with the efficacy of a certain therapy. However, as in the case of global assessment, it does not make explicit in which particular sector was improvement or deterioration felt. For this reason, as a method it is more evaluative than discriminative.

### ii. Sickness Impact Profile (SIP)

Health profiles, of which *Sickness Impact Profile* [21] is an example, encompass several aspects of patients’ life and behavior, both somatic and psychosocial, in terms of the disease perceived impact. This profile not only has a global score, but also has three sub-scores for physical aspects, four for psychosocial aspects and five for autonomous areas.

As a generic scale with discriminative capability, it can be used in planning healthcare policies, as it allows functional status comparisons between patients with different illnesses [5, 17].

### iii. Psychosocial Adjustment to Illness Scale (PAIS)

The *Psychosocial Adjustment to Illness Scale* [22], proposed by the author of the SCL-90, is another well-studied generic health profile [23] which may be used to explore several intervening factors in the psychosocial adjustment to illness. Besides a global score, it covers aspects of health orientation, vocational environment – work, school and home activities, – domestic environment, sexual relationships, extended family relationships, social environment, and psycho-affective disturbance. It can be applied either by patients themselves or some other person; and being a generic profile, it can be applied to patients with different pathologies, allowing comparison studies. However, existing standard groups refer to patients with lung cancer, renal dialysis, severe burns and essential hypertension.

Moreover, the 4 possible answers to each of the 46 questions offer some difficulty of application in clinical practice; either because of its lengthy and time-consuming format – necessary to ensure the data validation required to explore the several areas it is meant to assess –, or because of its elaborate and numerous nuances, which may constitute a serious obstacle for patients with a low cultural background and little academic qualification.

*iv. Quality of Life Scale*

The *Self-Assessment Quality of Life Scale* [24] is yet another generic instrument that has also been proposed, with the particularity of having a version which uses a computer as means of implementation as well as archive and automatic processing of the resulting data [25].

### 3. Specific assessment

Specific assessment uses instruments capable of evaluating certain statuses and worries of patients with a specific disease. This ought to be the case of an assessment aimed for instance, at Crohn's disease; which must include issues related to intestinal functioning, abdominal pain and sexual aspects. Whereas another assessment aimed at rheumatoid arthritis may instead evaluate prehensile strength and mobility.

The advantages of such specificity lie on the added sensitivity to variation in clinical status, which may occur with the passing of time [26]. This aspect, combined with the fact that the issues and areas explored overlap those usually performed and evaluated by clinicians, makes it readily applicable in clinical trials.

The disadvantages concern the inability to differentiate between patients with different diseases or even in the context of the same disease, on account that, as was previously noted, the population used to develop the instrument must be taken into account. This aspect is well illustrated by the "ceiling effect" [7]: a Quality of Life scale developed in IBD in-patients may not be sensitive enough to Quality of Life variations in ambulatory patients, as these are expected to belong to a less severe clinical condition. The same goes for the "floor effect", which undermines the sensitivity/reactivity of an instrument used on patients with low Quality of Life, as they can hardly present lower values in further assessments.

Generally speaking, it can be said that all instruments available in the context of Inflammatory Bowel Disease (IBD) have content validation, that is, the questions they explore represent effectively the aspects they propose to assess. The same can be said of concurrent validation, given that the respective scores correlate with those of other previously validated Health-related Quality of Life instruments. Finally, there is also construct validation regarding scales constructed following a hypothetical model and then put to test in groups of patients with certain characteristics, or whose health status was assessed by other means; thus confirming the model.

*i. Inflammatory Bowel Disease Questionnaire (IBDQ)*

The *Inflammatory Bowel Disease Questionnaire* (IBDQ) [27, 28, 29, 30], conceived for use in therapeutic trials, is a questionnaire covering intestinal and systemic symptoms as well as affective and social behavior aspects, which was initially meant to be applied as a structured interview. Widely used and translated into many different languages [31] – Dutch [32, 33], Portuguese [34, 35, 36], Spanish [37, 38, 39], Korean [40], UK English [41, 42], Greek [43, 44], Swedish [45, 46], Norwegian [47], Japanese [48, 49], German [50, 51, 52], Chinese [53], Lebanese [54], Brazilian [55], Italian [56] –, it has shown its cross-cultural stability, while also being recognized as robust in psychometric terms, with proven reproducibility, stability and sensitivity to variations among Inflammatory Bowel Disease (IBD) affected patients, both in ambulatory regime and as in-patients.

Aiming to improve its adequacy, some modified versions came to light. One of those first modified versions, a self-applied questionnaire with 36 Likert-type questions [57], although using many questions from the IBDQ, from which it was derived – contributing to a certain degree of concurrent validation –, should not be considered properly standardized, given that the control study was performed only on a group of healthy people. Moreover, its application was aimed at a sample of patients only mildly affected by Inflammatory Bowel Disease (IBD). Some other versions and new modes of administration [58] came forward later on; ultimately agreeing upon a light-footed 32-item revised version (IBDQ-R) with proven psychometrics and adequacy [59].

ii. Cleveland Clinic Inflammatory Bowel Disease Questionnaire

The *Cleveland Clinic Questionnaire* [60] is a structured interview with 47 questions evaluated on a Likert-type scale which was shown to be correlated with the *Sickness Impact Profile*. Its focus is less on clinical symptoms and more on functional aspects of patient daily life. This allows to some extent its use in generic terms, going so far as to discriminate, in a slightly altered version, Inflammatory Bowel Disease (IBD) patients from multiple sclerosis and rheumatoid arthritis patients; the latter showing lower values of HR-QoL [61].

Specifically conceived to be used with Inflammatory Bowel Disease (IBD) patients, it can discriminate between patients with Ulcerative Colitis and patients with Crohn's disease, as well as tell apart patients with more severe forms from those with less severe ones; as is the case, respectively, for those with and without a history of prior surgical intervention.

iii. Rating Form of IBD Patients Concerns (RFIPC)

Although it does not assess symptoms or functional statuses, as it was not specifically conceived to assess Health-related Quality of Life, the *Rating Form of IBD Patients Concerns* [62] was shown to correlate with well-being reports, the psycho-affective disturbance degree assessed by the SCL-90, and daily functioning. It is based on a self-applied questionnaire with 25 questions answered by means of an analogical scale and oriented towards patient fears and concerns. It was applied to a large sample of American IBD patients and claims to be an index capable of evaluating results from psychotherapeutic interventions or simple counseling.

In other cultural contexts this questionnaire showed a much more random and less reliable behavior; which gave rise to an explanation, put forward after further probing, that physicians dealing with these patients may be less prone to enlighten them about the implications of their condition [63].

iv. Ulcerative Colitis and Crohn's Disease Health Status Scales (UC/CD HSS)

Based on the assumption that health status and its evolution depend both on disease-related factors and psychosocial factors [3], the *UC/CD Health Status Scales* [64] were conceived integrating aspects related with medical assistance, daily functioning and psycho-affective discomfort to differentiate situations of mild affliction from more severe cases and to predict the outcome.

They would benefit from prospective validation in order to strengthen its warrant for correct predictions in terms of prognosis or therapeutic response. However, the included symptoms have revealed from the start, through a nation-wide American study, that they have a better predictive power than that of *Crohn's Disease Activity Index* (CDAI) [65].

#### 4. Quality of life findings in inflammatory bowel disease

Despite the vast number of published studies claiming to have assessed the Quality of Life, for the most part they were based on clinical evaluations or questionnaires of which there is

insufficient data concerning their standardization. This lends their possible conclusions a great degree of relativity and leads to restricted information available in this area. However, the general rule is that ambulatory Inflammatory Bowel Disease (IBD) patients have a reasonably good Health-related Quality of Life [5, 18, 60, 66].

In a wide-range study [18], Drossman's workgroup has studied a great deal of aspects related to Inflammatory Bowel Disease (IBD) in 997 members of the Crohn's & Colitis Foundation of America. This study concluded that, as compared to the general population, only a slight increase in psychological distress can be observed. Nevertheless, while the daily functional status was overall quite good, disturbances, if any, stemmed less from physical aspects and more from psychological or social functioning factors. Additionally, when compared to Ulcerative Colitis, Crohn's disease patients showed more psychosocial difficulties and resorted to healthcare services more often; although the differences are not significant when adjusted to the greater severity of their symptoms.

As for coping mechanisms, considering that strategies focused on the problem have been considered more adaptive in the sense that they dampen the psychosocial disturbances, it is exactly to this type of strategies that these patients resort more often: facing problems and making their positive reassessment, while resisting interference from emotional distress and also seeking social support.

Assuming that the common ground for a better or worse Health-related Quality of Life is the underlying personality, a study [67] was conducted among IBD patients aiming at disclosing any particular characteristics relevant to this population in terms of relationships with QoL dimensions as assessed by the IBDQ-R [60]. The framework considered to do so was the psychobiological model of temperament and character [68, 69], of which variables even have the proven ability to predict independent DSM diagnoses of personality disorders [70]. Just to conclude that QoL – both IBDQ Global score and all its dimensions –, is significantly modulated and may be predicted to some extent through a recognizable distressed type of personality. But also further suggest an adjustment typology relying on different aspects of personality. Namely, that harm avoidance by temperament is the main predictor of bowel symptoms, systemic symptoms and emotional status; while the relative strength of dimensionally assessed character disorder – after controlling for harm avoidance – mainly accounted for social malfunctioning [67].

Quality of Life and psychosocial factors – well-being, psychological disturbances and functional status – were shown to be much better predictive factors, in terms of the number of consultations taken, than the commonly used disease activity indexes; which are not even significant. But these latter indexes – severity of symptoms, steroid dosage and weight loss – are otherwise quite good predictors of hospital admission and surgery.

Moreover, the *Rating Form of IBD Patients Concerns* (RFIPC) has allowed to conclude that these patients' main worries and fears are: incertitude regarding the disease evolution, medication effects, energy level, surgery and having an ostomy bag, being a burden on others, loss of bowel control and the possibility of cancer. Furthermore, within this concern spectrum some differences have been established between patients with Crohn's disease and Ulcerative Colitis. The former are more concerned with their energy level, being a burden to others, full development, pain and suffering, expenses and the risk of contagion to others. While the latter fear mostly the possibility of cancer. Finally, there is a relation between these concerns and the psychological well-being and daily functioning; suggesting that a psycho-educational intervention aimed at these concerns can play an important role in improving these patients' health status and Quality of Life.

In yet another study [5] conducted by the same workgroup using the *Sickness Impact Profile* (SIP) among both in-patients and ambulatory as well, the results came to confirm that the psychological and social factors have a greater effect on the daily functioning status than do physical aspects. This is more so in Crohn's disease than in Ulcerative Colitis, but above all among in-patients as compared to those in ambulatory care. This also came out as a result from a study using *Cleveland Clinic Questionnaire* in ambulatory patients [60], which has shown a poorer Quality of Life among patients with Crohn's disease when compared to those with Ulcerative Colitis; and the same goes for patients with a surgery history when compared to those without surgery. This is hard to interpret in the case of Ulcerative Colitis patients, where colectomy is presumed to heal. However, the high rank of the health care facilities where the study has been conducted allows to conjecture that the sample may have been selected focusing on patients with postoperative complications.

While being aware that different questionnaires lead to different interpretations about Quality of Life after restorative proctocolectomy [71], the question raised here is knowing to what extent the colectomy may improve the Health-related Quality of Life; or whether there are significant differences according to the chosen procedure. In fact a study with such a focus, using utilitarian methods such as the *Time Trade-off Technique* (TTOT) [72], confirmed such improvement. In yet another study conducted one year after surgery, the authors found no differences among the several used procedures: conventional ileostomy, Kock pouch and ileal pouch anal anastomosis. Although the difference in methodologies prevents any direct comparisons, going as far back as 1981 another study which engaged 1000 patients operated for Ulcerative Colitis came to slightly different conclusions [73]. This study concluded, using a suitable questionnaire to assess Health-related Quality of Life, that, when compared to patients with Kock pouch, patients with ileal pouch anal anastomosis felt fewer difficulties both sexually and in sport activities. The same was true when compared to ileostomy patients; although these mentioned fewer problems with travelling. Drossman's workgroup also approached this issue with their *Rating Form of IBD Patients Concerns* (RFIPV) [74], reinforcing these studies' conclusions on the positive response in terms of Quality of Life among colectomized Ulcerative Colitis patients. Furthermore concluding that ostomies reduce the level of concern regarding cancer, surgery and ostomy itself; without significantly raising those related with bodily image – sexuality, intimacy, attraction –. The same cannot be said about Crohn's disease; possibly due to the post-operative severity of these patients condition [60].

## 5. Conclusions

The level of interest seen recently in assessing the Health-related Quality of Life led to the creation of a number of assessment instruments with applications in several areas of intervention, such as clinical practice, research and healthcare policy guidelines. However, in order to make an adequate choice and/or a correct use of these instruments, it is necessary to have some knowledge of the characteristics and limitations of both generic instruments and IBD-specific instruments. As for the countless studies published which refer to this concept, the main conclusion to be drawn still is the scarcity of standardized conditions. However, overall they all point to a relatively good Health-related Quality of Life among these patients.

An increase in the interest for this type of instruments is foreseeable in the near future, towards a better assessment of Inflammatory Bowel Disease (IBD) impact both on an

individual – clinical orientation in medical or surgical contexts – and a population levels – therapeutic efficacy, budget planning –.

## 6. References

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