Prevention of Refractive Defects of Vision by Means of Evolutionary Medicine
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Abstract
Refractive errors of vision (myopia, astigmatism and hyperopia) are widespread diseases with an increasing frequency and enormous costs. It has been estimated that, by the year 2020, about 3 billion people will be affected by them and that, in 2009, the related global economic productivity loss was $268,8 billion.
An effective prevention of these diseases is proposed, not by means of innovative technologies or sophisticated drugs, but through the application of simple measures based on known information, that is, the application of plain concepts of Evolutionary Medicine.
Epidemiological studies show that refractive defects in modern populations: a) are very frequent; b) vary greatly from population to population; c) vary greatly within the same population over one or two generations; in primitive populations, however, the same defects are rare. This demonstrates that they are, for the most part, caused not by genetic alterations but by a “mismatch” between the adaptation of our species and a modified lifestyle.
The most probable factor causing the defects appears to be the reduced exposition to natural light in the initial periods of life, a condition that alters the correct eye development (emmetropization).
It is, therefore, proposed that, if their eyes are to develop properly, babies should be exposed, as much as possible, to natural light conditions, with a view to creating a living environment similar to the one in which man originally lived.
This should reduce the frequency of refractive errors to the level observed in primitive conditions, thereby avoiding a great deal of discomfort, suffering and expense.

Keywords: refractive defects, evolutionary medicine, mismatch, myopia, astigmatism, hyperopia.

Introduction
In modern medicine, important advances are, in general, achieved through innovative technologies or sophisticated drugs.
In this work, I propose an effective prevention of a very widespread group of diseases, i.e. the refractive vision defects, through the use of known information and the application of simple measures that do not require special technologies or sophisticated drugs.
The proposed method is the application of simple concepts of Evolutionary Medicine. A brief introduction to them is indispensable for an understanding of what is to be put forward.

Discussion
a) Evolutionary Medicine
Evolutionary Medicine considers the diseases by which living beings are affected, not simply as alterations of the normal physiology, but more in the broader context of natural selection.
Current Medicine seeks to understand the alterations of the physiology and to find the best remedies for such alterations. Evolutionary Medicine seeks, first of all, to understand the primary cause of any disease, or the interpretation thereof, in the context of the natural selection that shapes every characteristic of a species.
We first find Evolutionary or Darwinian Medicine [1-6] referred to such in 1991 [1], but there are certain known forerunners quoted by Trevathan et al. [7] (e.g. Eaton, Konner and Shostak [8, 9]) and others not generally cited as forerunners (Price [10], Libertini [11]).
Evolutionary Medicine is not an alternative medicine (like homeopathy, iridology, ayurvedic medicine, naturopathy, traditional Chinese medicine, energy medicine, etc.) but a medicine that is more thoroughly scientific in that it involves the concepts of evolutionism.

A medicine that ignored the principles of chemistry, for example, would be partially scientific. Similarly, a medicine that ignores the principles of evolution is partially scientific. So, the difference is not between current medicine and alternative medicines but between current medicine (which in most cases ignores evolutionism) and evolutionary medicine (which is a more thoroughly scientific medicine).

This difference is not a theoretical or verbal nicety, but has strong, significant implications for the prevention and cure of many diseases and, in principle, implies a radical modification to the structure of medical studies and health organization.

b) Two important classes of diseases

In the classification of diseases based on evolutionary criteria that I proposed in 1983 [11], there are two categories of diseases that here require a brief explanation.

1) Diseases caused by alterations of the genotype

The harmful mutations that arise continuously are also continually eliminated by natural selection. If the inactive gene $C'$ has a harmful allele $C$, in which $C'$ changes with frequency $v$, supposing that the damage caused by $C$ is $-s$ ($0 < [s] <= 1$) and excluding, for the sake of simplicity, the notion that $C$ has any benefits, it is easy to calculate the equilibrium frequency of $C$ in natural conditions ($C_e$) as well as the equilibrium frequency, in natural conditions too, of its harmful phenotypic expression ($P_e$) [11, 12].

Figure 1 shows the values of $C_e$ and $P_e$, which, in the case of a harmful recessive gene, are:

\[
C_e = \sqrt{\frac{v}{[s]}} \tag{1}
\]

\[
P_e = C_e^2 = \frac{v}{[s]} \tag{2}
\]

and in the case of a harmful dominant gene:

\[
C_e = 1 + \sqrt{1 + 3 \frac{v}{[s]}} \approx 0.5 \frac{v}{[s]} \tag{3}
\]

\[
P_e = 2C_e - C_e^2 = (1 - \sqrt{1 + 3 \frac{v}{[s]}})(5 + \sqrt{1 + 3 \frac{v}{[s]}}) \approx \frac{v}{[s]} \tag{4}
\]

If a disease can be caused by $n$ recessive or dominant mutations, its equilibrium frequency ($D_e$) will be the summation of all the phenotypic frequencies, namely:

\[
D_e = \sum P_e \approx n \frac{v}{[s]} \tag{5}
\]

(The formulas are given in [12] and the mathematical steps necessary to obtain the values are expounded in [11].)

The important fact is that, if $[s]$ is not small, a disease caused by genotypic alterations cannot have a high frequency. Consequently, if a disease has a high frequency, the disease must have other causes, except for a small fraction that certainly can have a genetic cause [12].
2) Diseases caused by alterations of the ecological niche, i.e. caused by “mismatch”
“Ecological niche” is here defined as the range of conditions (including diet, environmental conditions, interrelations with other living beings, etc.) to which a species has adapted after countless generations of natural selection.
The interactive adaptation between a species and its ecological niche is a very complex matter. A random modification of a complex structure has an alteration of the structure as its most likely consequence. For example, in a PC or in a piece of software, the random modification of something
will most likely cause the PC or the software to have some malfunction. Only in a few rare cases will the random modification improve the efficiency of the PC or the program.

Similarly, for the biological system species-ecological niche, a change in the ecological niche will most likely lead to a discrepancy between the adaptation and the modified ecological niche [8, 9, 11, 12], a condition defined, in short, as “mismatch” [8].

In other words:

“a random modification of the ecological niche, given that it reduces the order of the system, alters, for the most part, the equilibrium between species and ecological niche - read: adaptation -, i.e. it entails a lesser aptitude for persistence in the individuals of the species. Lesser fitness means, by definition, damage or the possibility of damage for the individuals of the species.” (Translated from Italian in the 2011 edition of [11])

“When conditions of life for any animal population deviate from those to which it has genetically adapted, biological maladjustment – discordance – is inevitable. The human species is no exception.” [9]

The most important implication for a disease caused by mismatch is that there are no theoretical limits to its frequency. For example, if a species is adapted to a certain diet a critical modification of the diet can lead to diseases in a substantial percentage of a population. The modern diets that are unbalanced in various ways and the frequent illnesses caused by them (diabetes mellitus, atherosclerosis and its complications, etc.) are a well-known case, but other similar conditions are also well known [8, 9, 11, 12] (see Table 1).

<table>
<thead>
<tr>
<th>Alterations of the ecological niche</th>
<th>Diseases</th>
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<tbody>
<tr>
<td>Excessive ingestion of salt → hypertension [9, 13, 14] (→ heart hypertrophy, congestive heart failure, arrhythmia and sudden death [15])</td>
<td></td>
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<tr>
<td>Excessive ingestion of unsaturated fats, caloric foods, meat with high fat content → obesity (→ renal cell carcinoma [16], heart hypertrophy, congestive heart failure, arrhythmia and sudden death [15]), type 2-diabetes and increased vascular risk (→ myocardial infarct, cerebral ischemia, infarcts in all the vascular districts, heart hypertrophy and failure, etc.) [9]</td>
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<tr>
<td>Occupational noise, smoking, high Body Mass Index → hearing loss [17]</td>
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<tr>
<td>Excessive exposure to noise → hearing loss [9, 18]</td>
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<tr>
<td>Smoking and/or air pollution → chronic bronchitis [19], emphysema [20]</td>
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<tr>
<td>Excessive ingestion of simple and refined carbohydrates (in particular sugar) and other dietary modifications → dental caries, pyorrhoea, crowded teeth [9, 10]</td>
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<tr>
<td>Scarce ingestion of fibers → constipation, colon diverticulosis, colon carcinoma, stomach carcinoma, type 2-diabetes, metabolic syndrome and cardiovascular diseases [28], appendicitis [29, 30]</td>
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<tr>
<td>Scarce ingestion of calcium and reduced physical activity → osteoporosis [9, 31], back pain [9]</td>
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<td>Reduced exposure to natural allergens in the childhood → allergies [32]</td>
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<td>Exposure to chemical substances artificially synthesized → allergic diseases [33]</td>
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<tr>
<td>Altered conditions of sociality, stress of civilized condition → mental and psychiatric disorders [2, 9]</td>
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<td>Various factors → increased incidence of various types of cancer [9, 34]</td>
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<tr>
<td>Alcoholism → hepatic steatosis, steatohepatitis, cirrhosis [35], larynx carcinoma [23]</td>
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c) Methodology for studying a disease caused by mismatch

If the high frequency of a disease suggests that it stems from mismatch, it is possible to outline a methodology for the study of the disease in order to understand the primary causes and to find the best way to prevent and treat it.
First, it is necessary to study its frequency in modern populations, i.e. in populations with a lifestyle that has supposedly changed from that to which the species is adapted. If the disease is caused by mismatch, its frequency will be: a) high; b) varying, depending on lifestyles in genetically homogeneous populations; c) varying with time, over one or more generations, in the same population (Step 1).

It will be necessary, immediately afterwards, to compare the frequency of the disease among populations with modern lifestyles, and populations in primitive conditions, and also to study the variation of the frequency of the disease throughout the passage from primitive to modern conditions of life (Step 2). Confirmation of the facts in Steps 1 and 2 will demonstrate that it is impossible for the disease to have been caused by genotype alterations, with the exception of predictable rare individual cases.

It will then be necessary to determine which particular changes in the ecological niche are the key factors of the mismatch condition (Step 3). With the support of these data, it will subsequently be necessary to study the pathogenetic mechanism that leads from the mismatch condition to the physical manifestation of the disease (Step 4).

At this point, it is possible to conceive and apply changes, or rather corrections, of the ecological niche that nullify, or balance, or at least mitigate the mismatch. This will prevent disease, or at least, block or slow down its progression (Step 5).

Finally, the measures taken must be checked in their effectiveness and applicability. If necessary, they should be modified and/or replaced with other measures, which will, in turn, be verified in their effectiveness and applicability (Step 6).

d) Refractive defects of vision as mismatch diseases

The above-mentioned theoretical premises are not the discovery of something new, but rather the short exposure of simple and immediate consequences of certain concepts of Evolutionism applied to the disease phenomenon.

Now, by investigating a subject already studied [36], I want to verify whether refractive errors of vision can be usefully studied with the proposed methodology, in order to prevent and treat said diseases.

Step 1 - Epidemiological study of modern populations
Refractive defects of vision (myopia, astigmatism and hyperopia) are a group of related diseases with the following frequencies:
- very common [37-40]
- varying greatly from population to population (e.g.: “The prevalence of myopia in Asia is as high as 70-90%, in Europe and America 30-40%, and in Africa 10-20 %” [38])
- varying greatly within the same population with changing conditions [41-43]
- greatly varied within a population over a short time [42, 44-46] (see Figure 2)
Step 2 - Comparison between the frequency of a disease in modern populations and the frequency of the same disease in populations in primitive conditions

The study of primitive peoples shows that these defects are very rare or nonexistent. As regards Australian Aborigines: “The marvelous vision of these primitive people is illustrated by the fact that they can see many stars that our race cannot see. In this connection it is authoritatively recorded regarding the Maori of New Zealand that they can see the satellites of Jupiter which are only visible to the white man's eye with the aid of telescopes. These people prove that they can see the satellites by telling the man at the telescope when the eclipse of one of the stars occurs. It is said of these primitive Aborigines of Australia that they can see animals moving at a distance of a mile which ordinary white people can not see at all.” [10]

As regards the Yakuts (a Siberian people): “Many travelers observed what some of them call ‘telescopic’ eyesight among these peoples. A Yakut distinguished with the naked eye stars in the Pleiades not usually seen without a telescope. The Yakuts say there are many stars in this group, but only seven large ones.” [47]

As regards two hunter-gatherer populations: “Using a retinoscope and cycloplegia, Holm (1937) refracted 2364 members (aged 20–65 years) of several hunter-gatherer tribes in Gabon (formerly French Equatorial Africa) in 1936. Of the 3624 eyes examined, only 14 were classified as myopic (nine eyes from −0.50 to 1.00 D; five eyes from −3.00 to −9.00 D), thereby yielding a myopia incidence rate of 0.4%. Similar low rates for myopia were reported by Skeller (1954), who refracted the eyes of 775 Angmagssalik Eskimos as part of a comprehensive anthropological study carried out in 1954. Retinoscopy in conjunction with cycloplegia demonstrated that of the 1123 eyes examined, only 13 (1.2%) were classified as myopic (nine eyes =−1.00 D; four eyes =−1.25 D).” [42]
“a number of lines of evidence strongly reject the notion that [a] recent (in evolutionary terms) relaxation of natural selection pressures could be responsible for the high incidence of myopia in modern, technological societies.” [42]

Data from Step 1 and Step 2 indicate that refractive defects are surely a group of diseases caused by environmental factors, i.e. by presumable mismatch.

Step 3 - Hypotheses on the possible changes in the ecological niche underlying the disease

Excessive near-work, especially using artificial lighting (an improbable condition in the ecological niche to which we are adapted) is a common hypothesis regarding the causes of refractive defects, especially myopia [36, 48, 49].

Factors such as “increasing educational levels, higher educational income, professional or office-related occupations, better housing”, associated with refractive defects, have been interpreted as “indicator of near-work and support[ing] the use-abuse theory for myopia” [50].

Against this hypothesis: “In an earlier study of 977 school children (6-17 years of age) on the remote South Pacific island of Vanuatu, Garner et al. (1985) found that only 1.3% of subjects had myopia greater than −0.25 D, despite engaging in about 8 hrs of school work per day.” [42]

Another hypothesis ascribes the epidemic of myopia incidence to dietary alterations, in particular the “increase in high glycaemicload foods” [42]. But, in two homogeneous populations with no detectable difference in dietary habits, incidence of myopia was very different [43]. However, another factor appears to be the pivotal cause of these diseases.

A study was made of two homogeneous groups of 6-7-year-old children of Chinese ethnicity, living in Singapore and in Sidney, respectively, with the same frequency of myopia in their parents. “Children in Sidney read more books per week (P < .001) and did more near-work activity (P = .002). Children in Sidney spent more time on outdoor activities (13.75 vs 3.05 hours per week) (P < .001)”. The prevalence of myopia was 3.3% in Sidney and 29.1% in Singapore [43].

This suggests that the critical factor is the outdoor activity, i.e. the exposition to natural light, a hypothesis confirmed by other studies [51, 52].

In particular, “Higher levels of total time spent outdoors, rather than sport per se, were associated with less myopia” [51].

Milinski observed [36] that “There is increasing correlational evidence supporting the association of myopia … with increased education. The rapid rise in myopia may depend upon the introduction of schooling and modern life in many societies …”, but the subsequent work of Rose et al. [10] and the other cited papers [51, 52] indicate that this association is coincidental with that of fewer hours of exposition to natural light.

Near-work activities appeared to be an independent aggravating factor, but not the main cause of myopia [51, 52].

Step 4 - Study of the mechanisms linking the alteration of the ecological niche to the pathogenesis of the disease

This section confirms and adds evidence to what exposed and argued by Milinski [36].

It is known – from experiments on chickens - that the application (for 7 days, beginning at 5 days of age), of spherical defocus lenses or of translucent occluders to one eye, or exposure to constant light, cause astigmatism associated with myopia or hyperopia. In control birds, astigmatism is normal at birth and disappears, or decreases, over the following days [53].

Similar results were obtained in monkeys [54].

In our species too, astigmatism is normal at birth and disappears in the first years of life: “Infants have a high incidence of clinically significant astigmatism.” “Of 28 children who had large amounts of astigmatism in the first year, all showed elimination or a large reduction in the amount of the cylindrical error by 4 years” [55]

“Full term newborn babies are known to be on average hypermetropic at birth. Preterm babies tend to be myopic when examined at an age corresponding to term …” [56]
Thus, at birth, the eye is imperfect. The image is focused either too forward or too far behind the retina. There is also a deformation of the image on one plane versus the other (astigmatism). The genetic program of eye development means that, at birth, an eye will have only approximate vision. Immediately after birth, another program is activated, an “emmetropization mechanism” [57], which modulates the further development of the eye in order to achieve optimum vision. In other words, these data indicate that, at birth, the eye is hyperopic (a little too short) or myopic (a little too long) and astigmatic (different curvature on the vertical vs the horizontal plane). In the first period of life, by means of neurological and morphogenetic mechanisms, the length and the curvatures of the eye are adapted to achieve the best possible vision. It is like a camera with a very sophisticated hardware autofocus capacity in its rest position (remote viewing): when it comes out of the factory, it is not focused, but it achieves, by itself, an optimal hardware focusing for remote viewing if we respect the manufacturer’s instruction (e.g.: do not point the camera at anything which is too dark or too bright!).

Our eye / camera has a hardware focusing capacity only in the first period of life, and it is essential that the conditions are similar to those to which our species is adapted. In different conditions, proper functioning is not guaranteed and a malfunction is probable.

Step 5 – Possible restoration of the normal, i.e. primeval, conditions or possible compensatory conditions
Under modern living conditions, particularly in urban areas with high population densities, it is "normal" that babies do not grow up outdoors, with exposure to natural light. It is a widespread popular belief that babies should be protected as much as possible from the external environment, in particular from direct exposure to sunlight, as this will damage them in some way. Many infants spend their first months of life almost exclusively indoors, only exposed to artificial lighting, with uneven and weak brightness, and, in all cases, under conditions quite different from those to which our species is adapted. These habits, which certainly represent a change in our ecological niche, have never been shown to be harmless and healthy. On the contrary, the above-cited evidence indicates that they are surely an alteration of the ecological niche with harmful consequences for our vision. For proper eye development, babies should be exposed as much as possible to natural light conditions; sunlight should not be avoided and conditions should be as similar as possible to the original ones.

Step 6 - Analysis of the results achieved and ideation and proposal of further improvements
Such measures should be applied on a very large scale, because evidence indicates that the current epidemic of refractive defects is caused by alterations in the exposure rate to natural light in infants and children. Selected groups of infants and children, growing up under various conditions of compliance with these guidelines, should be carefully monitored from an ophthalmologic point of view and compared with control groups that fail to comply with them. It would be essential to know how much the exposure to natural light is needed to prevent the occurrence of refractive defects.

d) Possible objections
First Objection
It might be argued that, before applying the proposed measures of prevention, careful observations of controlled groups is necessary in order to confirm their validity. In fact, it is a fundamental rule of medicine that any type of treatment or prevention requires testing or confirmation before being adopted for anyone or even used on a large scale.
This argument, which may, at first glance, seem logical and necessary to safeguard the well-being of all concerned, can easily be countered.
In fact, when a new drug is proposed, following the preliminary stages, a rigorous procedure, divided into various phases, must be carefully observed [58]. Only after the drug has passed all stages, may be marketed, and even after this, the drug is subject to controls, which can also lead to its withdrawal from the market. This procedure, which follows what we could call the "precautionary principle", is fully justified in terms of the logic of Evolutionary Medicine. In reality, individuals of the species on which the drug is tested have no evolutionary experience thereof. In the terminology that we have adopted, the use of a new drug is a modification of the ecological niche and therefore must be considered as potentially harmful until the contrary is proved.

Let us now consider the case in which there is a habit that is new in evolutionary terms. The same logic requires that the new habit must be considered potentially dangerous until proven otherwise. According to the "precautionary principle", the new habit should be discouraged until it is demonstrated to be non-harmful. Moreover, we should not wait until the habit has been proven to be harmful before we advise people, on a large scale, not to indulge in the habit. This is not an abstract matter of no practical interest. For example, we have suffered as a result of actions based on opposing arguments, motivated by huge economic interests, and this has led to death and disease on a massive scale.

I am referring to the use of tobacco, a severe alteration of our ecological niche, which has been recognized as such for many years [9, 11]. The remedy, in terms of the logic of Evolutionary Medicine, was and is - simple and straightforward: to stop this habit, both individually and on a large scale, without waiting for proofs of non-harmfulness of this advice, which is clearly based on the "precautionary principle". Yet for many years, the tobacco industry has argued that, first of all, the harmfulness of smoking needed to be proven as certain and only then could measures be adopted to limit the use of tobacco on proper scientific grounds [59], a thesis that one could say is inspired by an "imprudence principle".

In short, returning to the prevention and treatment of refractive defects and to the afore-mentioned objection, the recommendation that a change in our ecological niche (i.e., a prolonged exposition to artificial lighting in the first periods of life) be corrected, given that are reasonable grounds in support of its harmfulness, should not be subject to the demonstration of its non-harmfulness before it is adopted.

For refractive defects, it is not acceptable to wait for decades of experimentation to prove that the restoration of conditions closer to the natural ones is not harmful. Measures of increased exposure to natural light conditions from birth, should be promoted and applied on a large scale in order to obtain a dramatic reduction in new cases of refractive disorders. The results in populations, and fractions of populations, which apply, to a greater or lesser extent, the restoration of more physiological, i.e. natural, conditions must be compared both to confirm the expected results and to evaluate the necessary degree of exposure to natural light for optimal results. However, one should not wait for the results of test samples before applying the aforesaid preventive actions on a large scale.

**Second Objection**

It might be observed that refractive errors are caused both by genetic and non-genetic factors [60]. Therefore, as correction of lifestyle may correct only non-genetic factors, research should be focused on genetic factors.

This is a misleading way of describing the case. Refractive errors are surely due, in some cases, to alterations of the genotype, where no correction of the ecological niche is a logical or effective measure of prevention. However, as it has been demonstrated in the case of diseases caused by alterations of the genotype, these diseases must have a low frequency under natural conditions. In accordance with this theoretical prediction, the incidence of cases of refractive errors in natural conditions is less than 1% and they are, in general, mild, as documented by evidence from populations living under primitive conditions.
In the modern large and growing epidemic of refractive defects, the portion of cases due to genetic defects is quite small and alterations of the ecological niche prevail by far. Certainly, when an individual is exposed to an ecological niche to which his genes are not adapted, in those diseases that are caused by the altered ecological niche, his genes, which are more or less resistant to the onset of diseases, come into play. But, it is not correct to consider the genes that are less resistant to the diseases as pathological: they are entirely normal genes that, in new conditions, to which the species is not adapted, have responses that are more or less effective against the onset of pathological changes. For example, our species is certainly not adapted to smoking. If, in smokers, some suffer respiratory failure, others chronic bronchitis and others cancer, it is not correct to say that those who develop these diseases have pathological genes that somehow must be corrected, or for which it is necessary to develop appropriate treatments. Logic dictates that we must avoid the alteration of the ecological niche and thus prevent the development of diseases that are the result thereof. Therefore, the attribution of responsibility to genetic factors, i.e. non-pathological genes that come into play in altered conditions, should not be an excuse to diminish or to avoid placing greater attention and effort on prevention by correcting the alterations of the ecological niche.

**Conclusion**

Refractive errors of vision are widespread diseases with an increasing frequency. It has been estimated that, by the year 2020, about 3 billion people will be affected by them [39]. Refractive defects involve significant costs arising from the adoption of artificial means to correct refraction (lenses, contact lenses, lenses inserted artificially, laser surgery or other methods). In cases where the defects are of a high level, there are complications that involve additional costs, worsening vision and sometimes the loss of sight. Even in cases where there is no loss of sight, artificial means of correction only partially remedy the defect and are a source of limitation or disability in many activities. Moreover, it has been estimated that the global economic productivity loss in 2009 was $268,8 billion [61]. Overall, refractive defects involve poor quality of life and enormous costs weighing on vast number of people.

Modern medicine aims to pursue means of correction that are increasingly sophisticated and refined. But the ultimate objective would certainly be to minimize new cases of refractive defects, reserving the cures for exceptional cases. This would limit the degradation in quality of life, a great deal of suffering, and - last but by no means least - rising costs. This is possible by correctly applying simple principles of Evolutionary Medicine. Modern doctors, largely unaware even of the most basic principles of Evolutionism, do not know these possibilities. At the same time, evolutionary biologists are unaware of the extreme importance of these possibilities for a rational organization of a health system that should primarily prevent diseases. It is, therefore, essential the integration of the Evolutionism into the active body of modern medicine, transforming it into Evolutionary Medicine, which is more than simply adding Evolutionary Medicine concepts to medical school curriculum [62, 63]. This would be a disruptive but beneficial change in medicine.

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**Conflicts of interests**

None.

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