**Beyond oral hygiene, are capacity-altering biologically based interventions within the moral domain of dentistry?**

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**Running Title**: Beyond oral hygiene, enhancement in dentistry

**Abstract**
Oral diseases such as dental caries (DC) and periodontitis (P) are widely prevalent, and existing approaches to managing these conditions have only a limited effect. Accordingly, there is growing interest in the development of novel biological interventions (including, amongst others CRISPR-Cas9) that might in the future be used to prevent the development or cure these conditions. However, in addition to familiar concerns about using biological interventions in children who cannot provide valid consent, it is not clear whether the provision of these interventions would fall within the proper domain of dentistry. In this opinion paper, we defend the view that the provision of reasonably safe and effective novel biological interventions aimed at preventing DC and P should be understood to fall within the proper domain of dentistry. To do so, we first argue that they may substantially increase the recipient's well-being and future autonomy. We then argue(i) that their use would be consistent with existing practice in dentistry, and (ii) that their use could constitute a form of indirect preventative medicine by addressing a threat to systemic health.

**Key words:** Dental Caries; Periodontitis; human enhancement; biological intervention; well-being; preventative medicine

**Introduction**

Oral diseases such as dental caries (DC) and periodontitis are highly prevalent around the world[1-4]. At the biological level, it is natural for DC, P and TL to arise widely in our species[5-7], making it a statistical norm for the human species to live with these oral 'diseases'**.** Once established, these conditions are highly associated with systemic diseases and can ultimately lead to tooth loss (TL), which impacts social and psychological well-being[8-11].

Conditions such as DC and P are complex to treat, and as yet no cure has been found for them. Instead, current treatments offered in day-to-day practice aimed at managing DC, P, and its sequelae TL, are either generally restorative, or aim to halt disease progression. Furthermore, dentists will commonly recommend behavioural strategies (such as flossing and tooth brushing) that aim to prevent the onset of DC and P. Yet, as we shall explain below, all of these existing interventions have only limited effects.

Technological advances in dentistry are raising the prospect of new strategies for tackling these conditions. Indeed, it is likely that DC and P will be targets for novel capacity-altering biologically based interventions that aim to tackle direct biological risk factors beyond individual fronts of oral disease. However, the prospect of these novel interventions raises moral questions about the proper domain of dentistry.

In this article we shall argue that dentistry should seek the prevention and cure of DC and P using novel biological capacity altering interventions, in view of considerations of wellbeing, and consistency with accepted dental practices.

**Existing Approaches in Dentistry and New Frontiers**

The destroyed dental and oral structures in DC and P result in burdens for life, requiring restoration and additional maintenance throughout one's lifetime. Such interventions aim to restore oral health functionality/hygiene, aiding life extension of the dental organ(s), not to cure. Therefore, seeking to prevent/generate immunity for common oral conditions is still of great importance for oral health.

Although behaviour change has been shown to be efficient in significantly decreasing the number of affected teeth over time[12,13], there are three key factors influencing the effectiveness of that approach. First, independently of socio-economic status, the personal perceptions of a patient or patient's family on the importance of the behavioural change, ultimately influences treatment adherence[14,15]. Second, manual dexterity[16], and third, genetic and epigenetic factors[17-20]. Furthermore, some patients can develop DC and P even in an optimal (behaviour) oral hygiene regime scenario; for example, they may do so if they suffer from Amelogenesis/Dentinogenesis imperfecta[21], Hereditary Gingival Fibromatosis (HGF), or experience periodontitis as a manifestation of systemic disease[22,23].

Therefore, there is a need for novel interventions that prevent and/or cure DC and P at a more fundamental level, targeting the biological processes underlying these diseases. Gene-editing technologies such as CRISPR-Cas9 offer some promise in this regard[24-26]. A reliable predictive genetic marker for DC or P does not currently exist, but many candidate genes have been proposed[17-19]. Moreover, DC and P develop as a result of gene-environmental interaction[17-20,27,28], suggesting that gene-editing offers a potential therapeutic avenue in dentistry, in addition to behavioural enhancements approaches. The use of CRISPR-Cas9 for dental conditions has not been widely discussed, in part because the technology is still in its infancy outside of dentistry, and its safety and efficacy has not yet been established for more serious life-threatening conditions. However, should the safety of the technique be established in the future, such an approach could offer a potential avenue for altering host regulatory genes that are an integral part of fighting against the infectious aspect of DC and P[29].

Moreover, somatic gene-editing interventions could also potentially have important preventative effects. First, somatic interventions could be used to modulate the composition of the native oral microbiome[29], or the pathogenicity of the bacteria causative of DC and P. If successful, such an approach could decrease the damage caused to the dental organ and supportive tissues, preventing early disease stage development[30]. Alternatively, gene-editing could be used to modulate dental organ tissues and their supportive apparatus[31,32]. Such tissues are constantly exposed to pathogens and commensal microorganism. Therefore, the ability of local cell populations to respond to the environmental factors could be enhanced via gene editing.

**Consistency With Current Practice**

As we suggested above, dentists already attempt to prevent DC and P by advocating behavioural change. Oral hygiene habits have shown to be successful in TL decrease[12,13], even though such measure was initially met with scepticism in his early days in the mid twentieth century[33].

Of course, it may be argued that there is a difference between advocating behavioural changes and performing biologically based interventions. For instance, one might appeal to the fact that the latter infringe on a right to bodily integrity that the former do not. However, whether or not there is a morally significant disanalogy between advocating behavioural changes and performing biologically based interventions is something of a moot point, since dentistry has also already fought to universally implement and perform a biological intervention that is still widely used today, universal systemic water fluoridation. This intervention has been shown to be effective in reducing levels of tooth decay among children[34]**.** Moreover, topical fluoride application to teeth in the dental practice and fissure sealants are also used to prevent DC[35]. Whether it is via changing behaviour or through the use of biological interventions, we believe that it is (and always has been) within the professional and ethical domain of dentistry to pursue novel biological preventative and curative strategies against DC, P and TL.

**Considerations for using capacity-altering biologically based approaches in dentistry.**

Many of the biological interventions we consider would be either performed prenatally or before adulthood. This has significant implications for their potential moral permissibility, as the recipients cannot provide valid consent to the intervention. However, we often rely on parents to make proxy decisions for their children with regards to preventative medicine. For example, we already allow parents to exercise parental autonomy in order to prevent children developing dental disease by ensuring oral hygiene in their children. Notably, there are also some risks with providing children with oral hygiene; if parents are neglectful or lazy, they may risk causing fluoride associated conditions in the children, which in extreme levels can be toxic and fatal[36].

The reason that parental autonomy appears justifiable here is that choosing to prevent oral disease in one's children by ensuring oral hygiene meets the following criteria of the kinds of biological interventions that parents may permissibly choose for their children. The intervention in question must be:

1. Safe
2. Unlikely to result in harm to others;
3. Compatible with the demands of distributive justice;
4. Such that the parent's choices are based on a plausible conception of well-being and a better life for the child.
5. Consistent with development of autonomy in the child and a reasonable range of future life plans.[37]

As we have already mentioned, one of the main concerns about the use of gene-editing in any context is safety. In the context of dentistry, there is risk of disruption of neural crest commitment to craniofacial formation[38], therefore, there is a very long way to go before we have a safe and reliable gene-editing technique that would be morally permissible to use for even the most serious medical conditions. Accordingly, our discussion of the use of gene-editing in dentistry is naturally oriented towards a future time where the safety and reliability of gene-editing techniques has reached a satisfactory level, such that they might be considered for preventing the harms associated with oral disease.

In the interests of brevity, we shall thus set aside issues raised by safety, as well as harm to others and distributive justice. However, we shall argue that novel biological interventions in dentistry could meet conditions 4 and 5.

**Well-being and Future Autonomy**

DC and P are detrimental to well-being. The greater the number of reported toothaches, decayed teeth, periodontal disease, and missing teeth, the poorer a person's quality of life is[9,39,40]. Negative judgments are made about people with flawed dentition, affecting their everyday experiences[41,42], and raising the chances for bulling in children[43]. Safe and effective biological interventions that prevent or cure DC, P and TL would enhance the child's well-being on any plausible conception, and they would be consistent with the development of the child's future autonomy.

There is of course scope for debate about the level and type of well-being that it is the professional responsibility of dentists to achieve. It might be argued that DC, P and TL are universal diseases, and so it does not fall within the domain of dentistry to cure (rather than simply treat) these conditions. However, this line of objection overlooks a significant body of research suggesting that these conditions also affect systemic health[44-61]. Oral diseases are directly linked to systemic health and some life-threatening diseases. Therefore, capacity-altering interventions for prevention and cure of DC and P may not only result in common oral diseases benefits but may also result in systemic health benefits.

Seeking to cure and prevent these conditions can thus be viewed as a form of indirect preventative medicine. As such, we should not assume that novel biological interventions aimed at securing these benefits will only be permissible if they pose *no* risk. Some low level of risk may be proportionate, although the precise level of risk that it would be reasonable to expose children to for the sake of these benefits is a question that we cannot adequately address here.

**Conclusion**

The real problem with existing oral diseases preventive measures is their ineffectiveness, rather than the strategy of prevention *per se*. DC is still the most common noncommunicable disease worldwide, consuming 5–10% of healthcare budgets in industrialized countries, and is among the main reasons for hospitalization of children in some high-income countries[3]. We suggest that DC and P cure and prevention by means of novel biological capacity-altering interventions is consistent with the historic and current pursuit of preventative measures already adopted in dentistry. Therefore, potential future use of novel biological capacity-altering interventions should fall within the moral domain of dentistry.

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