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| Question |
| **Should tap water vs. milk be used for avulsed human teeth?** |
| **Population:** | Avulsed permanent human teeth |
| **Intervention:** | Storage in tap water, or buttermilk, or castor oil, or turmeric extract |
| **Comparison:** | Storage in cow’s milk (skim milk, 2.5 % fat milk, unspecified milk)  |
| **Main outcomes:** | Cell viability after 30, 45, 60 or 180 minutes immersion; Cell viability after 6 h or 24 h immersion Rate of cell growth (2, 7 or 14 days) after 120 minutes immersion |
| **Setting:** | Clinical and laboratory in relation to prehospital management |
| **Perspective:** | First aid |
| **Background:** | While it is recognized that immediate replantation of an avulsed permanent tooth provides the best opportunity for tooth survival, this may not be possible in the first aid setting. This review evaluates means of temporarily storing an avulsed tooth until the tooth can be replanted. |
| **Conflict of interests:** | None declared |

# Assessment

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| ProblemIs the problem a priority? |
| Judgement | Research evidence | Additional considerations |
| ○ No○ Probably no● Probably yes○ Yes○ Varies○ Don't know | The oral region comprises 1% of the total body area, yet it accounts for 5% of all bodily injuries. In preschool children, oral injuries estimated at 17% of all bodily injuries. The incidence of traumatic dental injuries is estimated at 1%-3%. Prevalence is steady at 20%-30% (Anderson 2013 S2). Several groups investigating injury rates across non–mouthguard mandated sports (e.g., baseball, basketball, soccer) estimated that orofacial injury rates ranged from 3%-38% of all sport-specific injuries (Kvittem 1998 288; Kumamoto 2004 270).During the last decade traumatic dental injuries were recognized as a public dental health problem worldwide (Zaleckiene 2014 7). |  |
| Desirable EffectsHow substantial are the desirable anticipated effects? |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial○ Small○ Moderate○ Large○ Varies● Don't know | No desirable effects for tap water, castor oil or turmeric extract were reported. | Treatment of dental and oral injuries can cost upwards of US$15,000 over an individual’s lifetime.Important public health implications such as how to best – organize emergency dental care and how to prevent dental injuries, decrease cost, and increase lay knowledge are important factors needed to change epidemiologic data toward more favorable figures in the future (Gould 2016 821). |
| Undesirable EffectsHow substantial are the undesirable anticipated effects? |
| Judgement | Research evidence | Additional considerations |
| ○ Large○ Moderate● Small○ Trivial○ Varies○ Don't know | **Tap water**:For the critical outcome of cell viability (percentage of viable PDL cells), we have identified very-low-certainty evidence (downgraded for risk of bias, indirectness and imprecision) from 1 randomized study (Talebi 2018 203) including 120 extracted teeth, showing harm from 60 min, 180 min, 6 h and 24 h of immersion in tap water when compared with skim milk (MD, -18.53%; 95% CI, -23.53– -13.53; MD, -16.47; 95% CI, -22.56– -10.38; MD, -15.2%; 95% CI, -18.52– -18.22; MD, -7.33%; 95% CI, -9.26– -5.40; P<0.00001, respectively).One observational study (Pileggi 2002 186) did not report the number of extracted teeth in the groups but showed harm from 45 min immersion in tap water when compared with milk (unspecified) (MD, -45.42; 95% CI could not be calculated; P<0.05).

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| **Certainty assessment** | **№ of patients** | **Effect** | **Certainty** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **tap water** | **milk** | **Relative(95% CI)** | **Absolute(95% CI)** |
| **Cell viability after 6 h immersion (Talebi 2018)** |
| 1  | randomised trials  | serious a,h,i | not serious  | serious b,c | serious d | none  | 15  | 15  | -  | MD **15.2 % lower**(18.52 lower to 11.88 lower)  | ⨁◯◯◯VERY LOW  | CRITICAL  |
| **Cell viability after 24 h immersion (Talebi 2018)** |
| 1  | randomised trials  | serious a,h,i | not serious  | serious b,c | serious d | none  | 15  | 15  | -  | MD **7.33 % lower**(9.26 lower to 5.4 lower)  | ⨁◯◯◯VERY LOW  | CRITICAL  |

**Buttermilk**:For the critical outcome of viability (number of viable PDL cells), we have identified very-low-certainty evidence (downgraded for risk of bias, indirectness and imprecision) from 1 randomized study (Kokkali 2017 209) including 30 extracted teeth showing harm from 45 min of immersion in buttermilk when compared with milk (unspecified) (MD, -12646; 95% CI, -14084.66– -11208.48; P<0.00001).

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| **Certainty assessment** | **№ of patients** | **Effect** | **Certainty** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **buttermilk** | **milk** | **Relative(95% CI)** | **Absolute(95% CI)** |
| **Cell viability after 45 minutes immersion (Kokkali 2017)** |
| 1  | randomised trials  | serious a,b,c | not serious  | serious d,e | serious f | none  | 15  | 15  | -  | MD **12646 lower**(14084.66 lower to 11208.48 lower)  | ⨁◯◯◯VERY LOW  | CRITICAL  |

**Castor oil:**For the critical outcome of viability (percentage of viable PDL cells), we have identified very-low-certainty evidence (downgraded for risk of bias, indirectness and imprecision) from 1 randomized study (Nabavizadeh 2018 28) including 20 extracted teeth showing harm from 45 min immersion in castor oil when compared with 2.5 % fat milk (only median cell viability reported, thus absolute effects could not be calculated; P<0.05).

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| **Certainty assessment** | **№ of patients** | **Effect** | **Certainty** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **castor oil** | **milk** | **Relative(95% CI)** | **Absolute(95% CI)** |
| **Cell viability after 45 minutes immersion (Nabavizadeh 2018)**  |
| 1  | randomised trials  | serious a,b,c | not serious  | serious d,e | serious f,g | none  | 10  | 10  | -  | median **8.17 % lower** h | ⨁◯◯◯VERY LOW  | CRITICAL  |

**Turmeric extract:**For the critical outcome of viability (percentage of viable PDL cells), we have identified very-low-certainty evidence (downgraded for risk of bias, indirectness and imprecision) from 1 randomized study (Dhimole 2019 140) including 60 extracted teeth showing harm from 30 min of immersion in turmeric extract when compared with milk (unspecified) (MD, -8.35%; 95% CI, -11.29– -5.41; P<0.00001).

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| **Certainty assessment** | **№ of patients** | **Effect** | **Certainty** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **turmeric extract** | **milk** | **Relative(95% CI)** | **Absolute(95% CI)** |
| **Cell viability after 30 minutes immersion (Dhimole 2019 140)** |
| 1  | randomised trials  | serious a,b,c | not serious  | serious d,e | serious f | none  | 30  | 30  | -  | MD **8.35 % lower**(11.29 lower to 5.41 lower)  | ⨁◯◯◯VERY LOW  | CRITICAL  |

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| Certainty of evidenceWhat is the overall certainty of the evidence of effects? |
| Judgement | Research evidence | Additional considerations |
| ● Very low○ Low○ Moderate○ High○ No included studies | There are limitations in study design, indirectness and imprecision. |  |
| ValuesIs there important uncertainty about or variability in how much people value the main outcomes? |
| Judgement | Research evidence | Additional considerations |
| ○ Important uncertainty or variability○ Possibly important uncertainty or variability● Probably no important uncertainty or variability○ No important uncertainty or variability |  | Developed countries may place more value on personal hygiene and personal appearance, thus, the ability to save a tooth in developed countries is likely more desirable. |
| Balance of effectsDoes the balance between desirable and undesirable effects favor the intervention or the comparison? |
| Judgement | Research evidence | Additional considerations |
| ○ Favors the comparison● Probably favors the comparison○ Does not favor either the intervention or the comparison○ Probably favors the intervention○ Favors the intervention○ Varies○ Don't know | The included evidence shows harm for the outcome of cell viability after immersion in tap water, buttermilk, castor oil and turmeric extract.  |  |
| Resources requiredHow large are the resource requirements (costs)? |
| Judgement | Research evidence | Additional considerations |
| ○ Large costs○ Moderate costs● Negligible costs and savings○ Moderate savings○ Large savings○ Varies○ Don't know | No research evidence identified. | In developed countries, much of the cost of saving a tooth can be outweighed by the overall cost needed to replace a tooth. However, the cost of commercial devices could be a challenge for many developing countries.The cost for tap water is negligible.Turmeric extract costs around 0.20$ per capsule (Amazon.com). Castor oil costs 9.60€ for 150 ml. Buttermilk costs 1.09€ for 1 L (Belgium). |
| Certainty of evidence of required resourcesWhat is the certainty of the evidence of resource requirements (costs)? |
| Judgement | Research evidence | Additional considerations |
| ○ Very low○ Low○ Moderate○ High● No included studies | No studies were identified on resource requirements. |  |
| Cost effectivenessDoes the cost-effectiveness of the intervention favor the intervention or the comparison? |
| Judgement | Research evidence | Additional considerations |
| ○ Favors the comparison● Probably favors the comparison○ Does not favor either the intervention or the comparison○ Probably favors the intervention○ Favors the intervention○ Varies○ No included studies | No research evidence is identified. |  |
| EquityWhat would be the impact on health equity? |
| Judgement | Research evidence | Additional considerations |
| ○ Reduced○ Probably reduced● Probably no impact○ Probably increased○ Increased○ Varies○ Don't know | No research evidence required. | Tap water, castor oil and buttermilk are available in most countries. |
| AcceptabilityIs the intervention acceptable to key stakeholders? |
| Judgement | Research evidence | Additional considerations |
| ○ No○ Probably no● Probably yes○ Yes○ Varies○ Don't know | No research evidence identified. |  |
| FeasibilityIs the intervention feasible to implement? |
| Judgement | Research evidence | Additional considerations |
| ○ No● Probably no○ Probably yes○ Yes○ Varies○ Don't know | No research evidence identified. | Tap water is available in most settings. From a practical perspective, buttermilk, castor oil or turmeric extract might not be easy to carry and are not routinely available in a first aid kit.  |

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# Summary of judgements

|  | **Judgement** |
| --- | --- |
| **Problem** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |
| **Desirable Effects** | Trivial | Small | **Moderate** | Large |  | Varies | Don't know |
| **Undesirable Effects** | Large | **Moderate** | Small | Trivial |  | Varies | Don't know |
| **Certainty of evidence** | **Very low** | Low | Moderate | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | **Probably no important uncertainty or variability** | No important uncertainty or variability |  |  |  |
| **Balance of effects** | Favors the comparison | **Probably favors the comparison** | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | Don't know |
| **Resources required** | Large costs | Moderate costs | **Negligible costs and savings** | Moderate savings | Large savings | Varies | Don't know |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | **Probably favors the comparison** | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | No included studies |
| **Equity** | Reduced | **Probably reduced** | Probably no impact | Probably increased | Increased | Varies | Don't know |
| **Acceptability** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |
| **Feasibility** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |

# Type of recommendation

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| Strong recommendation against the intervention | **Conditional recommendation against the intervention** | Conditional recommendation for either the intervention or the comparison | Conditional recommendation for the intervention | Strong recommendation for the intervention |
| ○  | **●**  | ○  | ○  | ○  |

# Conclusions

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| Recommendation |
| We suggest the use of cow’s milk, any percent fat or form, compared with tap water, buttermilk, castor oil, turmeric extract for temporary storage of an avulsed tooth (weak recommendation, very low certainty evidence). |
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| Justification |
| Despite the limited number of studies available for the interventions, findings show a lower number or percentage of viable PDL cells suggesting lack of benefit as compared with storage of an avulsed tooth in cow’s milk. |

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| Subgroup considerations |
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| Implementation considerations |
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| Monitoring and evaluation |
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| Research priorities |
| Additional studies from a laboratory setting could confirm findings detailed in the included studies. |