Chapter 15
Prognosis of Healing in Treated Teeth with Endodontic Infections
Shimon Friedman

15.1 Introduction: The critical importance of prognosis

The term *prognosis* in the context of health care is defined as the forecast of the course of a disease. In the context of endodontic infection, the associated disease is apical periodontitis, and prognosis means the chance of the affected tissues to heal after treatment of the offending tooth. In common language, however, the term *prognosis of treatment* is often used as synonym for the expected positive outcome.

Prognosis is a critically important element in clinical decision-making, particularly when different alternatives are available for treatment of a given disease. The
current ethical concepts of health care delivery require that clinical decision-making be based on sound evidence and involve the patient. Evidence to support the benefits and risks of available treatment alternatives is shared with the patient, who then selects a specific treatment based on his/her individual values, priorities, and resources (Pellegrino 1994; Ambrosio and Walkerley 1996; Wertz 1998; Schattner and Tal 2002; Fournier 2005). To conform to this concept, health care providers must be well versed in the evidence that supports the prognosis of alternative treatments they suggest to patients. Clinical decision-making in endodontics is no exception to this prevailing concept; therefore, dentists and endodontic specialists should be well informed about the prognosis of different endodontic treatment modalities.

Information about prognosis of endodontic treatment is available from over 260 studies on nonsurgical and surgical treatment. While all this evidence appears abundant, it has been highly inconsistent because of methodologic and technical variations, precluding indiscriminate review of the many available studies. Supported by inconsistent evidence, answers to the main questions related to the prognosis of endodontic treatment modalities have remained equivocal (Friedman 1998). Specifically, careful review is required of the prognosis in teeth with endodontic infections, known to be compromised relative to teeth without infections (Friedman 1998).

It is well established that questions about the prognosis following state-of-the-art treatment should be addressed in structured reviews that focus on studies selected according to well-defined criteria. Accordingly, this chapter aims to define the prognosis of nonsurgical and surgical endodontic treatment of teeth with preoperative lesions indicative of active infective process, and to identify prognostic variables, based on selected studies.

15.2 Outcome measures and criteria in assessment of endodontic prognosis

Much of the confusion regarding the prognosis of endodontic treatment is caused by inconsistent use of outcome criteria, resulting in highly variable “success” rates among the different studies (Friedman 1998). This inconsistency has affected current studies on initial root canal treatment (Table 15.1), orthograde retreatment (Table 15.2), apical surgery (Table 15.3), and intentional replantation (Table 15.4). The inconsistencies result from use of ambiguous or older terms such as “success” and “failure,” and from lack of calibration in outcome assessment. This section of the chapter focuses on outcome measures, assessment strategies, and criteria for assessment of prognosis after nonsurgical and surgical endodontic treatment.

15.2.1 Clinical outcome measures

Clinical outcome measures have been widely used to assess the health state of endodontically treated teeth. Patients’ reporting on presence or absence of pain (subjective measure) and clinical recording of presence or absence of swelling, sinus tract, and tenderness to percussion and palpation (objective measures) have been commonly used. Inasmuch as any one of these clinical outcome measures can be an expression of persistent endodontic infection, they are not specific signs of apical periodontitis; therefore, they have been coupled with radiographic measures in most studies. Nevertheless, in many studies on nonsurgical treatment (Orstavik et al. 1987; Molven and Halse 1988; Murphy et al. 1991; Orstavik and Hörsted-Bindslev 1993; Smith et al. 1993; Orstavik 1996; Trope et al. 1999; Heling et al. 2001; Pettiette et al. 2001; Waitimo 2001; Cheung 2002; Huunonen et al. 2003; Peters et al. 2004; Marending et al. 2005), and in at least one apical surgery study (Rapp et al. 1991), only the radiographic appearance was used to assess the outcome without use of clinical outcome measures. In this manner, the “success” rate can be overestimated by inclusion of teeth that appear radiographically normal but that are symptomatic (Friedman 2002b).

15.2.2 Radiographic outcome measures

Assessment of radiographs is subject to bias (Goldman et al. 1972, 1974; Reit and Hollender 1983; Zakariasen et al. 1984; Eckerbom et al. 1986). Calibration and specific observer strategies have been advocated for endodontic studies (Rud et al. 1972a; Reit 1987b; Molven et al. 2002a), to improve the consistency of assessment. A frequently used strategy uses the Periapical Index (PAI) (Orstavik et al. 1986) for calibration purposes and as reference for assessment of radiographs. Assessed radiographs are compared with five sets of radiographic images and their schematic representations (see Chapter 2). These images are derived from a histologic–radiographic correlation
Table 15.1 Follow-up studies published since 1990, reporting specific data on the outcome of initial treatment in infected teeth. Highlighted studies have been selected as “current best evidence”

<table>
<thead>
<tr>
<th>Study</th>
<th>Cases observed</th>
<th>Follow-up (years)</th>
<th>Cohort</th>
<th>Exposure</th>
<th>Assessment</th>
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<td>5</td>
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<td>n</td>
<td>n</td>
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<td>de Chevigny et al. 2008a</td>
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</table>

- Asymptomatic, without or with residual radiolucency (≥ not reported; rate is sum of healed and healing).
- With at least one criterion for acceptable quality.
- Without or with residual radiolucency (≥ not reported; rate is sum of healed and healing).
- Includes repeated material.
- All canals obliterated to some extent.
- Teeth treated in two sessions without intraoral medication excluded.
- HIV-positive patients.
- Conventional treatment group.
- Assessment with periapical radiographs.
- Does not satisfy criteria of acceptable quality.
- Satisfies criteria of acceptable quality.
Table 15.2  Follow-up studies published since 1988, reporting specific data on the outcome of orthograde retreatment in teeth with endodontic infection. Highlighted studies have been selected as “current best evidence”

<table>
<thead>
<tr>
<th>Study</th>
<th>Examined sample</th>
<th>Follow-up (years)</th>
<th>Cohort</th>
<th>Exposure</th>
<th>Assessment</th>
<th>Analysis</th>
<th>Healed</th>
<th>Healing</th>
<th>Functional*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molven and Halse 1988</td>
<td>98</td>
<td>10-17</td>
<td>n</td>
<td>n</td>
<td>y</td>
<td>y</td>
<td>71b</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Allen et al. 1989</td>
<td>315</td>
<td>≥0.5</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>73</td>
<td>12</td>
<td>≥85</td>
</tr>
<tr>
<td>Sjögren et al. 1990</td>
<td>94a</td>
<td>8-10</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>62</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>van Nieuwenhuyzen et al. 1994</td>
<td>561c</td>
<td>≥0.5</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>y</td>
<td>78</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Friedman et al. 1995</td>
<td>86</td>
<td>0.5-1.5</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td>56</td>
<td>34</td>
<td>≥90</td>
</tr>
<tr>
<td>Danin et al. 1996</td>
<td>18</td>
<td>1</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td>28</td>
<td>28</td>
<td>≥56</td>
</tr>
<tr>
<td>Sundqvist et al. 1998</td>
<td>54</td>
<td>4</td>
<td>n</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>74</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Pietrowska et al. 1997</td>
<td>60c</td>
<td>−</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td>43</td>
<td>42</td>
<td>≥85</td>
</tr>
<tr>
<td>Abbott 1999</td>
<td>43c</td>
<td>0.3-4</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>98</td>
<td>1</td>
<td>−</td>
</tr>
<tr>
<td>Kvist and Reit 1999</td>
<td>47</td>
<td>4</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>58</td>
<td>d-</td>
<td>−</td>
</tr>
<tr>
<td>Chugal et al. 2001</td>
<td>85c</td>
<td>4</td>
<td>n</td>
<td>n</td>
<td>y</td>
<td>y</td>
<td>79</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Hoskinson et al. 2002b</td>
<td>76c</td>
<td>4-5</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>y</td>
<td>78</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Farzaneh et al. 2004a</td>
<td>69</td>
<td>4-6</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td>y</td>
<td>81</td>
<td>5</td>
<td>≥86</td>
</tr>
<tr>
<td>Gorni and Gagliani 2004</td>
<td>452c</td>
<td>2</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td>y</td>
<td>65</td>
<td>4</td>
<td>−</td>
</tr>
<tr>
<td>Fristad et al. 2004</td>
<td>112c,c,e</td>
<td>20-27</td>
<td>n</td>
<td>n</td>
<td>y</td>
<td>y</td>
<td>96</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Imura et al. 2007</td>
<td>404</td>
<td>1.5-5</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>y</td>
<td>81</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Erkan et al. 2007</td>
<td>64</td>
<td>1</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td>64</td>
<td>14</td>
<td>≥78</td>
</tr>
<tr>
<td>de Chevigny et al. 2008b</td>
<td>147</td>
<td>4-6</td>
<td>y</td>
<td>n</td>
<td>y</td>
<td>y</td>
<td>80</td>
<td>6</td>
<td>93</td>
</tr>
<tr>
<td>Hsiao et al. 2009</td>
<td>13</td>
<td>≥0.6</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>70</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Ng et al. 2011</td>
<td>763c</td>
<td>≥2</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>74</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Ricucci et al. 2011</td>
<td>71</td>
<td>5</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>83</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Touboul et al. 2014</td>
<td>108</td>
<td>2-4</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>y</td>
<td>80</td>
<td>11</td>
<td>−</td>
</tr>
<tr>
<td>Azim et al. 2016</td>
<td>41a</td>
<td>0.5-8</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>68</td>
<td>5</td>
<td>−</td>
</tr>
</tbody>
</table>

*a Asymptomatic, without or with residual radiolucency (≥ not reported; rate is sum of healed and healing).
*b Cases classified as "uncertain" excluded.
*c May include unspecified number of teeth without infection.
*d Approximate figure deduced from graph.
*e Includes repeated material.
*f Does not satisfy criteria of acceptable quality.
*g Satisfies criteria of acceptable quality.”
Table 15.3  Follow-up studies published since 1995, reporting specific data on the outcome of apical surgery in teeth with endodontic infection. Highlighted studies have been selected as "current best evidence"

<table>
<thead>
<tr>
<th>Study</th>
<th>Cases observed</th>
<th>Follow-up (years)</th>
<th>Cohort</th>
<th>Exposure</th>
<th>Assessment</th>
<th>Analysis</th>
<th>Outcome (%)</th>
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</thead>
<tbody>
<tr>
<td>Jessen et al. 1995</td>
<td>93</td>
<td>5</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td>59</td>
</tr>
<tr>
<td>August 1996</td>
<td>39</td>
<td>10-23</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>74</td>
</tr>
<tr>
<td>Danin et al. 1996</td>
<td>19</td>
<td>1</td>
<td>n</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>58</td>
</tr>
<tr>
<td>Rud et al. 1996</td>
<td>351</td>
<td>0.5-1.5</td>
<td>n</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>82</td>
</tr>
<tr>
<td>Sumi et al. 1996</td>
<td>157</td>
<td>0.5-3</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td>31</td>
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<tr>
<td>Jansson et al. 1997</td>
<td>62</td>
<td>0.9-1.3</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td>79</td>
</tr>
<tr>
<td>Rud et al. 1997</td>
<td>551</td>
<td>0.5-1.5</td>
<td>n</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>97</td>
</tr>
<tr>
<td>Bader and Lejeune 1998</td>
<td>254</td>
<td>1</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td>50</td>
</tr>
<tr>
<td>Danin et al. 1999</td>
<td>10</td>
<td>1</td>
<td>n</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>60</td>
</tr>
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<td>Kvist and Reit 1999</td>
<td>45</td>
<td>4</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>97</td>
</tr>
<tr>
<td>Rubinstein and Kim 1999</td>
<td>94</td>
<td>1.2</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>y</td>
<td>50</td>
</tr>
<tr>
<td>Testorf et al. 1999</td>
<td>134</td>
<td>1-6</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td>82</td>
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<tr>
<td>von Arx and Kurt 1999</td>
<td>43</td>
<td>1</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td>82</td>
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<td>Zuolo et al. 2000</td>
<td>102</td>
<td>1-4</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>91</td>
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<tr>
<td>Rahbaran et al. 2001</td>
<td>129</td>
<td>0.5-1.5</td>
<td>n</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>92</td>
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<td>Rud et al. 2001</td>
<td>834</td>
<td>0.5-12.5</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td>88</td>
</tr>
<tr>
<td>von Arx et al. 2001</td>
<td>25</td>
<td>1</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td>92</td>
</tr>
<tr>
<td>Rubinstein and Kim 2002</td>
<td>59</td>
<td>5-7</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td>73</td>
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<tr>
<td>Jensen et al. 2002</td>
<td>60</td>
<td>1</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td>90</td>
</tr>
<tr>
<td>Chong et al. 2003</td>
<td>108</td>
<td>2</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>90</td>
</tr>
<tr>
<td>Wesson and Gale 2003</td>
<td>790</td>
<td>5</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>90</td>
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<td>Maddalone and Gagliani 2003</td>
<td>120</td>
<td>0.3-3</td>
<td>n</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>93</td>
</tr>
<tr>
<td>Schwartz-Arad et al. 2003</td>
<td>262</td>
<td>0.3-0.9</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>y</td>
<td>44</td>
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<tr>
<td>Wang et al. 2004</td>
<td>94</td>
<td>4-8</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>74</td>
</tr>
<tr>
<td>Gagliani et al. 2005</td>
<td>231</td>
<td>5</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td>78</td>
</tr>
<tr>
<td>Lindeboom et al. 2005</td>
<td>100</td>
<td>1</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td>89</td>
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<tr>
<td>Taschieri et al. 2005</td>
<td>28</td>
<td>1</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td>93</td>
</tr>
<tr>
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<td>Year</td>
<td>Sample Size</td>
<td>Range</td>
<td>Mortality</td>
<td>Recovery</td>
<td>Other Notes</td>
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<td>0.5–1.5</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>91</td>
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</tr>
<tr>
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<td>71</td>
<td>1</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>93</td>
<td></td>
</tr>
<tr>
<td>Marin-Boero 2006</td>
<td>30†</td>
<td>1</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>von Arx et al. 2007</td>
<td>191</td>
<td>1</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>84</td>
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<tr>
<td>Yazdi et al. 2007f</td>
<td>60#</td>
<td>6.5–9</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>78</td>
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<tr>
<td>Taschieri et al. 2007a†</td>
<td>28</td>
<td>1</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>80</td>
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<td>Wallivaara et al. 2007</td>
<td>55</td>
<td>1</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>80</td>
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<tr>
<td>Perharrocha et al. 2007f</td>
<td>333</td>
<td>1</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>74</td>
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</tr>
<tr>
<td>Taschieri et al. 2008kh</td>
<td>100</td>
<td>2</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>75</td>
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<td>Garcia et al. 2008</td>
<td>106</td>
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<td>y</td>
<td>n</td>
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<td>75</td>
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<td>y</td>
<td>n</td>
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<td>Jonasson et al. 2008</td>
<td>192</td>
<td>1–5</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>91</td>
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<tr>
<td>Kim et al. 2008</td>
<td>37</td>
<td>0.5–1.5</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>75</td>
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</tr>
<tr>
<td>Ortega-Sánchez et al. 2009</td>
<td>25†</td>
<td>1</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>97</td>
<td></td>
</tr>
<tr>
<td>Christiansen et al. 2009</td>
<td>147</td>
<td>1–3</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>87</td>
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</tr>
<tr>
<td>Wallivaara et al. 2009</td>
<td>134p</td>
<td>4–10</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>74</td>
<td></td>
</tr>
<tr>
<td>Barone et al. 2010</td>
<td>339</td>
<td>1</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>86</td>
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<tr>
<td>von Arx et al. 2010</td>
<td>54</td>
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<td>n</td>
<td>y</td>
<td>n</td>
<td>79</td>
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<td>Song et al. 2011a</td>
<td>81p</td>
<td>4</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>85</td>
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<tr>
<td>Taschieri et al. 2010k</td>
<td>194</td>
<td>1</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>88</td>
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<tr>
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<td>491</td>
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<td>y</td>
<td>n</td>
<td>84</td>
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<tr>
<td>Song et al. 2011a</td>
<td>43†</td>
<td>4</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>88</td>
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</tr>
<tr>
<td>Song et al. 2012p</td>
<td>104</td>
<td>6–10</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>88</td>
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</tr>
<tr>
<td>von Arx et al. 2012n</td>
<td>170</td>
<td>5</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>76</td>
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<td>Song and Kim 2012</td>
<td>192</td>
<td>1</td>
<td>y</td>
<td>y</td>
<td>n</td>
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<tr>
<td>Villa-Machado et al. 2013</td>
<td>171</td>
<td>1–16</td>
<td>n</td>
<td>y</td>
<td>y</td>
<td>74</td>
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</tr>
<tr>
<td>Asgary and Ehsani 2013</td>
<td>13</td>
<td>1–2</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>91</td>
<td></td>
</tr>
<tr>
<td>Taschieri et al. 2013k</td>
<td>102</td>
<td>4</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>93</td>
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<tr>
<td>Song et al. 2013</td>
<td>431</td>
<td>1–10</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>96</td>
<td></td>
</tr>
</tbody>
</table>

(continued)
Table 15.3  (Continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Cases observed</th>
<th>Follow-up (years)</th>
<th>Cohort</th>
<th>Exposure</th>
<th>Assessment</th>
<th>Analysis</th>
<th>Appraisal categories</th>
<th>Outcome (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Song et al. 2013</td>
<td>135</td>
<td>1–7</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>y</td>
<td></td>
<td>Healed: 85%, Healing: 32%, Functional: 92%</td>
</tr>
<tr>
<td>Kurt et al. 2014</td>
<td>40</td>
<td>1</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td></td>
<td>Healed: 42%, Healing: 32%, Functional: 92%</td>
</tr>
<tr>
<td>Lui et al. 2014</td>
<td>93</td>
<td>1–2</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>y</td>
<td></td>
<td>Healed: 71%, Healing: 8%, Functional: 85%</td>
</tr>
<tr>
<td>von Ax et al. 2014</td>
<td>134</td>
<td>1</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td></td>
<td>Healed: 85%, Healing: 32%, Functional: 92%</td>
</tr>
<tr>
<td>Li et al. 2014</td>
<td>101</td>
<td>2</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td></td>
<td>Healed: 93%, Healing: 32%, Functional: 92%</td>
</tr>
<tr>
<td>Taiw et al. 2015</td>
<td>155</td>
<td>3</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>y</td>
<td></td>
<td>Healed: 69%, Healing: 32%, Functional: 92%</td>
</tr>
<tr>
<td>Shinburi et al. 2015</td>
<td>113</td>
<td>1–3</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td></td>
<td>Healed: 81%, Healing: 32%, Functional: 92%</td>
</tr>
<tr>
<td>Song et al. 2014</td>
<td>115</td>
<td>4</td>
<td>n</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td></td>
<td>Healed: 88%, Healing: 32%, Functional: 92%</td>
</tr>
<tr>
<td>Çalışkan et al. 2016</td>
<td>90</td>
<td>2–6</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td></td>
<td>Healed: 83%, Healing: 32%, Functional: 92%</td>
</tr>
<tr>
<td>Dhiman et al. 2015</td>
<td>30</td>
<td>1</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td></td>
<td>Healed: 83%, Healing: 32%, Functional: 92%</td>
</tr>
</tbody>
</table>

*Asymptomatic, without or with residual radiolucency (≥ reported; rate is sum of healed and healing).
**Roots considered as unit of evaluation, rather than teeth.
***Some sample as in Rud et al. 1991a, b and 1996.
****Includes only treatments performed in the endodontic clinic.
*****Same sample as in Rubinstein and Kim 1999.
******Only teeth treated by “modern technique.”
*******Randomized controlled trial with inadequate analysis.
********Some sample as Jensen et al. 2002.
*********Most teeth managed by retrograde root canal treatment or retreatment.
**********Only teeth treated with MTA root-end filling.
***********All teeth treated with repeat surgery.
************May include samples from previous studies.
*************Only teeth treated without previous retreatment.
**************All teeth treated with application of guided tissue regeneration membranes.
***************Same sample as in Kim et al. 2008.
****************Same sample as in von Ax et al. 2007.
*****************Includes repeated sample from Wang et al. 2004.
******************Only teeth treated with Recuplast.
*******************Assessed with cone-beam CT.
********************Same sample as in von Ax et al. 2010.
Table 15.4 Follow-up studies since 1987, reporting specific data on the outcome of intentional replantation in teeth with endodontic infection

<table>
<thead>
<tr>
<th>Study</th>
<th>Cases observed</th>
<th>Follow-up (years)</th>
<th>&quot;Success&quot;</th>
<th>Root resorption</th>
<th>Persistent infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tegsjö et al.</td>
<td>56</td>
<td>4</td>
<td>86</td>
<td>14</td>
<td>–</td>
</tr>
<tr>
<td>Warivinge and Kahnberg 1989b</td>
<td>26</td>
<td>2</td>
<td>75</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>Koenig et al. 1989b</td>
<td>177</td>
<td>0.5-4</td>
<td>82</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>Kahnberg 1988b</td>
<td>58</td>
<td>2-7</td>
<td>71</td>
<td>0</td>
<td>29</td>
</tr>
<tr>
<td>Keller 1990</td>
<td>34</td>
<td>3</td>
<td>91</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Bender and Rossman 1993</td>
<td>31</td>
<td>0-22</td>
<td>81</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>Raghoebar and Vissink 1999</td>
<td>29</td>
<td>1-11</td>
<td>72</td>
<td>14</td>
<td>–</td>
</tr>
<tr>
<td>Kahnberg 1996b</td>
<td>21</td>
<td>10</td>
<td>90</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>Çalıkan et al. 1998b</td>
<td>34</td>
<td>0.5-3</td>
<td>95</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>Choi et al. 2014</td>
<td>287</td>
<td>0.5-4.5</td>
<td>90</td>
<td>3</td>
<td>–</td>
</tr>
<tr>
<td>Cho et al. 2016</td>
<td>159</td>
<td>0.5-12</td>
<td>95</td>
<td>3</td>
<td>5</td>
</tr>
</tbody>
</table>

a Teeth rotated 180°.
bCoronally repositioned teeth.

study (Brynolf 1967). They represent a healthy periapex (score 1), minor changes perceived as consistent with a healthy periapex (score 2), and increasing extent and severity of apical periodontitis (scores 3–5). Radiographs are assigned a score according to which of the reference images they match best. Such “blinded” and reference-based assessment reduces bias and improves the sensitivity of assessment, compared with the common assessment of success or failure (Ørstavik et al. 1986, 2004). The PAI has been used mainly in studies on nonsurgical treatment (Ørstavik and Hørsted-Bindslev 1993; Ørstavik 1996; Trope et al. 1999; Waltimo et al. 2001, 2005; Friedman et al. 2003; Huumonen et al. 2003; Farzaneh et al. 2004a,b; Ørstavik et al. 2004; Peters et al. 2004; Marengini et al. 2005; Agribawi 2006; Marquis et al. 2006; Cotton et al. 2008; de Chevigny et al. 2008a,b; Penesis et al. 2008; Mente et al. 2009; Suter et al. 2009; Tervit et al. 2009; Saini et al. 2012; Cheung et al. 2013; Martins et al. 2013), but also apical surgery studies (Wang et al. 2004; Barone et al. 2010) to minimize bias and to facilitate comparisons with nonsurgical treatment studies from the same group (Friedman et al. 2003; Farzaneh et al. 2004a,b; Marquis et al. 2005; de Chevigny et al. 2008a,b). Although the PAI was originally designed to observe changes in mean scores as the main outcome, they can be used to dichotomize outcomes as health (scores 1 and 2) and disease (scores 3, 4, and 5) (Trope et al. 1999; Waltimo et al. 2001, 2005; Boucher et al. 2002; Dugas et al. 2003; Friedman et al. 2003; Huumonen et al. 2003; Farzaneh et al. 2004a,b; Peters et al. 2004; de Chevigny et al. 2008a,b; Kirkevang 2006; Marquis et al. 2006).

In recent years, increasing use of cone-beam computerized tomography (CBCT) imaging in endodontics has drawn attention to possible use of this novel technology for outcome assessment (Velvart et al. 2001; Lofthag-Hansen et al. 2007; Estrela et al. 2008; Low et al. 2008; Christiansen et al. 2009; Patel 2009; Wu et al. 2009; Liang et al. 2011, 2012, 2013; Patel et al. 2012a,b; Cheung et al. 2013; Esposito et al. 2013; Fernandez et al. 2013; van der Borden et al. 2013; Pope et al. 2014; Tanomaru et al. 2015; von Arx et al. 2015, 2016; Zhang et al. 2015). While interpretation of CBCT images allows for excellent repeatability and reproducibility (Estrela et al. 2008; von Arx et al. 2016), suggesting it is less prone to bias than two-dimensional periapical radiographs, use of CBCT imaging may result in overdiagnosis and lower intervention thresholds in the absence of clear definition of
the appearance limits of normal, healthy tissues (Pope et al. 2014). In studies where both periapical radiographs and CBCT imaging were used to detect periapical lesions associated with apical periodontitis, lesion detection with CBCT was consistently more sensitive and more specific and the proportion of healthy teeth confirmed by CBCT was about 10–30% lower than that observed in periapical radiographs (Velvart et al. 2001; Loftag-Hansen et al. 2007; Estrela et al. 2008; Low et al. 2008; Christiansen et al. 2009; Patel 2009; Wu et al. 2009; Liang et al. 2011, 2012, 2013; Patel et al. 2012a, b; Cheung et al. 2013; Esposito et al. 2013; Fernandez et al. 2013; van der Borden et al. 2013; Pope et al. 2014; Tanomaru et al. 2015; von Arx et al. 2015, 2016; Zhang et al. 2015). However, it should be noted that, as yet, CBCT is not the gold standard radiographic outcome measure for periapical health; it is not routinely used preoperatively and, therefore, its should not be routinely applied for posttreatment outcome assessment.

15.2.3 Outcome criteria

Criteria and terminology used for outcome assessment in endodontic studies have varied, mainly in the use of “strict” and “lenient” classifications of “success” (Ng et al. 2007, 2008). Whereas in the majority of the studies “success” or “complete healing” is defined as complete radiographic and clinical normalcy, in many current studies “success” is defined primarily as clinical normalcy that may be accompanied by a residual radiolucency, which is either decreased in size or unchanged. The difference in “success” between these two sets of criteria can be approximately 15% (Friedman et al. 1995; Wang et al. 2004; Ng et al. 2007, 2008, 2011). Adding to the confusion, outcome categories of “uncertain,” “doubtful,” “questionable,” and “improved” have been used inconsistently, to imply uncertainty of the outcome, improved outcomes after nonsurgical treatment and apical surgery, and even nonimproved outcomes after apical surgery. These inconsistencies result for the major part from use of the ambiguous and value-laden terms “success” and “failure” (Ørstavik 1996); therefore, these terms should be replaced with neutral expressions to facilitate communication with patients. The terms used should preferably relate to the specific goals of treatment.

In teeth with endodontic infection, the primary goal of treatment is to heal the tissues affected by apical periodontitis (Ørstavik and Pitt Ford 1998). Thus, the primary outcome of treatment should be related to healing (Rud et al. 1972a; Byström et al. 1987; Ørstavik 1996; Friedman 2002a, b, 2005; Friedman and Mor 2004). The term healed is used for complete clinical and radiographic normalcy (no signs, symptoms, residual radiolucency) (Figures 15.1, 15.2, and 15.3).

![Fig. 15.1 Primary infection healed after initial treatment. (a) Maxillary second molar with apical periodontitis extending along the mesial root surface, and associated sinus tract (traced with a gutta-percha cone). (b) Completed treatment. (c) At 8 years, radiographic and clinical normalcy suggest that the tooth has healed. Source: Friedman (2002). Reproduced with permission of Blackwell Munksgaard.](image)
Prognosis of Healing in Treated Teeth with Endodontic Infections

Fig. 15.2 Persistent infection healed after orthograde retreatment. (a) Maxillary first premolar with posttreatment apical periodontitis restored with a cast post and crown. (b) Completed retreatment with the original crown re-cemented in place. (c) At 4 years, radiographic and clinical normalcy suggest that the tooth has healed. Source: Friedman (2002). Reproduced with permission of John Wiley and Sons.

Fig. 15.3 Persistent infection healed after apical surgery. (a) Maxillary canine with a large excess of sealer and persistent infection. (b) Completed surgery, including root-end filling with MTA. (c) At 3 months, some bone deposition is suggested, but the lesion is not reduced. (d) At 6 months, the tooth is symptom free and the lesion appears to be healing. (e) At 1 year and 8 months, radiographic and clinical normalcy suggest that the tooth has healed. Source: Friedman (2005). Reproduced with permission of John Wiley and Sons.
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Fig. 15.4 Persistent infection healed by scar formation (incomplete healing) after apical surgery. (a) Maxillary lateral incisor with a root filling extruded beyond the root end, and persistent apical periodontitis. (b) Completed surgery, including root-end filling with Super EBA. (c) At 1 year, radiographic and clinical normalcy suggest that the tooth has healed with a small scar formed several millimeters from the root end. Courtesy of Dr. Richard Rubinstein. Source: Friedman et al. (2005). Reproduced with permission of John Wiley and Sons.

This category includes the typical appearance of a scar after apical surgery (Andreasen and Rud 1972a, b; Rud et al. 1972a; Molven et al. 1987, 1996) (Figure 15.4). The term healing is used for decreased radiolucency and clinical normalcy after a follow-up period shorter than 4 years (Figure 15.3d). The term nonhealed or persistent apical periodontitis is used for persistent radiolucency regardless of clinical presentation (Figure 15.5), or persistent symptoms. The secondary goal of treatment is to retain the tooth in a symptom-free function. Thus, the respective outcome of treatment should be related to retention of the tooth, and the term functional retention used for clinical normalcy even in presence of persistent radiolucency. Importantly, individual patients may define elimination of symptoms as their specific treatment goal, particularly when clinical conditions suggest a poor prognosis for healing.

15.3 Levels of evidence in assessment of endodontic prognosis

Reports on prognosis are frequently inconsistent in methodology and in the level of evidence they provide (Sackett et al. 1991). Consequently, structured analysis of the literature is necessary to differentiate clinical studies according to the level of evidence, and to gather valid evidence from selected studies.

15.3.1 Study designs

Design categories of clinical studies are defined by the Cochrane Collaboration (http://www.cochrane.org/glossary/5-letterc) as follows:

- **Clinical trial:** “An experiment to compare the effects of two or more healthcare interventions. Clinical trial is an umbrella term for a variety of designs of healthcare trials, including uncontrolled trials, controlled trials, and randomised controlled trials.” Among the latter, N-of-1 randomized trial is “A randomized trial in an individual to determine the optimum treatment for that individual. The individual is given repeated administrations of experimental and control interventions (or of two or more experimental treatments), with the order of the treatments being randomized.”
• **Cohort study:** "An observational study in which a defined group of people (the cohort) is followed over time. The outcomes of people in subsets of this cohort are compared, to examine people who were exposed or not exposed (or exposed at different levels) to a particular intervention or other factor of interest. A prospective cohort study assembles participants and follows them into the future. A retrospective (or historical) cohort study identifies subjects from past records and follows them from the time of those records to the present. Because subjects are not allocated by the investigator to different interventions or other exposures, adjusted analysis is usually required to minimize the influence of other factors (confounders)."

• **Case–control study:** "A study that compares people with a specific disease or outcome of interest (cases) to people from the same population without that disease or outcome (controls), and which seeks to find associations between the outcome and prior exposure to particular risk factors. This design is particularly useful where the outcome is rare and past exposure can be reliably measured. Case–control studies are usually retrospective, but not always."

• **Cross-sectional study:** "A study measuring the distribution of some characteristic(s) in a population at a particular point in time."

• **Case series:** "A study reporting observations on a series of individuals, usually all receiving the same intervention, with no control group."

Different designs are appropriate for different assessment aims, such as effectiveness of therapy interventions, prognosis, or risks associated with interventions; therefore, reviews geared to answer specific questions should focus on studies with matched design (Fletcher et al. 1996). While randomized controlled trial (RCT) is the appropriate design for assessing effectiveness of different interventions, the appropriate design for assessment of prognosis is a cohort study (Green and Byar 1984; Fletcher et al. 1996).

### 15.3.2 Methodologic rigor

A primary concern in clinical studies is different forms of bias. Data may be distorted so that differences are demonstrated between groups that may not really exist, while existing differences may not be shown (Fletcher
et al. 1996). Bias can occur during assembly of the study cohort, when groups characteristics differ in variables that may influence the outcome or in capacity to heal (Fletcher et al. 1996). Bias can also occur during assessment of the outcome (Fletcher et al. 1996), particularly if assessment is carried out by the providers of treatment, who may be biased towards favorable outcome (Goldman et al. 1972). A structured checklist can be used to identify bias in studies on prognosis so as to determine their internal validity (Department of Clinical Epidemiology and Biostatistics 1981; Sackett et al. 1991; Laupacis et al. 1994; Fletcher et al. 1996; Sutherland 2001):

- Was the study cohort defined, assembled at the inception of the study, at a common point in the course of the disease, described in detail?
- Was the referral pattern described?
- Were baseline features measured reproducibly?
- Was the follow-up achieved in at least 80% of the inception cohort, the follow-up period described, and long enough for the outcome of interest to occur?
- Were the criteria used for outcome assessment described, either objective or applied in a blinded fashion, clinically important and reproducibly measured?
- Was adjustment for extraneous or important prognostic factors carried out?

The checklist criteria can be grouped into four general categories, used as the basis for appraisal of the endodontic studies below.

15.3.2.1 Cohort, at inception and end-point of the study

The inception cohort should be clearly characterized for variables that can potentially influence the outcome, pattern of referral of treated subjects, type of cases treated, and case selection criteria used (Fletcher et al. 1996). Case selection is likely to determine the results (Ingle et al. 1994), because subjects are included or excluded according to perceived prognosis.

At the end-point of the study, failure to examine the majority of treated subjects may skew and invalidate the results (Strindberg 1956; Fletcher et al. 1996); therefore, at least 80% of the treated subjects should be examined (Department of Clinical Epidemiology and Biostatistics 1981; Laupacis et al. 1994; Sutherland 2001). Those who are not examined should be explicitly accounted as “dropouts” who do not present for follow-up at their own volition (their absence may be related to the outcome of interest) or “discontinuers” who are excluded from the study for accountable reasons, for example death or relocation (their absence is not related to the outcome of interest).

The examined sample is a determinant of the study’s validity (Fletcher et al. 1996), and of its statistical power when associations are analyzed between the outcome and different variables. Small differences in outcome require large samples to achieve significance (Fletcher et al. 1996).

15.3.2.2 Exposure (treatment, intervention)

Treatment providers should be characterized, as their expertise may determine the results (Ingle et al. 1994). Treatment procedures performed should be current and explicitly described to avoid the need for interpretation. Studies may be excluded if the treatment procedures are considered irrelevant or unacceptable.

15.3.2.3 Outcome assessment

To minimize bias (Fletcher et al. 1996), objective outcome measures should be used consistently in a blinded manner; therefore, examiners should be independent and calibrated with established reliability. The follow-up period should be long enough to capture the outcome of interest (Figure 15.6). Specifically for endodontic studies, the conclusion of the dynamic healing processes must be captured in the majority of the study sample.

15.3.2.4 Data reporting and analysis

Data pertaining to the study cohort, intervention, outcome assessment, and analysis should be reported in detail to allow identification of potential bias and assessment of validity. Statistical analyses should be designed to minimize bias, and take into account extraneous factors and their potential confounding effects. Preferably, multivariate analyses should be used to account for all the variables.

15.3.3 “Current best evidence” for the prognosis of endodontic treatment

Evidence-based practice is “the conscientious, explicit and judicious use of current best evidence in making
decisions about the care of individual patients” (Sackett et al. 1991). Accordingly, to support evidence-based endodontic practice, the current best evidence for endodontic prognosis needs to be identified. The level of evidence of clinical studies is determined by the research question, study design, and methodologic rigor. Studies are ranked by descending hierarchy of evidence (http://www.cebm.net/index.aspx?o = 5653). Note that the level of evidence may be graded down on the basis of study quality; it may be graded up if there is a large or very large effect.

Evidence for treatment benefits:

- **Level 1**: systematic review of randomized trials or N-of-1 trials;
- **Level 2**: randomized trial or observational study with dramatic effect;
- **Level 3**: nonrandomized controlled cohort/follow-up study;
- **Level 4**: case-series, case–control or historically controlled studies;
- **Level 5**: mechanism-based reasoning.

Evidence of prognosis:

- **Level 1**: systematic review of inception cohort studies;
- **Level 2**: inception cohort studies;
- **Level 3**: cohort study or control arm of randomized trial;
- **Level 4**: case-series or case–control studies, or poor quality prognostic cohort study.

Systematic reviews have been published on the outcome of nonsurgical endodontic treatment (Sathorn et al. 2005; Ng et al. 2007, 2008; Peng et al. 2007; Figini et al. 2008; Naito 2008; Panitsai et al. 2010; Su et al. 2011; McGuigan et al. 2013; Aminosharie and Kulild 2015; Kang et al. 2015) and apical surgery (Peterson and Gutmann 2001; Niederman and Theodosopoulou 2003; Torabinejad et al. 2009; Tsesis et al. 2009, 2011; Del Fabbro and Taschieri 2010; Setzer et al. 2010, 2012; Tang et al. 2010; von Arx et al. 2010; Tsesis et al. 2013; Kang et al. 2015; Serrano-Gimenez et al. 2015), where methodologic rigor was not used as a consideration for inclusion of studies in the review and where the prognosis for teeth with endodontic infections was not always specified. While these reviews satisfy many criteria for systematic reviews, they do not exclude short-term outcome studies and they do not highlight the current best evidence for endodontic prognosis in teeth with apical periodontitis. In contrast, Friedman (2002b, 2005) has
been reviewing clinical endodontic studies focusing on methodologic rigor, so as to identify the current best evidence supporting prognosis of endodontic nonsurgical and surgical treatment beyond the short-term of 1 year. The methodologic rigor of clinical studies is a crucial consideration (Barton 2000), so much so that rigorous cohort studies can outweigh compromised RCTs and structured reviews of rigorous cohort studies can yield consistent conclusions with those of systematic reviews of RCTs (Benson and Hartz 2000; Concato et al. 2000). Accordingly, Friedman’s reviews on prognosis have excluded RCTs and rather included prospective cohort studies that comply with three of the four methodology criteria: cohort, intervention, assessment, analysis/reporting. This chapter represents an update on the previous reviews (Friedman 2002b, 2005) and the data reported in the first edition of this textbook. Inclusion criteria were further restricted, to samples of at least 50 teeth, without treatment history of orthograde retreatment prior to apical surgery, publication since 1990 to capture current interventions, follow-up of at least 2 years for nonsurgical treatment and 4 years for apical surgery to avoid short-term outcomes, availability of data on the proportion of healed teeth, and multivariate analysis of outcome predictors. Excluding studies with samples that have been repeated, eight studies (Table 15.1) represent the current best evidence for the prognosis of primary apical periodontitis after initial root canal treatment (Sjögren et al. 1990, 1997; Ørstavik 1996; Peters et al. 2004; de Chevigny et al. 2008a; Weiger et al. 2000; Ng et al. 2011; Ricucci et al. 2011). In addition, five studies (Table 15.2) represent the current best evidence for the prognosis of posttreatment apical periodontitis after orthograde retreatment (Sjögren et al. 1990; Sundqvist et al. 1998; de Chevigny et al. 2008b; Ng et al. 2011; Ricucci et al. 2011) and three studies (Table 15.3) represent the current best evidence for the prognosis of posttreatment apical periodontitis after apical surgery (Barone et al. 2010; von Arx et al. 2012, 2014). None of the current studies on intentional replantation (Table 15.4) meet the methodology criteria; thus, the level of evidence to support the prognosis of this specific treatment modality is the lowest. Collectively, the current best evidence studies form the basis for the prognosis of treatment in teeth with endodontic infections several years after treatment. They also serve as reference for identifying outcome predictors that significantly influence the prognosis.

15.4 Prognosis of primary apical periodontitis after initial treatment

Treatment providers are expected to advise patients of the prognosis of treatment and to maximize the prognosis by using treatment methods based on solid evidence. Therefore, the prognosis is reported along with outcome predictors that may influence it. Although the methodology among the eight current studies reviewed in this section (Sjögren et al. 1990, 1997; Ørstavik 1996; Weiger et al. 2000; Peters et al. 2004; de Chevigny et al. 2008a; Ng et al. 2011; Ricucci et al. 2011) is rather uniform, they still differ in case selection, study materials, and, consequently, in reported outcomes. Several of these studies have also not controlled for nonendodontic variables that could be of importance in periapical healing. Included among these potential confounding variables are restorative issues, periodontal disease, presence of neighboring teeth, the patient’s smoking habits, systemic diseases, bone modulatory medications, as well as genetic and epigenetic variables.

15.4.1 Potential for healing

The proportion of completely healed teeth after initial treatment ranges from 75% (Ørstavik 1996) to 86% (Sjögren et al. 1990). Considering the uniform outcome assessment among the selected studies, the results may have varied because of differences in tooth types, definition of the tooth or root as the evaluated unit (Friedman 2002b), case selection (Ingel et al. 1994), and restoration.

In addition to the healed teeth, “healing” has been reported in 8% (de Chevigny et al. 2008a) to 16% (Weiger et al. 2000) of the teeth. Typically, the proportion of healing captured in a study is inversely proportional to the follow-up period, because the healing process often requires years to be completed (Friedman 2002b). Thus, the potential of teeth with apical periodontitis to heal within 2–4 years after initial treatment is 75–86%, while an additional 10–15% may still be healing at this time interval. It also is noteworthy that regardless of whether the periapical tissues heal or not, about 90–95% of the teeth remain symptom-free.
and functional (Ørstavik 1996; Weiger et al. 2000; de Chevigny et al. 2008a; Ng et al. 2011).

15.4.2 Time-course of healing

The healing process of primary apical periodontitis lesions is initiated within the first year after treatment (Reit 1987a; Kvist and Reit 1999); however, its completion often requires longer. Therefore, of all the teeth that heal eventually, only 50–70% appear completely healed by 1 year (Adenubi and Rule 1976; Ng et al. 2011), with the proportion increasing up to 90% by 2–4 years and up to 95% by 6 years (Byström et al. 1987; Sjögren et al. 1990; Ørstavik 1996; Kvist and Reit 1999; Ng et al. 2011). The remaining 5–6% of treated teeth may continue healing for years and appear healed only in the second or third decade after treatment (Molven et al. 2002b; Fristad et al. 2004). As long as 4–6 years after treatment, about 8–13% of the teeth may still appear healing (Ørstavik 1996; Farzaneh et al. 2004b; Marquis et al. 2006; de Chevigny et al. 2008a). Considering the rather lengthy time-course of healing, studies with short follow-up periods underestimate the potential prognosis of the treated sample.

Infrequently after nonsurgical treatment, very extensive lesions can heal without total resolution of the radiolucency, when fibrous tissue occupies the periapical space (apical scar) (Penick 1961; Bhaskar 1966; Byström et al. 1987; Nair et al. 1999; Selden 1999; Kabak et al. 2005; Saunders 2008; Schultz et al. 2009; Zhang et al. 2015; Çalışkan et al. 2016) (Figure 15.7). Because this occurrence is infrequent, persisting lesions should be considered

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**Fig. 15.7** Primary infection healed by scar formation after initial treatment. (a,b) Mandibular lateral incisor and canine with primary infection associated with an orofacial fistula. (c) Completed treatment. (d,e) At 2 years, the fistula has healed with minimal scarring of the skin. The residual radiolucency may suggest persistence of infection. (f) Clinical view after reflection of a full thickness flap reveals a thick fibrous bundle connecting the periapical lesion and the soft tissues over the chin. Histologic examination of the dissected bundle confirmed it to be fibrous (scar) tissue. (g) At 6 months after surgery, further decreased radiolucency and better defined periodontal ligament space suggest healing in progress. Source: Friedman (2002). Reproduced with permission of Blackwell Munksgaard.
as persistent apical periodontitis rather than fibrous scars.

Reversal of the healing process is uncommon (Ørstavik 1996; Kvist and Reit 1999), suggesting that extended follow-up of teeth that demonstrate signs of healing after 1 year may be unnecessary (Ørstavik 1996). Nevertheless, root-filled teeth remain constantly at risk of recurrent infection in the long term. For example, over 1% of teeth observed to be healed 10–17 years after treatment reverted to disease a decade later (Molven et al. 2002b). To address this long-term risk, periodic follow-up of root-filled teeth is advocated.

### 15.4.3 Prognostic variables

Outcome predictors can be divided into those that have been identified in multivariate analyses, those that appear to be nonsignificant, and those that are equivocal and require further study. They can also be divided into preoperative variables that inform the projected prognosis before treatment (best derived from cohort studies), and intraoperative variables that are considered during treatment to maximize the prognosis (best derived from RCTs).

#### 15.4.3.1 Significant outcome predictors

**Adjunctive irrigation with chlorhexidine (intraoperative).** One current best evidence study (Ng et al. 2011) suggests a poorer prognosis in teeth with canals are irrigated with chlorhexidine as an adjunct to principal irrigation with sodium hypochlorite (66% healed) compared to canals where chlorhexidine is not used (83% healed). Note that based on a cohort study, the evidence supporting this predictor is weak.

**Extruded root filling (intraoperative).** Poorer prognosis (about 67% healed) has been reported in three studies (Sjögren et al. 1990; Ng et al. 2011; Ricucci et al. 2011) for root fillings extruded beyond the root end, compared to adequate filling length (about 86% healed). Although comparable outcomes for adequate and extruded root fillings have been reported in two other studies (Weiger et al. 2000; de Chevigny et al. 2008a), the collective evidence supporting the adverse impact appears to outweigh that refuting this impact.

**Defective or no restoration (intraoperative).** Poorer prognosis (about 50% healed) is reported in one study (Ng et al. 2011) for teeth with defective or missing restorations, compared to adequate restorations (about 80% healed). Although comparable outcomes for adequate and defective/missing restorations are reported elsewhere (Ricucci et al. 2011), the evidence supporting the adverse impact appears to outweigh that refuting this impact.

#### 15.4.3.2 Equivocal variables

**Systemic health (preoperative).** One current best evidence study (Ng et al. 2011) reports no association between systemic health and prognosis. Another study where the cohort is not differentiated for teeth without or with infection (Marending et al. 2005) suggests that a compromised nonspecific immune system impairs the prognosis, but this conclusion is not well supported by the statistical data. It is possible that healing in the immune-compromised patients requires a longer time than the 2-year observation in these studies.

**Number of roots (preoperative).** Two studies (Ng et al. 2011; Ricucci et al. 2011) have shown no association of prognosis with the numbers of roots. Conversely, one study (de Chevigny et al. 2008a) reports on poorer prognosis of multi-rooted teeth (79% healed) compared to single-rooted teeth (90% healed), suggesting that the risk of persistent disease in multi-rooted teeth is multiplied by the number of roots.

**Radiolucency size (preoperative).** Better prognosis in teeth with small lesions (≤5 mm in diameter) than larger lesions has been reported in two current best evidence studies (Weiger et al. 2000; Ng et al. 2011), while comparable outcomes have been reported for small and large lesions in four other studies (Sjögren et al. 1990, 1997; de Chevigny et al. 2008a; Ricucci et al. 2011).

**Sinus tract (preoperative).** Sinus tracts have not been significantly associated with prognosis in four studies (Sjögren et al. 1990; Weiger et al. 2000; de Chevigny et al. 2008a; Ricucci et al. 2011). Conversely, in another study (Ng et al. 2011) a poorer prognosis was reported for teeth with a sinus tract (67% healed) than when no tract was present (85% healed).
Flareup (intraoperative). Flareups have not been significantly associated with prognosis in two studies (Sjögren et al. 1990; de Chevigny et al. 2008a), but in another study (Ng et al. 2011) teeth where flareup occurred had a poorer prognosis (62% healed) than teeth where flareup did not occur (83% healed).

Root filling method (intraoperative). Two studies have suggested no association between the vertically and laterally compacted root fillings and prognosis (Peters et al. 2004; Ng et al. 2011), while The Toronto Study series (de Chevigny et al. 2008a) has reported a better prognosis (87% healed) in teeth treated with flared canal preparation and vertically compacted warm gutta-percha than in teeth treated with step-back instrumentation and lateral compaction of gutta-percha (77% healed). Their finding notwithstanding, the authors emphasize the requirement to validate this variable in a randomized controlled trial (de Chevigny et al. 2008a).

Short root filling (intraoperative). Poorer prognosis has been reported in two studies (Sjögren et al. 1990; Ricucci et al. 2011), while comparable outcomes for adequate and short root fillings have been reported in three other studies (Weiger et al. 2000; Peters et al. 2004; de Chevigny et al. 2008a).

Bacterial culture before root filling. Bacteriologic root canal samples showing no growth before root filling were associated with better prognosis in one study (Sjögren et al. 1997). Nevertheless, the limited aptitude of root canal bacterial sampling techniques and culture (Paquette et al. 2007) undermine the ability to conclusively answer this research question.

Complications. Perforation, file breakage, and massive extrusion of filling materials have all been suggested to impair healing (Sjögren et al. 1990; de Chevigny et al. 2008a) and measures must be taken to avoid them. However, when they occur, endodontists currently may successfully manage complications associated with perforation (Main et al. 2004; Ghoddusi et al. 2007; Pace et al. 2008; Mente et al. 2010; Ree and Schwartz 2012; Krupp et al. 2013; Pontius et al. 2013; Mente et al. 2014; Gorni et al. 2016) and fractured instruments (Spili et al. 2005; Panitvisai et al. 2010; Fu et al. 2011; Murad and Murray 2011; Ng et al. 2011; McGuigan et al. 2013; Ungerechts et al. 2014). Thus, the negative influence of mid-treatment complications on the prognosis may be mitigated by current management strategies.

15.4.3.3 Nonpredictive variables

The following preoperative variables have not been significantly associated with the prognosis of primary apical periodontitis:

- Age, gender (Sjögren et al. 1990; de Chevigny et al. 2008a; Ng et al. 2011; Ricucci et al. 2011);
- Jaw, specific anatomy (Weiger et al. 2000; de Chevigny et al. 2008a; Ng et al. 2011);
- Periodontal support (Sjögren et al. 1990; de Chevigny et al. 2008a; Ng et al. 2011). Yet, if present, advanced periodontal disease should be expected to progress over time (Figure 15.8).

The following intraoperative variables have not been significantly associated with the prognosis of primary apical periodontitis.

Root canal instrumentation. The type of instruments used (Sjögren et al. 1990; de Chevigny et al. 2008a), degree of taper (Ng et al. 2011), and apical enlargement size (Sjögren et al. 1990; de Chevigny et al. 2008a). Although extensive apical enlargement has been suggested to enhance disinfection in the apical portion of the root canal (Orstavik et al. 1991; Yared and Dagher 1994; Card et al. 2002), the inability in studies to consistently assess the extent of apical enlargement without knowing the initial canal dimensions undermines the ability to address this research question.

Restoration type. The type of restoration (temporary, definitive, filling, cast) (Sjögren et al. 1997; de Chevigny et al. 2008a; Ng et al. 2011). Yet, one study (Sjögren et al. 1990) reported less healing in teeth restored with crowns and those serving as bridge abutments, than in teeth restored with fillings. Posts have not been associated with the outcome either (Sjögren et al. 1990; de Chevigny et al. 2008a).

Number of treatment sessions. (de Chevigny et al. 2008a; Ng et al. 2011) Though intracanal medication applied between treatment sessions has been suggested to improve root canal disinfection (Bystöm and Sundqvist 1981, 1983, 1985; Bystöm et al. 1985; Molander et al. 1990; Örstavik et al. 1991; Yared and Dagher 1994; Shuping et al. 2000), a systematic review of studies assessing treatment outcomes after one or
more treatment sessions concludes that “the biological benefit of multi-session treatment has not been supported by clinical evidence” (Sathorn et al. 2005).

15.5 Prognosis of posttreatment apical periodontitis after orthograde retreatment

Similarly to the studies in initial treatment, considerable differences exist in case selection and composition of study materials among the five selected current studies on retreatment (Sjögren et al. 1990; Sundqvist et al. 1998; de Chevigny et al. 2008b; Ng et al. 2011; Ricucci et al. 2011), and their results vary even more than those of initial treatment.

15.5.1 Potential for healing

The proportion of completely healed teeth after orthograde retreatment ranges from 62% (Sjögren et al. 1990) to 84% (in teeth without perforation) (de Chevigny et al. 2008b). Falling below the range reported in the other studies, the reported 62% (Sjögren et al. 1990) appears to be an outlier. The variability of the results may be attributed to the same factors as those suggested above for initial treatment. In addition to the healed teeth, progressive healing has been reported in 6% of the teeth (de Chevigny et al. 2008b). Thus, the potential of teeth with persistent apical periodontitis to heal within 2–4 years after orthograde retreatment is 74–84%, while additional 5–6% may still be healing at this time interval. It also is noteworthy that even if complete healing does not occur, 90–93% of the teeth may remain symptom-free and functional (de Chevigny et al. 2008b; Ng et al. 2011).

15.5.2 Time-course of healing

In the same way as healing of primary apical periodontitis after initial treatment, healing of persistent apical periodontitis requires considerable time after
orthograde retreatment. Apparently, as many as 50% of teeth that were not healed 10–17 years after retreatment were completely healed a decade later (Fristad et al. 2004). The late healing was mainly characteristic of teeth with surplus root-filling material (Fristad et al. 2004).

15.5.3 Prognostic variables

The similarities between initial treatment and orthograde retreatment justify the consideration of the same outcome predictors. It is noteworthy that the current best evidence for retreatment is limited to only a few studies that do not allow conclusive assessment of the influence of many variables on the prognosis. Also, specifically for retreatment, characteristics of the previous root canal treatment history have to be considered, including the previous root filling, a perforation that may be present in a minority of retreated teeth, and the time elapsed since initial treatment.

15.5.3.1 Significant outcome predictors

Previous perforation (preoperative). Two studies (de Chevigny et al. 2008b; Ng et al. 2011) have reported a poorer prognosis for retreated teeth with previous perforations sealed with a variety of repair materials (about 50% healed), compared to teeth without perforations (84% healed). It is noteworthy, however, that limited-size case series (Main et al. 2004; Ghodduzi et al. 2007; Pace et al. 2008; Mente et al. 2010, 2014; Rea and Schwartz 2012; Krupp et al. 2013; Pontius et al. 2013) have reported that 73–100% of teeth healed after perforations were sealed with mineral-trioxide aggregate (MTA) (Figure 15.9). Thus, a previous perforation’s impact on the prognosis, or the lack thereof, may depend on the material used for repair.

Apical patency (intraoperative). One study (Ng et al. 2011) reports a better prognosis in teeth where apical patency was regained during retreatment (82% healed), compared to no patency regained (70% healed). Note that based on a cohort study, the evidence supporting this predictor is weak.

Adjunctive irrigation with ethylenediaminetetraacetic acid (EDTA) (intraoperative). One study (Ng et al. 2011) reports a better prognosis in teeth where canals were irrigated with EDTA in addition to sodium hypochlorite (87% healed), compared to no use of EDTA (78% healed). Note that based on a cohort study, the evidence supporting this predictor is weak.

Number of treatment sessions. Unlike initial treatment (see earlier), one study (de Chevigny et al. 2008b) reports a better prognosis in teeth retreated in one
session (100% healed), compared with retreatment in two sessions (77% healed). Note that based on a cohort study, the evidence supporting this predictor is weak.

15.5.3.2 Equivocal variables

Radiolucency size (preoperative). One current best evidence study (Ng et al. 2011) reports a better prognosis in teeth with small lesions (<5 mm in diameter; 86% healed) than larger lesions (67% healed), while comparable outcomes have been reported for small and large lesions in two other studies (de Chevigny et al. 2008b; Ricucci et al. 2011).

Sinus tract (preoperative). One study (Ng et al. 2011) reports a poorer prognosis in teeth with a sinus tract (67% healed) than when no tract is present (85% healed), while sinus tracts have not been significantly associated with prognosis in one study (de Chevigny et al. 2008b).

Apparent quality of the previous root filling (preoperative). One study (de Chevigny et al. 2008b) reports a better prognosis (86% healed) in teeth with adequate length or density of the previous root filling, compared with teeth with apparently adequate root fillings (50% healed). Previous root filling quality was not associated with the prognosis in another study (Ng et al. 2011).

15.5.3.3 Nonpredictive variables

The following preoperative variables have not been significantly associated with the prognosis of posttreatment apical periodontitis after orthograde retreatment:

- Age, gender (de Chevigny et al. 2008b; Ng et al. 2011);
- Jaw, specific anatomy (de Chevigny et al. 2008b; Ng et al. 2011);
- Periodontal support (de Chevigny et al. 2008b; Ng et al. 2011);
- Number of roots (de Chevigny et al. 2008b; Ng et al. 2011);
- Symptoms (de Chevigny et al. 2008b; Ng et al. 2011);
- Elapsed time after previous treatment (de Chevigny et al. 2008b).

The following intraoperative variables have not been significantly associated with the prognosis of posttreatment apical periodontitis after orthograde retreatment:

- Root canal instrumentation (de Chevigny et al. 2008b; Ng et al. 2011);
- Type of root filling (de Chevigny et al. 2008b; Ng et al. 2011);
- Restoration type (de Chevigny et al. 2008b; Ng et al. 2011).

15.6 Prognosis of posttreatment apical periodontitis after apical surgery

Techniques and materials applied in apical surgery have evolved considerably over the past two decades, leading to a surge in the number of studies reporting on prognosis and outcome predictors. Systematic reviews of older and contemporary studies have highlighted the benefits of state-of-the-art apical surgery approaches including the use of magnification and illumination (microscope or endoscope), ultrasonic root-end cavity preparation, and MTA and super ethoxy-benzoic acid (Super-EBA) for root-end filling (Tsesis et al. 2009, 2013; Del Fabbro and Taschieri 2010; Setzer et al. 2010, 2012; Tang et al. 2010; von Arx et al. 2010; Kang et al. 2015; Serrano-Gimenez et al. 2015). Collectively, these current techniques, often referred to as “apical microsurgery” (Setzer et al. 2010), have been reported to yield high “success” rates in the range of 89–94% (Tsesis et al. 2009; Del Fabbro and Taschieri 2010; Setzer et al. 2010, 2012; Tang et al. 2010; von Arx et al. 2010; Tsesis et al. 2013; Kang et al. 2015; Serrano-Gimenez et al. 2015). While the recent systematic reviews satisfy the literature searching and statistical analysis criteria, they have consistently fallen short in critically appraising the studies they selected, ignoring flaws in outcome assessment and short-term observation periods. In this regard, those systematic reviews have generally overestimated the prognosis of apical surgery and their conclusions are the subject of controversy (Friedman 2011).

The most contentious methodologic issues are the following.

Short follow-up periods. The 1-year observation in many studies reporting on the outcome of apical microsurgery (Table 15.3, from Rubinstein and Kim 1999 onwards) does not capture longer-term regression,
reported in 6–10% of teeth that appeared healed in the short-term after microsurgical treatment (Rubinstein and Kim 2002; Wesson and Gale 2003; Song et al. 2012, 2014; von Arx et al. 2012, 2014; Tawil et al. 2015) (Figure 15.10). As result of such long-term regression, the healed rates in given populations declined from 84% to 76% at 5 years (von Arx et al. 2007) and from 91% to 88% at 4–8 years (Song et al. 2014), although the decline was occasionally offset by an atypical progression in a few teeth from “not healed” at 1 year to “healed” at 5 years (von Arx et al. 2014; Tawil et al. 2015). By relying primarily on short-term studies, the recent systematic reviews (Tsisis et al. 2009; Del Fabbro and Tsuchi 2010; Setzer et al. 2010, 2012; Tang et al. 2010; von Arx et al. 2010; Tsisis et al. 2013; Kang et al. 2015; Serrano-Gimenez et al. 2015) have overestimated the prognosis of apical microsurgery.

Misclassification of “incomplete healing”. The majority of studies on the prognosis of apical microsurgery appear to classify outcomes based on well-established criteria (Rud et al. 1972a; Molven et al. 1987; Grung et al. 1990), although with critical discrepancies. According to the classic criteria, both “complete” and “incomplete” healing represent a favorable outcome or success, while “uncertain” and “unsatisfactory” healing represent unfavorable outcome or failure. “Incomplete healing” is strictly reserved for fibrous scars, occurring in less than 10% of cases (Molven et al. 1987; Grung et al. 1990; Yazdi et al. 2007; von Arx et al. 2012, 2014; Çalışkan et al. 2016). Instead, it has been erroneously assigned to teeth showing reduced radiolucency (Gagliani et al. 2005; Ortega-Sanchez et al. 2009; Li et al. 2014), which should be classified as “uncertain healing.” The importance of this misclassification cannot be overstated: it counts many teeth (often 12–32% of the cohort) with an unfavorable outcome as having a favorable outcome, thus overestimating the prognosis. In specific studies, outcomes can be properly interpreted when both complete and incomplete healing categories are specified (Chong et al. 2003; Maddalena and Gagliani 2003; Lindeboom et al. 2005; Marin-Botero et al. 2006; Yazdi et al. 2007; Walivaara et al. 2009, 2011; Song and Kim 2012; Song et al. 2012; von Arx et al. 2012, 2014); however, some researchers lump both outcome categories together without breakdown, precluding reinterpretation of misclassified outcomes (Tsuchi et al. 2005, 2006a,b, 2007a,b 2008, 2010, 2011, 2013).

Misclassification of “uncertain healing”. The prognosis has been further inflated by a specific research.
The proportion of healed teeth (including scars) after first-time apical microsurgery ranges from 74% (Barone et al. 2010) to 84% (von Arx et al. 2014). The reported outcomes may have varied somewhat because of differences in proportions of previously retreated teeth and in treatment procedures. Beyond the assessment of healing, some 85–95% of the teeth may remain symptom-free and functional (Barone et al. 2010; von Arx et al. 2012, 2014).

15.6.1 Potential for healing

The proportion of healed teeth (including scars) after first-time apical microsurgery ranges from 74% (Barone et al. 2010) to 84% (von Arx et al. 2014). The reported outcomes may have varied somewhat because of differences in proportions of previously retreated teeth and in treatment procedures. Beyond the assessment of healing, some 85–95% of the teeth may remain symptom-free and functional (Barone et al. 2010; von Arx et al. 2012, 2014).

15.6.2 Time-course of healing

Healing after apical surgery progresses rapidly within the first year (Halse et al. 1991; Kvist and Reit 1999). Of all the teeth that heal eventually, 35–60% appear completely healed by 1 year (Grung et al. 1990; Halse et al. 1991; Molven et al. 1996; Maddalone and Gagliani 2003; Wesson and Gale 2003), while approximately 85% appear healed by 3 years (Grung et al. 1990). Healing by a fibrous scar occurs frequently (Rud et al. 1972a; Molven et al. 1996) (Figure 15.4), when both the buccal and lingual bone plates are perforated at the conclusion of the surgical procedure (Molven et al. 1991). Postsurgery apical scars usually remain stable over time (Molven et al. 1996) and are considered at par with a healed site (Rud et al. 1972a; Molven et al. 1996).

Unlike the very low occurrence of healing regression after nonsurgical treatment, recurrent infection in the long term after apical microsurgery has been reported in 6–10% of healed teeth (Rubinstein and Kim 2002; Wesson and Gale 2003; Song et al. 2011, 2014; von Arx et al. 2012, 2014; Tawil et al. 2015) (Figure 15.10). To address this risk of regression, it is advisable to re-examine teeth 3 years or longer after apical microsurgery.

15.6.3 Prognostic variables

Many variables associated with the prognosis of apical microsurgery differ from those that have been examined in relation to nonsurgical treatment.

15.6.3.1 Significant outcome predictors

Interproximal bone level (preoperative). One study consistent with the current best evidence reported better prognosis in teeth where the measured distance between the interproximal bone level and the cementoenamel junction was ≤3 mm (78% healed) compared to >3 mm (53% healed) (von Arx et al. 2012). This finding supported earlier observations in a rather large number of nonselected studies (Rud et al. 1972b; Fimme et al. 1977; Hirsch et al. 1979; Skoglund and Persson 1985; Forssell et al. 1988; Kim et al. 2008; Saunders 2008) of poor outcomes in teeth with considerable vertical or marginal bone loss, which can compromise periodontal reattachment. Taken together, both higher and lower level evidence suggests that the prognosis may be compromised by considerable attachment loss of the treated tooth.

Type of root-end filling material (intraoperative). Studies based on an in vivo model developed to simulate clinical conditions (Friedman et al. 1991b) have
highlighted intermediate restorative material (IRM) (Andreasen and Pitt Ford 1994; Pitt Ford et al. 1994; Tawil et al. 2009), Super-EBA (Pitt Ford et al. 1995; Trope et al. 1996), MTA (Torabinejad et al. 1995; Tawil et al. 2009), and Diaket (Witherspoon and Gutmann 2000) as potentially superior root-end filling materials. However, animal studies do not rank as evidence for effectiveness of clinical interventions. While several RCTs (Jensen et al. 2002; Chong et al. 2003; Lindeboom et al. 2005), a nonrandomized trial (von Arx et al. 2007), and a systematic review (Tang et al. 2010) have suggested equivalence of IRM, Super-EBA, MTA, and Retroplast (Figure 15.11) in the short-term, recent 5-year studies consistent with the current best evidence reported a better prognosis in teeth root-end filled with MTA (86–93% healed) compared to Retroplast (77–79% healed) and Super-EBA (67% healed) (von Arx et al. 2012, 2014). Note that based on cohort studies, the evidence supporting this predictor is weak.

Surgical crypt size (intraoperative). One study (Barone et al. 2010) reports a better prognosis in teeth with smaller crypt size (≤10 mm in diameter; 80% healed) than larger crypts (>10 mm; 53% healed). Note that this finding was not correlated with preoperative radiolucency size in the same study and this variable has not been addressed in the other current best evidence studies.

15.6.3.2 Equivocal variables

Patient’s age (preoperative). One current best evidence study (Barone et al. 2010) reports a better prognosis for older patients (>45 years; 84% healed) than for younger patients (≤45 years; 68% healed), while comparable outcomes have been reported for younger and older patients in two other current best evidence studies (von Arx et al. 2012, 2014).

Length of the existing root filling (preoperative). One current best evidence study (Barone et al. 2010) reports a better prognosis in teeth with root fillings of inadequate length (≥2 mm short of the root end or extruded; 84% healed) than adequate length (68% healed), while comparable outcomes have been reported for all root filling lengths in another study (von Arx et al. 2012).
15.6.3.3 Nonpredictive variables

The following preoperative variables have not been significantly associated with the prognosis of posttreatment apical periodontitis after apical microsurgery:

- Tooth type, jaw, specific anatomy (Barone et al. 2010; von Arx et al. 2012). Note that incomplete healing by scar tissue occurs more frequently in maxillary lateral incisors than in other teeth (Molvæ et al. 1991; von Arx et al. 2014).
- Symptoms (Barone et al. 2010; von Arx et al. 2012).
- Radiolucency size (Barone et al. 2010; von Arx et al. 2012). Note that healing by scar tissue frequently occurs in very large lesions (>10 mm in diameter) (Molvæ et al. 1991).
- Material and density of existing root-filling (Barone et al. 2010).
- Restoration type, post (Barone et al. 2010; von Arx et al. 2014).

- Elapsed time after nonsurgical treatment (Barone et al. 2010).
- Second-time surgery (Barone et al. 2010; von Arx et al. 2012, 2014). Note that modified case selection criteria and techniques have been suggested to improve the outcome of second-time surgery (Wang et al. 2004) (Figure 15.12).
- Nature of pathologic lesion as revealed by biopsy (Barone et al. 2010).

The following intraoperative variables have not been significantly associated with the prognosis of posttreatment apical periodontitis after apical microsurgery:

- Method of hemostasis (Barone et al. 2010). Note that effective hemostasis is critical for quality root-end filling (Carr 1998) and bonding of Retroplast apical caps (Jensen et al. 2002).
- Depth of root-end filling (Barone et al. 2010). Note that with the use of conventional ultrasonic tips, root-end cavities can vary in depth from 1 to 3 mm.
healing, must be considered as a risk when mandibular molars are treated. Paresthesia was reported in 20% of patients after apical surgery in mandibular molars; it was transient in 19% of patients but lingered for 2 years in 1% of patients (Wesson and Gale 2003).


15.6.3.4 Variables not addressed at the level of current best evidence

The following pre- and postoperative variables have been addressed in different studies but are not consistent with the current best evidence.

Root dentin defects (intraoperative). A pioneering but nonselected study (Tawil et al. 2015) reports a better 3-year healed rate (97%) in teeth where no root dentin defects were evident under microscopic and transillumination examination, than in roots where root dentin defects were evident (32%). This variable requires further investigation.

Presence or absence of a root-end filling (intraoperative). A root-end filling is placed to establish an effective barrier against interaction of intracanal bacteria with the periapical tissues (Friedman 1991). Many nonselected studies have reported better outcomes with root-end fillings than without (Friedman et al. 1991a; Rapp et al. 1991). Collectively, these low-evidence studies suggest that placement of a root-end filling to curtail persistent root canal infection improves the prognosis.

Operator’s skill (intraoperative). Three nonselected studies suggest that the prognosis is associated with the individual operator’s skill (Nord 1970; Altonen and Mattila 1976; Lustmann et al. 1991). While it is widely accepted that apical surgery is technique-sensitive, the evidence supporting this predictor is suggestive at best.

Laser irradiation, bone grafts, and barriers (intraoperative). Application of laser irradiation (Bader and Lejeune 1998), guided regeneration barriers, and bone grafting substances (Saad and Abdellatif 1991; Grimes 1994; Pecora et al. 1995; Rankow and Kranner 1996; Tobon et al. 2002; Lin et al. 2010) have not been shown to influence the prognosis. Bone regeneration after apical surgery may be improved by

(Figure 15.13); cavities extending further coronally qualify as retrograde retreatment.

- Procedural complications, including perforation of the opposing bone plate or sinus (Barone et al. 2010). Note that sensory deficit, while unrelated to

Fig. 15.13 Root-end cavity preparation with ultrasonic tips. (a) Assortment of ultrasonic tips for root-end cavity preparation. (b) Clinical view of root-end cavity preparation with an ultrasonic tip. Source: Friedman (2005). Reproduced with permission of John Wiley and Sons.
application of guided regeneration barriers only in teeth with through-and-through defects (Tsesis et al. 2011).

Level of apical resection (intraoperative). A more coronal resection (approximately 3 mm from the apex) may avoid exposing canal ramifications that can allow intracanal bacteria to sustain disease after surgery (Carr and Bentkover 1998), while also facilitating preparation of the root-end cavity and filling.

Concurrent surgical and orthograde management (intraoperative). When surgical and orthograde treatment are performed concurrently “infection is eliminated and reinfection is prevented” (Molven et al. 1991), augmenting the prognosis compared to apical surgery alone (Friedman 1991; Hepworth and Friedman 1997). While contemporary treatment planning for persistent endodontic infections usually prescribes either orthograde or surgical management, in selected cases both procedures can be performed concurrently to comprehensively manage anatomic and technical complexities.

Retrograde root canal retreatment (intraoperative). Retrograde retreatment comprises instrumentation, irrigation, and filling the root canal as far coronally as can be reached from the apical end (Figure 15.14) (Nygård-Osbrøy 1971; Storms 1978; Serota and Krakow 1983; Reit and Hirsch 1986; Flath and Hicks 1987; Amagasa et al. 1989; Goldberg et al. 1990; Jonasson et al. 2008), with reported healed rates ranging from 71% to 100% (Reit and Hirsch 1986; Amagasa et al. 1989; Goldberg et al. 1991; Wang et al. 2004; Jonasson et al. 2008). While the coronally extended barrier offers an advantage over the standard root-end filling, continued bacterial ingress into the canal under restorations and along posts may result in recurrence of disease (Figure 15.10).

Type of magnification and illumination (intraoperative). Contemporary systematic reviews of short-term studies (Tsesis et al. 2009, 2013; Del Fabbro and Taschieri 2010; von Arx et al. 2010; Setzer et al. 2012) suggest that the prognosis may be improved when apical microsurgery is performed with the aid of the operating microscope, compared to the endoscope.

15.7 Prognosis of posttreatment apical periodontitis after intentional replantation

In accordance with current concepts, intentional replantation may be used as an alternative to extraction when both treatment and apical surgery are not feasible in situ (Guy and Goerig 1984; Dumsha and Gutmann 1985) (Figure 15.15). The expected goal is survival of the replanted tooth, considered as success (Grossman 1982; Torabinejad et al. 2015) even if pathologic processes persist. Healing of the attachment apparatus without root resorption depends on survival of the periodontal ligament and cementum along the root surface (Andreasen 1985; Andreasen et al. 1995), and prevention of infection (Tronstad 1988; Trope and Friedman 1992). Reattachment without resorption is conditional on controlled trauma associated with

Fig. 15.14 Persistent infection healed after retrograde retreatment. (a) Maxillary second premolar with persistent infection. (b) Retrograde retreatment is carried out with ultrasonic files. (c) Completed surgery, including root filling with sealer and injectable gutta-percha. (d,e) At 1 and 7 years, respectively, radiographic and clinical normalcy suggest that the tooth has healed. Source: Friedman (2005). Reproduced with permission of John Wiley and Sons.
may not have followed the current clinical protocols for replantation of teeth. For example, on occasion roots were only sealed apically without a root filling, predisposing them to inflammatory root resorption (Koenig et al. 1988; Keller 1990).

Consideration of prognosis after intentional replantation takes into account not just periapical healing, but also reattachment without external root resorption (Hammarström et al. 1986; Torabinejad et al. 2015; Cho et al. 2016). Reported incidence of root resorption in contemporary studies has varied from zero (Kahnberg 1988; Warfvinge 1989; Keller 1990; Kahnberg 1996; Çalışkan 1998) to 6% (Kingsbury and Wiesnbau 1971; Will 1974; Koenig et al. 1988; Bender and Rossman 1993; Choi et al. 2014; Cho et al. 2016), likely thanks to optimal extraoral time and conditions. Nevertheless, incidence of resorption as high as 14% and 35% has been reported in several studies (Tegsjo et al. 1987; Raghoebar and Vissink 1999). Persistent infection ranges from 5% (Cho et al. 2016) to 29% (Kahnberg 1988), because the infected root canal can be effectively sealed with a root-end filling that is easily placed. The predictable healing potential after intentional replantation performed in well-controlled conditions has been further demonstrated, albeit at the lowest level of evidence, in many case reports (Feldman et al. 1971; Rosenberg et al. 1980; Solomon and Abelsohn 1981; Stoner and Laskin 1981; Kaufman 1982; Lubin 1982; Guy and Goerg 1984; Nosonowitz and Stanley 1984; Ross 1985; Dryden 1986; Lindeberg et al. 1986; Lu 1986; Madison 1986; Messkoub 1991; Kawai and Masaka 2002; Penarrocha et al. 2007; Subay et al. 2014).
15.7.1 Dynamics of external root resorption

Resorption after intentional replantation is usually discernible within 1 year (Emmertsen and Andreasen 1966). This is definitely true regarding inflammatory resorption. Replacement resorption may be first observed radiographically several years after replantation (Andreasen et al. 1995; Cho et al. 2016). For example, in a recent long-term study (Cho et al. 2016), occurrence of external root resorption increased from 2/159 teeth (1%) by 1 year to 5/129 teeth (3%) by 3 years. However, it may be indicated clinically much earlier than radiographically, by a specific pitch (or metallic sound) upon percussion.

15.8 Etiology of persistent apical periodontitis after endodontic treatment

While persistence of apical periodontitis after endodontic treatment may occur in the absence of microbial factors, due to foreign materials, cholesterol crystals, and true cysts (Penick 1961; Bhaskar 1966; Byström et al. 1987; Nair et al. 1990b, 1993, 1999; Selden 1999; Nair 2003a,b; Saunders 2008; Lin et al. 2009; Schulz et al. 2009; Barone et al. 2010; Lui et al. 2014; Siqueira et al. 2014; Bornstein et al. 2015), this is not a common occurrence (Sjögren et al. 1990). For the major part, persistent apical periodontitis is sustained by persistent or recurrent infection (Siqueira 2001; Friedman 2002a). The sites colonized by bacteria and the pathways of bacteria-host interactions may differ after nonsurgical and surgical treatment. Furthermore, the reason for nonhealing or delayed healing seen in some cases may be related to the presence of specific virulent microorganisms in these cases that exert significant impact on periapical tissues and elicit a pronounced host response.

15.8.1 Persistent infection after nonsurgical treatment

Microorganisms, mainly bacteria, sustain the infection process by colonizing different sites within or outside the affected tooth.


Extraradicular sites. Specific bacteria, particularly Actinomyces israelii and Propionibacterium propionicum, can colonize in the periapical tissues (Sundqvist and Reuterving 1980; Weir and Buck 1982; Martin and Harrison 1984; Nair and Shroder 1984; Happonen et al. 1985; Happonen 1986; Nishimura 1986; Haapasalo et al. 1987; O’Grady and Reade 1988; Sjögren et al. 1998; Iwu et al. 1990; Figueres and Douglas 1991; Wayman et al. 1992; Sakellarious 1996; Kalfa et al. 2001; Hirshberg et al. 2003; Siqueira 2003; Sundqvist and Figdor 2003; Figdor 2004; Ricucci and Siqueira 2008; Subramanian and Mickel 2009; Signoretti et al. 2011; Siqueira et al. 2014), after penetrating the host tissues during a long-term infection of the root canal system, or when inoculated periapically during treatment. Other bacterial species also have been implicated in extraradicular infection (Gatti et al. 2000; Sunde et al. 2000a,b, 2002, 2003; Tronstad and Sundt 2003). They can colonize the cementum on the root surface (Pitt Ford 1982; Nair 1987; Kiryu et al. 1994) and around the apical foramina (Tronstad et al. 1987, 1990a,b; Siqueira and Lopes 2001; Leonardo et al. 2002; Noiri et al. 2002; Tronstad and Sundt 2003; Ricucci et al. 2005; Vera et al. 2012; Wang et al. 2012; Siqueira et al. 2014), or in dentin debris inadvertently extruded during treatment (Yusuf 1982). Whether these bacteria can exclusively sustain infection is unclear, however, current knowledge suggests that the predominant cause of persistent apical periodontitis is root canal infection.
while exclusive extraradicular infection comprises a small percentage of cases (Friedman 2002a); (see also Chapter 6).


### 15.8.2 Persistent infection after apical surgery

Persistence of infection after apical surgery usually suggests that root canal bacteria are not effectively enclosed within the canal space by the root-end filling (Friedman 1991). Placement of a root-end filling is a challenging procedure and several pathways may remain that allow continued interaction of root canal bacteria with the host tissues, resulting in persistent or recurrent infection.

**Margins of the root-end filling.** Compromised placement, adaptation to the canal walls, and sealing ability of the filling material, can all compromise the seal of the root-end filling (Friedman 1991).

**Accessory canals or isthmuses.** Accessory foramina and, in specific teeth, isthmuses are frequently present in the apical portion of root canals. A root-end filling may not seal these pathways, particularly when it is placed without magnification and illumination aids (Hsu and Kim 1997; Carr and Bentkover 1998).

**Exposed dentinal tubules.** Apical resection is typically performed with a bevel, exposing dentinal tubules at the cut surface (Gilheany et al. 1994). A shallow root-end filling does not internally seal all the tubules. The exposed tubules provide a pathway for root canal bacteria to interact with the host tissues (Vertucci and Beatty 1986; Tidmarsh and Arrowsmith 1989; Gilheany et al. 1994).

**Vertical root defect, crack, or fracture.** Oral bacteria can colonize the crack or fracture line and sustain the infection even if a root-end filling effectively seals the root canal. Presence of a root crack or fracture should be ruled out before further treatment. Occasionally, there are dentinal defects that are not extensive enough to be diagnosed as fractures, but may adversely impact the prognosis (Tawil et al. 2015).

Because persistent infection after apical surgery is likely to be sustained by persistent root canal bacteria (Friedman 1991), the treatment of choice for its management is orthograde retreatment, perhaps with an MTA plug (Mente et al. 2015). When retreatment is not feasible, apical surgery should be repeated with an emphasis on effective sealing of the infected root canal.

### 15.9 Conclusions

The projected prognosis of treatment is a key consideration in selection of cases for endodontic treatment. Well-informed clinicians should project a specific prognosis for every tooth considered for treatment. As highlighted in this chapter, the chance of teeth with primary and persistent apical periodontitis to heal after appropriate endodontic treatment ranges from good to very good, depending on specific outcome predictors. Furthermore, the chance for functional retention of the tooth in the long term is excellent. Therefore, whenever patients consider it feasible and acceptable, nonsurgical or surgical endodontic treatment should be attempted before considering tooth extraction and replacement. This is certainly the most conservative and, frequently, the most economic manner in which to treat endodontic infections. Given that the lack of healing is primarily mediated by persistent infective process, more research is required to define microbial virulence factors that mediate the disease, as well as the microbial loads necessary to sustain clinically detectable disease. In addition, a better definition of the
acceptable follow-up periods should be determined to help the practitioner make treatment decisions on cases that do not respond to treatment with complete radiographic and clinical healing.

15.10 References


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