

Table S1. Summary of clinical (in vivo) studies.

| Author(s) & Year               | Study type | Total sample size | Intervention group | Sample size (per group) | Gender (F/M) | Age           | Duration                        | Main outcomes measured   |
|--------------------------------|------------|-------------------|--------------------|-------------------------|--------------|---------------|---------------------------------|--|
| Egli et al., 2017              | RCT        | 60 P              | DB                 | 30 P                    | Not stated   | Not stated    | 2Y                              | •Bond Failure<br>•Post-Treatment Changes   |
|                                |            |                   | IB                 | 30 P                    |              |               |                                 |  |
| Agarwal et al., 2017           | CT         | 25 P              | DB                 | Split mouth design      | Not stated   | Not stated    | -                               | • Accuracy   |
|                                |            |                   | IB                 |                         |              |               |                                 |  |
| Yildirim et al., 2018          | RCT        | 30 P              | DB                 | 15 P                    | 13/2         | 14.6 ± 2.4    | 0 M<br>1 M<br>2 M<br>6 M<br>End | • Chair-Time<br>• Overall-Time<br>• Plaque<br>• WSL<br>• Effectiveness<br>• Treatment-Time<br>• Bond-Failure |
|                                |            |                   | IB                 | 15 P                    | 10/5         | 16.7 ± 6.5    |                                 |  |
| Atilla et al., 2020            | RCT        | 51 P              | DB                 | 26 P                    | 12 / 14      | 14.73 ± 1.65  | 1.75 ± 0.45 Y                   | • WSL  |
|                                |            |                   | IB                 | 25 P                    | 12/13        | 15.42 ± 1.71  | 1.22 ± 0.31 Y                   |  |
| Ayyed et al., 2020             | CT         | 30 P              | DB                 | 15 P                    | Not stated   | 14-24         | -                               | • Bond-Failure   |
|                                |            |                   | IB                 | 15 P                    |              |               |                                 |  |
| Gelin et al., 2020             | RCT        | 61 P              | DB                 | 30 P                    | 23/7         | 16.0 ± 3.18   | 0 M<br>1 M<br>6 M<br>12 M       | • Bond-Failure<br>• Plaque<br>• Stability  |
|                                |            |                   | CAD/CAM            | 31 P                    | 20/11        | 18.0 ± 5.14   |                                 |  |
| Czolgosz et al., 2021          | RCT        | 27 P              | DB                 | Split mouth design      | 15/12        | 16.9 ± 8.6    | -                               | • Chair-Time<br>• Overall-Time<br>• Immediate Bond-Failure<br>• Cost   |
|                                |            |                   | CAD/CAM            |                         |              |               |                                 |  |
| Hegele et al., 2021            | CT         | 38 P              | DB                 | 20 P                    | 13/7         | 12.4 -22.2    | -                               | • Effectiveness<br>• Treatment-Time<br>• Bond- Failure   |
|                                |            |                   | CAD/CAM            | 18 P                    | 10/8         | 13.1-18.5     |                                 |  |
| Shim et al., 2022              | RCT        | 46 P              | DB                 | 14 P                    | 9/5          | 15.2          | 3 M<br>6 M                      | • Effectiveness<br>• Bond-Failure  |
|                                |            |                   | IB                 | 16 P                    | 12/4         | 15.8          |                                 |  |
|                                |            |                   | CAD/CAM            | 16 P                    | 7/9          | 16.5          |                                 |  |
| Cornelis et al., 2022          | RCT        | 52 P              | DB                 | 26 P                    | Not Stated   | 19.9 ± 6.4    | 5 Y                             | • Bond Failure<br>• Post-Treatment Changes   |
|                                |            |                   | IB                 | 26 P                    |              | 17.5 ± 4.0    |                                 |  |
| Wang et al., 2022              | CT         | 40 P              | DB                 | 20 P                    | 15/5         | 18.75 ± 6.50  | -                               | • Effectiveness<br>• Treatment-Time  |
|                                |            |                   | CAD/CAM            | 20 P                    | 17/3         | 21.35 ± 10.99 |                                 |  |
| Gera et al., 2023              | RCT        | 181 P             | DB                 | 91 P                    | 52/39        | 12.1-25.8     | 0 M<br>1 M<br>3 M<br>6 M        | • Stability<br>• Bond-Failure  |
|                                |            |                   | CAD/CAM            | 90 P                    | 44/46        | 12.1-25.8     |                                 |  |
| Kono et al., 2024              | RCT        | 124 P             | DB                 | 66 P                    | 52/14        | 23.17 ± 8.83  | 1-3 Y                           | • Chair-Time<br>• Treatment- Time<br>• Bond Failure<br>• Effectiveness<br>• Plaque                           |
|                                |            |                   | IB                 | 58 P                    | 38/20        | 20.63 ± 5.69  |                                 |  |
| Tran et al., 2024              | RCT        | 43 P              | DB                 | 14 P                    | 9/5          | 13.6-15.6     | 0 M                             | • Bond-Failure<br>• Stability  |
|                                |            |                   | IB                 | 15 P                    | 12/3         | 13.7-17.7     | 6 M                             |  |
|                                |            |                   | CAD/CAM            | 14 P                    | 6/8          | 15.2-19.9     | 1 Y<br>2 Y                      |  |
| Hoekstra-van Hout et al., 2024 | RCT        | 35 P              | DB                 | Spilt mouth design      | 20/15        | 14 ± 5 years  | 6 M                             | • Accuracy<br>• Bond- Failure  |
|                                |            |                   | IB                 |                         |              |               |                                 |  |
| Pullisaar et al., 2024         | RCT        | 153 P             | DB                 | 72                      | Not stated   | Not specified | 2 Y                             | • Bond-Failure<br>• Post treatment Changes<br>• Cost   |
|                                |            |                   | CAD/CAM            | 81                      |              |               |                                 |  |

Note: CAD/CAM: Computer-Aided Design/Computer-Aided Manufacturing; CT: Clinical Trial; DB: Direct Bonding; F: Female; IB: Indirect Bonding; M: Male; Mo: Month; P: Patient; RCT: Randomized Controlled Trial; WSL: White-Spot Lesions; Y: Year.

\* Values are presented as single number, median ± standard deviation (SD) or range (minimum–maximum), as appropriate.

Table S2. Summary of study design, sample allocation, follow-up duration, techniques compared, and bond failure incidence.

| Study                          | Design             | Total sample size | Duration                     | Techniques compared | Sample size (per group) | Bond failure rate                    |            | Notes   |
|--------------------------------|--------------------|-------------------|------------------------------|---------------------|-------------------------|--------------------------------------|------------|---|
| Egli et al., 2017              | RCT                | 60 P              | 2 Y                          | DB                  | 30 P                    | 11 of 30 (37%)                       |            | •No Diff<br>•Md retainers<br>• <i>p</i> -value = 0.64                                       |
|                                |                    |                   |                              | IB                  | 30 P                    | 13 of 30 (43%)                       |            |   |
| Cornelis et al., 2022          | RCT                | 52 P              | 5 Y                          | DB                  | 26 P                    | 14 of 26 (54%)                       |            | •No Diff<br>•Md Retainers<br>• <i>p</i> -value = 0.91                                       |
|                                |                    |                   |                              | IB                  | 26 P                    | 14 of 26 (54%)                       |            |   |
| Yildirim et al., 2018          | RCT                | 30 P              | Whole treatment time         | DB                  | 15 P                    | 7.14%                                |            | •No Diff<br>•Inclusion of first & second molar<br>• <i>p</i> -value = 0.32                  |
|                                |                    |                   |                              | IB                  | 15 P                    | 10.71%                               |            |   |
| Czolgosz et al., 2021          | RCT                | 27 P              | Immediate                    | DB                  | Split mouth design      | 0%                                   |            | •CAD/CAM more failure<br>• <i>p</i> -value = 0.0001   |
|                                |                    |                   |                              | CAD/CAM             |                         | 5,1%                                 |            |   |
| Ayyed et al., 2020             | CT                 | 30 P              | During levelling & alignment | DB                  | 15 P<br>294 Br          | 39/294                               |            | •No Diff  |
|                                |                    |                   |                              | IB                  | 15 P<br>290 Br          | 47/290                               |            |   |
| Gelin et al., 2020             | RCT                | 61 P              | 12 Mo                        | DB                  | 30 P                    | 0.14 ± 0.35                          |            | •No Diff<br>•Md Retainer<br>• <i>p</i> -value = 0.77  |
|                                |                    |                   |                              | CAD/CAM             | 31 P                    | 0.11 ± 0.32                          |            |   |
| Hegele et al., 2021            | CT                 | 38 P              | Whole treatment time         | DB                  | 20 P                    | 1.0 [0–3]                            |            | •CAD/CAM more failure<br>• <i>p</i> -value = 0.035  |
|                                |                    |                   |                              | CAD/CAM             | 18 P                    | 2.0 [0–19]                           |            |   |
| Gera et al., 2023              | RCT                | 178 P             | 6 Mo                         | DB                  | 90 P                    | Mx: 20 /90 (22%)<br>Md: 26 /90 (29%) |            | •No Diff<br>•Mx & Md Retainer<br>•Mx: <i>p</i> -value=0.99<br>•Md: <i>p</i> -value=0.80     |
|                                |                    |                   |                              | CAD/CAM             | 88 P                    | Mx: 19 /88 (22%)<br>Md: 26 /88 (30%) |            |   |
| Shim et al., 2022              | RCT                | 46 P              | 6 Mo                         | DB                  | 14 P                    | 2/25 (8%)                            |            | •IB most failure<br>•DB least failure<br>•Md Retainer<br>• <i>p</i> -value= 0.045           |
|                                |                    |                   |                              | IB                  | 16 P                    | 7/30 (23.3%)                         |            |   |
|                                |                    |                   |                              | CAD/CAM             | 16 P                    | 4/20 (20%)                           |            |   |
| Pullisaar et al., 2024         | RCT                | 153 P             | 2 Y                          | DB                  | 72 P                    | Mx:38 %<br>Md: 40%                   |            | •No Diff<br>•Mx & Md Retainer<br>•Mx: <i>p</i> -value = 0.46<br>•Md: <i>p</i> -value = 0.94 |
|                                |                    |                   |                              | CAD/ CAM            | 81 P                    | Mx: 34%<br>Md: 42%                   |            |   |
| Kono et al., 2024              | RCT                | 124 P             | Whole treatment time         | DB                  | 66 P                    | 7.75%                                |            | •IB more failure<br>• <i>p</i> -value < 0.001   |
|                                |                    |                   |                              | IB                  | 58 P                    | 20.10%                               |            |   |
| Tran et al., 2024              | RCT                | 43 P              | 2 Y                          | DB                  | 14 P                    | 4/14 (28.6%)                         |            | •No Diff<br>•Md Retainer<br>• <i>p</i> -value = 0.14  |
|                                |                    |                   |                              | IB                  | 15 P                    | 5/15 (33.3%)                         |            |   |
|                                |                    |                   |                              | CAD/CAM             | 14 P                    | 3/14 (21.4%)                         |            |   |
| Hoekstra-van Hout et al., 2024 | RCT                | 35 P              | 6 Mo                         | DB                  | Split mouth design      | Immediate: 0 %                       | Late: 2.5% | •IB more failure<br>• <i>p</i> -value = 0.008   |
|                                |                    |                   |                              | IB                  | Split mouth design      | Immediate: 3.9%                      | Late: 5.4% |   |
| Demirovic et al., 2018         | In-vivo & In-vitro | 30 P              | 6 Mo                         | DB                  | 15 P                    | 1.4%                                 |            | •No Diff<br>• <i>p</i> -value <0.05   |
|                                |                    |                   |                              | IB                  | 15 P                    | 1.7%                                 |            |   |

Note: Br: Bracket; CAD/CAM: Computer-Aided Design/Computer-Aided Manufacturing; CT: Controlled Trial; DB: Direct Bonding; Diff: Difference; IB: Indirect Bonding; Md: Mandibular; Mo: Month; Mx: Maxillary; P: Patient; RCT: Randomized Controlled Trial; Y: Year.

\*Values are reported as number or ratio (e.g., n/N), mean ± standard deviation, median [range], or percentage of bond failures within each group, as appropriate.

Table S3. Mechanical and adhesive properties.

| Study  | Total sample size | Techniques compared | Sample Size (per group) | Microleakage | SBS            | ARI       | Precision Fit (mm) | Notes   |
|--|-------------------|---------------------|-------------------------|--------------|----------------|-----------|--------------------|---|
| Shaheen et al., 2016   | 60 PM             | DB                  | 30 PM                   | 0.0988 mm    | -              | -         | -                  | •No Diff<br>•p-value<0.05   |
|  |                   | IB                  | 30 PM                   | 0.0916 mm    | -              | -         | -                  |   |
| Demirovic et al., 2018   | 60 PM             | DB                  | 30 PM                   | -            | 7.48±1.61 MPa  | 1.2 ± 0.6 | -                  | •No Diff  |
|  |                   | IB                  | 30 PM                   | -            | 7.82±1.61 MPa  | 1.3 ± 0.5 | -                  |   |
| Sohail et al., 2024  | 360 Md Teeth      | DB                  | 120 Teeth Braided SS    | -            | 112.75±25.83 N | 29.18     | 0.204±0.065        | •CAD/CAM better<br>•Md retainer<br>•p-value (SBS)<0.001<br>•p-value (ARI)=0.509<br>•p-value (FIT)=0.009 |
|  |                   |                     | 120 teeth Co-axial      | -            | 83±15.93 N     | 28.43     |                    |   |
|  |                   | CAD/CAM             | 120 Teeth               | -            | 189±55.10 N    | 33.90     | 0.038±0.022        |   |
| Note: ARI: Adhesive Remnant Index; CAD/CAM: Computer-Aided Design/Computer-Aided Manufacturing; DB: Direct Bonding; Diff: Difference; IB: Indirect Bonding; Md: Mandibular; mm: Millimeter; MPa: Megapascal; N: Newton, PM: Premolar; SBS: Shear-Bond Strength; SS: Stainless steel.<br>*Values are reported either as single means or as mean ± standard deviation, where applicable. |                   |                     |                         |              |                |           |                    |   |

Table S4. Summary of study design, total and per-group sample sizes, techniques compared, and measured deviations from ideal angulation and position.

| Study                          | Design    | Total sample size    | Techniques compared | Sample size (per group) | Angulation deviations from Ideal (degree) | Mesio-Distal deviations from Ideal (mm) | Height deviations from Ideal (mm) | Notes   |
|--------------------------------|-----------|----------------------|---------------------|-------------------------|---|---|-----------------------------------|---|
| Kalra et al., 2018             | In -Vitro | 13 Models            | DB                  | 6 Sets                  | 2.884                                     | 0.284                                   | 0.431                             | •No Diff<br>•p-value: Angulation=0.475<br>Mesiodistal=0.221<br>Height=0.430     |
|                                |           |                      | IB                  | 6 Sets                  | 3.099                                     | 0.252                                   | 0.395                             |   |
| Oliveira et al., 2019          | In-Vitro  | 560 Teeth<br>1654 Br | DB                  | 827 Br                  | 3.18                                      | 0.33                                    | 0.58                              | •IB better<br>•p-value: Angulation=0.004<br>Mesiodistal=0.004<br>Height < 0.001 |
|                                |           |                      | IB                  | 827 Br                  | 2.89                                      | 0.24                                    | 0.49                              |   |
| Agarwal et al., 2017           | CT        | 25 P                 | DB                  | Split mouth design      | 1.78 ±0.54                                | 0.57 ±0.14                              | 0.53 ±0.13                        | •IB better<br>•p-value <0.0001 except angulation of Canine: p-value=0.0002      |
|                                |           |                      | IB                  | Split mouth design      | 0.80 ±0.38                                | 0.20 ±0.18                              | 0.26 ±0.19                        |   |
| Hoekstra-van Hout et al., 2024 | RCT       | 35 P                 | DB                  | Split mouth design      | 8.24 ±5.15                                | 0.73 ± 0.46                             |                                   | •IB Better<br>•p-value: angulation<0.001<br>translation=0.017                   |
|                                |           |                      | IB                  | Split Mouth design      | 3.40 ±2.15                                | 0.38 ± 0.27                             |                                   |   |

Note: Br: Bracket; CT: Controlled Trial; DB: Direct Bonding; Diff: Difference; IB: Indirect Bonding; mm: Millimeter; P: Patient; RCT: Randomized Controlled Trial.

\* Values are reported either as single means or as mean ± standard deviation, where applicable.

Table S5. Summary of study design, total and per-group sample sizes, techniques compared, chair-time (min), overall time (min), and treatment duration (months).

| Study   | Design | Sample size | Techniques compared | Sample size per group | Chair-time (minute) | Overall-time (minute) | Treatment time (months) | Notes   |
|---|--------|-------------|---------------------|-----------------------|---------------------|-----------------------|-------------------------|---|
| Yildirim et al., 2018   | RCT    | 30 P        | DB                  | 15 P                  | 53.02 ± 4.72        | 53.02 ± 4.72          | 12.0 ± 3.1              | •Chair-Time: IB better<br>p-value <0.001<br>•Treatment time: No Diff<br>p-value=0.55    |
|   |        |             | IB                  | 15 P                  | 26.51 ± 3.33        | 72.05 ± 5.2           | 11.4 ± 2.4              |   |
| Czolgosz et al., 2021   | RCT    | 27 P        | DB                  | Split mouth design    | *16.47 ± 5.36       | *16.47 ± 5.36         | -                       | *Per half mouth<br>•Chair-Time: IB better<br>•Total time: DB better<br>•p-value < 0.001 |
|   |        |             | CAD/CAM             | Split mouth design    | 12.52 ±5.32         | 28.14 ± 8.49          | -                       |   |
| Kono et al., 2024   | RCT    | 124 P       | DB                  | 66 P                  | 58.52 ± 25.24       | -                     | 34.27 ±8.87             | •IB better<br>•p-value:<br>Chair-Time < 0.001<br>Treatment-Time < 0.01                  |
|   |        |             | IB                  | 58 P                  | 35.91 ± 15.51       | -                     | 30.51 ±7.27             |   |
| Hegele et al., 2021   | CT     | 38 P        | DB                  | 20 P                  | -                   | -                     | 16.8                    | •No Diff<br>•p-value = 0.654  |
|   |        |             | CAD/CAM             | 18 P                  | -                   | -                     | 16.7                    |   |
| Wang et al., 2022   | CT     | 40 P        | DB                  | 20 P                  | -                   | -                     | 21.20 ±7.14             | •CAD/CAM better<br>•p-value=0.04  |
|   |        |             | CAD/CAM             | 20 P                  | -                   | -                     | 17.17 ±4.16             |   |
| Note: CAD/CAM: Computer-Aided Design/Computer-Aided Manufacturing, CT: Controlled Trial, DB: Direct Bonding, Diff: Difference, IB: Indirect Bonding, P: Patient, RCT: Randomized Controlled Trial.<br>**Values are reported either as single means or as mean ± standard deviation, where applicable. |        |             |                     |                       |                     |                       |                         |   |

Table S6. Summary of study design, sample size, techniques compared, duration (months), plaque index, WSL index, and PCR (%).

| Study                 | Design | Sample size | Techniques compared | Duration | Plaque index  | WSL index        | PCR: (%)      | Notes   |
|-----------------------|--------|-------------|---------------------|----------|---------------|------------------|---------------|---|
| Yildirim et al., 2018 | RCT    | 30 P        | DB                  | 0M       | 3.33 [6.67]   | 0 [0.16]         | -             | <ul style="list-style-type: none"> <li>•No Diff</li> <li>•Plaque index: <math>p</math>-value = 0.02 (T4 only)</li> <li>•WSL: <math>p</math>-value &gt;0.05</li> </ul>                       |
|                       |        |             |                     | 1M       | 16.67 [22.67] |                  |               |   |
|                       |        |             |                     | 2M       | 10 [20]       |                  |               |   |
|                       |        |             |                     | 6M       | 5 [11.67]     |                  |               |   |
|                       |        |             |                     | End      | 5 [10]        | 0 [0.16]         |               |   |
|                       |        |             | IB                  | 0M       | 1.67 [6.67]   | 0 [0.08]         |               |   |
|                       |        |             |                     | 1M       | 11.67 [31.67] | -                |               |   |
|                       |        |             |                     | 2M       | 15 [26.67]    | -                |               |   |
|                       |        |             |                     | 6M       | 13.33 [26.67] | -                |               |   |
|                       |        |             |                     | End      | 11.67 [16.66] | 0 [0.08]         |               |   |
| Atilla et al., 2020   | RCT    | 51 P        | DB                  | 0M       | -             | scored per tooth | -             | <ul style="list-style-type: none"> <li>•IB better</li> <li>•<math>p</math>-value &lt; 0.05</li> <li>•QLF Method</li> </ul>  |
|                       |        |             | IB                  | End      |               |                  |               |   |
| Gelin et al., 2020    | RCT    | 61 P        | DB                  | 0M       | 1.17 ± 0.65   | -                | -             | <ul style="list-style-type: none"> <li>•No Diff</li> <li>•<math>p</math>-value &gt; 0.05</li> <li>•Gingival index CAD/CAM higher, (<math>p</math> = 0.039)</li> <li>•Md Retainer</li> </ul> |
|                       |        |             |                     | 1M       | 0.77 ± 0.57   |                  |               |   |
|                       |        |             |                     | 6M       | 1.16 ± 0.62   |                  |               |   |
|                       |        |             |                     | 12M      | 0.95 ± 0.49   |                  |               |   |
|                       |        |             | CAD/CAM             | 0M       | 1.07 ± 0.74   |                  |               |   |
|                       |        |             |                     | 1M       | 0.73 ± 0.67   |                  |               |   |
|                       |        |             |                     | 6M       | 0.92 ± 0.65   |                  |               |   |
|                       |        |             |                     | 12M      | 1.05 ± 0.62   |                  |               |   |
| Kono et al., 2024     | RCT    | 124 P       | DB                  | 0M       | -             |                  | 14.79±3.02    | <ul style="list-style-type: none"> <li>•No Diff</li> <li>•<math>p</math>-value &gt; 0.05</li> </ul>   |
|                       |        |             |                     | End      | -             |                  | 29.38±16.13   |   |
|                       |        |             | IB                  | 0M       | -             |                  | 14.55 ± 4.23  |   |
|                       |        |             |                     | End      | -             |                  | 29.08 ± 16.84 |   |

Note: CAD/CAM: Computer-Aided Design/Computer-Aided Manufacturing; DB: Direct Bonding; Diff: Difference; IB: Indirect Bonding; M: Month; Md: Mandibular; P: Patient; PCR: Plaque Control Record; QLF: Quantitative Light-Induced Fluorescence; RCT: Randomized Controlled Trial; WSL: White-Spot-Lesion.  
 \*Values are presented as mean ± standard deviation (SD) or median [interquartile range, IQR], as appropriate.

Table S7. Overview of studies: sample size, techniques compared, follow-up duration, and outcome parameters.

| Study                  | Design | Total sample size | Techniques compared         | Duration             | Parameters measured   | Notes   |
|------------------------|--------|-------------------|-----------------------------|----------------------|---|---|
| Egli et al., 2017      | RCT    | 60 P              | DB vs. IB                   | 24 Mo                | -ICW<br>-IPD  | •No Diff<br>•Md Retainer  |
| Yildirim et al., 2018  | RCT    | 30 P              | DB vs. IB                   | Whole treatment time | -OGS/ABO scores   | •Total Score IB better:<br>$\Delta = -3.999$<br>(95% CI: -6.000 to -0.005)<br>$p$ -value = 0.03<br>•Marginal ridge IB better:                       |
| Gelin et al., 2020     | RCT    | 62 P              | DB vs.<br>CAD-CAM           | 12 M                 | -ICW<br>-IPD<br>-IIL<br>-Cephalometric                                      | •No Diff<br>•Md Retainer  |
| Hegele et al., 2021    | CT     | 38 P              | DB vs.<br>CAD/CAM           | Whole treatment time | -ABO scores<br>-ICW<br>-IPD<br>-LII<br>-Cephalometric<br>-wire bends/Change | •CAD/CAM slightly better<br>•Wire changes more in CAD/CAM,<br>$p$ -value < 0.001<br>•Lower incisors in DB more protruded,<br>$p$ -value < 0.05      |
| Shim et al., 2022      | RCT    | 46 P              | DB vs.<br>IB vs.<br>CAD/CAM | 6 M                  | -ICW<br>-LII  | •Md Retainer<br>•CAD/CAM best<br>•ICW: CAD/CAM better than DB (3M & 6M):<br>$p$ -value < 0.001 & < 0.05<br>•LII: CAD/CAM better than IB (3M):       |
| Cornelis et al., 2022  | RCT    | 52 P              | DB vs. IB                   | 5 Y                  | -ICW<br>-IPD<br>-Torque /Rotation   | •Md Retainer<br>•ICW, IPD: No Diff<br>•Changes in torque of mandibular incisors and canines in DB (6/26P)   |
| Wang et al., 2022      | CT     | 40 P              | DB vs.<br>CAD/CAM           | Whole treatment time | -ABO Scores (Cephalometric)   | •No Diff<br>• $p$ -value > 0.05   |
| Gera et al., 2023      | RCT    | 181 P             | DB vs.<br>CAD/CAM           | 6 M                  | -IIL<br>-Arch dimension   | •No Diff<br>• $p$ -value > 0.05<br>•Mx/Md Retainer  |
| Tran et al., 2024      | RCT    | 43 P              | DB vs.<br>IB vs.<br>CAD/CAM | 24 M                 | -ICW<br>-LII  | •Md Retainer<br>•ICW: CAD/CAM better than DB<br>$p$ -Value < 0.05<br>•ICW: CAD/CAM better than IB (6M),<br>$p$ -Value = 0.038<br>•LII: CAD/CAM best |
| Pullisaar et al., 2024 | RCT    | 153 P             | DB vs. CAD/CAM              | 24 M                 | -IIL<br>-Arch dimension   | •No Diff<br>• $p$ -value > 0.05<br>•Mx/Md Retainer  |
| Kono et al., 2024      | RCT    | 124 P             | DB vs. IB                   | -                    | -ABO Occlusal index (CR-Eval)   | •IB better<br>•CR-Eval:<br>DB: 53.24 ± 7.74<br>IB: 47.31 ± 8.17   |

Table S8.

| Study  | Design | Sample size | Techniques compared | Total cost                 | Notes                   |
|--|--------|-------------|---------------------|----------------------------|-------------------------|
| Czoglosz et al., 2021  | RCT    | 27          | DB                  | Per half-mouth: €112       | •CAD/CAM more expensive |
|  |        |             | CAD/CAM             | Per half-mouth: €128-€132. |                         |
| Pulisaar et al.,2024   | RCT    | 152         | DB                  | Per Patient: €327          | •DB 10% more expensive  |
|  |        |             | CAD/CAM             | Per patient: €290          |                         |
| Note: RCT: Randomized controlled trial; DB: Direct Bonding; CAD/CAM: Computer-Aided Design/Computer-Aided Manufacturing. |        |             |                     |                            |                         |