

## Online Supplementary Material

### Economic Effects of Fixed-Dose Versus Loose-Dose Combination Therapy for Type 2 Diabetes Patients

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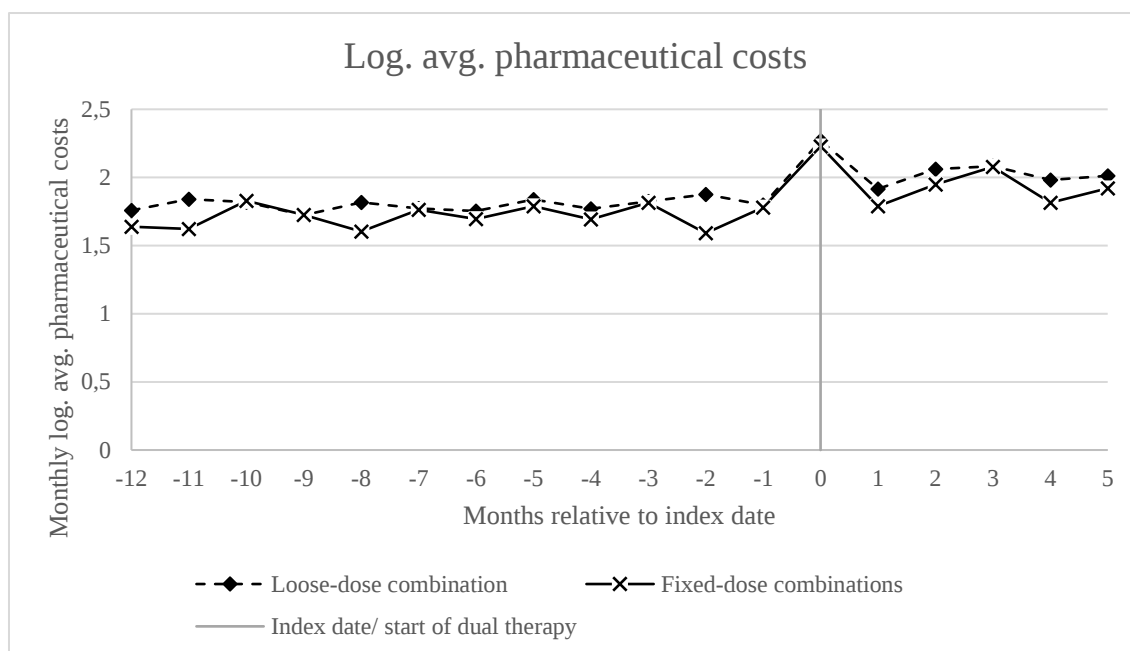
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**Conflicts of interest:** The authors declare no conflicts of interest.

#### Supplementary Table S1: ICD-10 codes of disease-related morbidities

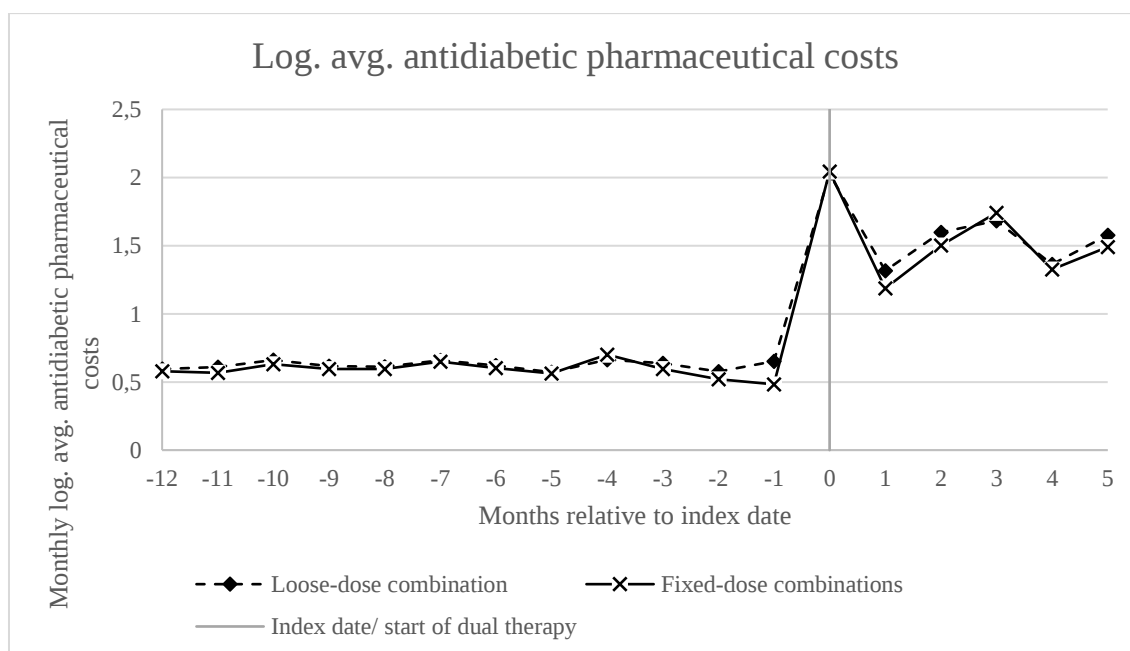
| Diagnoses                                        | Codes (ICD-10)                                                                                                                                     |
|--------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|
| <i>Microangiopathic complications</i>            |                                                                                                                                                    |
| Eye complications                                | H280, H54, H431, H358, H350, H352, H360, E113, E143                                                                                                |
| Renal failure                                    | E112, E112, N049, N059, N083, N17, N26, N289, T824, T861                                                                                           |
| Diabetic foot syndrome/<br>Peripheral neuropathy | E114, E115, Z894, Z895, Z896, Z897, Z898, Z899, R02, L97, L984, G590, G632, G990, G730, G62, G629, G63, M142, M146, I792, I739, I702, E1174, E1175 |
| <i>Macroangiopathic complications</i>            |                                                                                                                                                    |
| Angina pectoris                                  | I20                                                                                                                                                |
| Myocardial infarction                            | I21-I23                                                                                                                                            |
| Ischemic heart disease                           | I24, I25                                                                                                                                           |
| Cerebrovascular disease                          | I63-I66, I69                                                                                                                                       |

Based on Ferber L von, Köster I, Hauner H. Kosten der antihyperglykämischen Behandlung des Diabetes mellitus: Einfluss von Lebensalter, Therapieart und Komplikationsstatus: Ergebnisse der KoDiM-Studie 2001. Med Klin (Munich). 2006; 101(5):384–93.

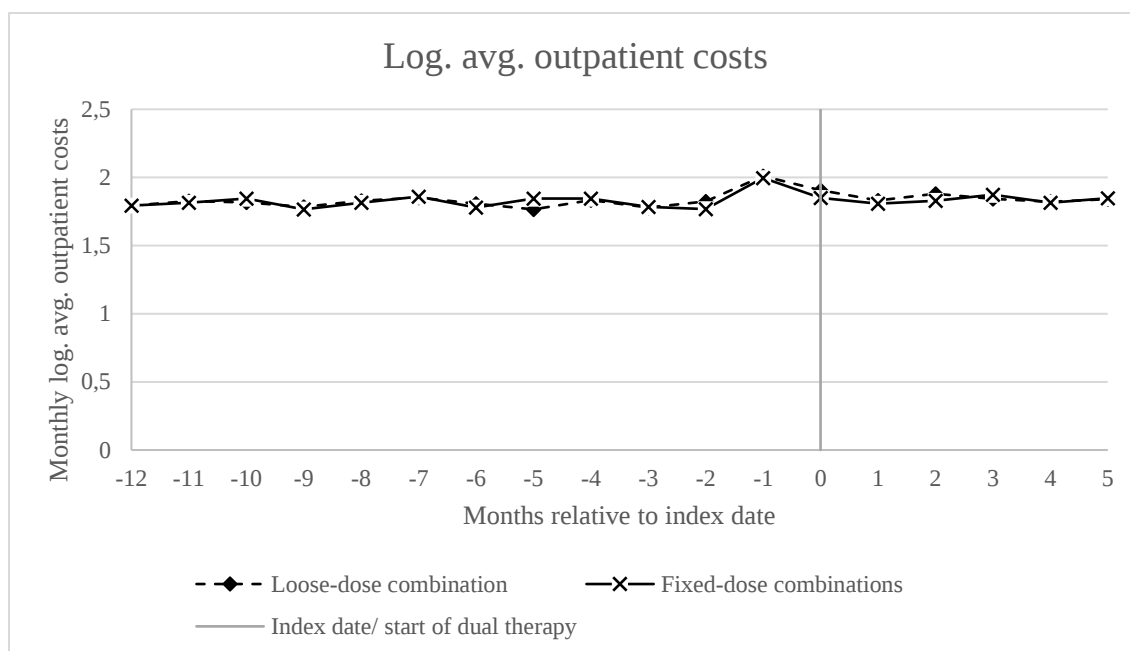


### Supplementary Fig. F1: Common trends graphs

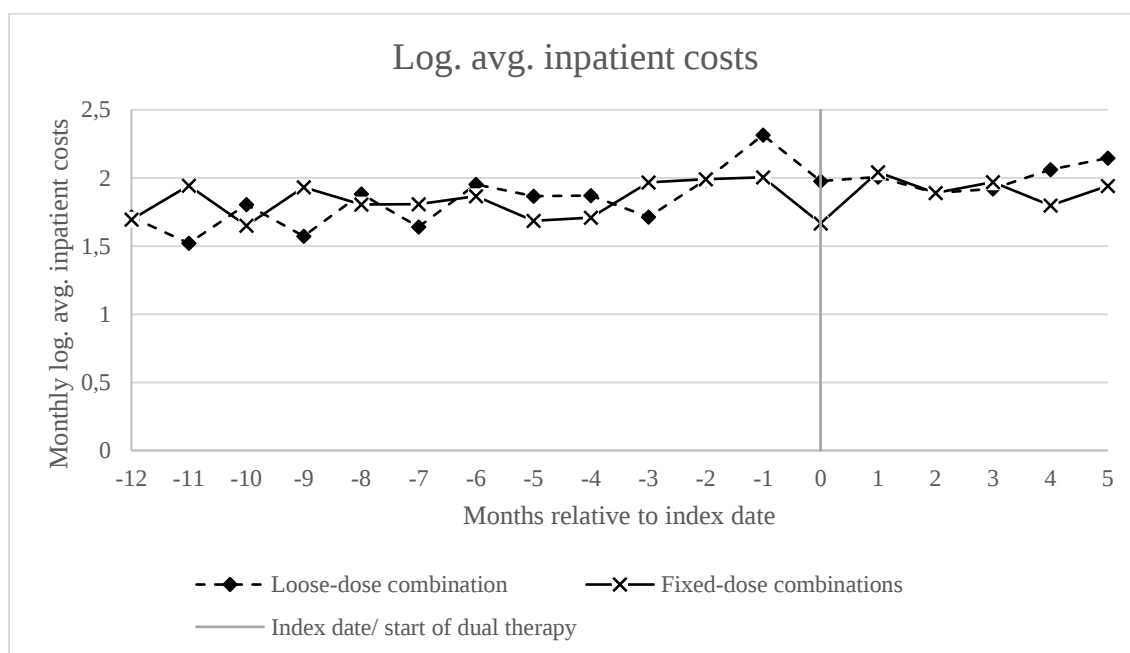
The index date was defined as the first prescription fill of the dual therapy. The vertical line displays the first value of the post-index period (i.e., the index date belongs to month zero)



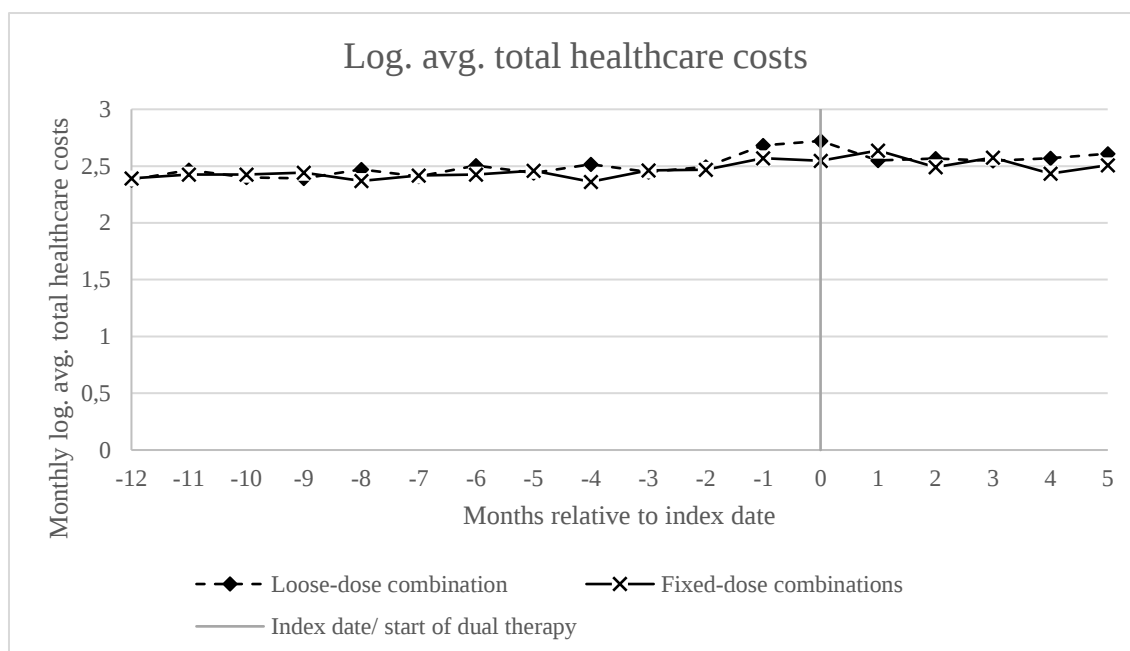
### Supplementary Fig. F1: Common trends graphs (continued)



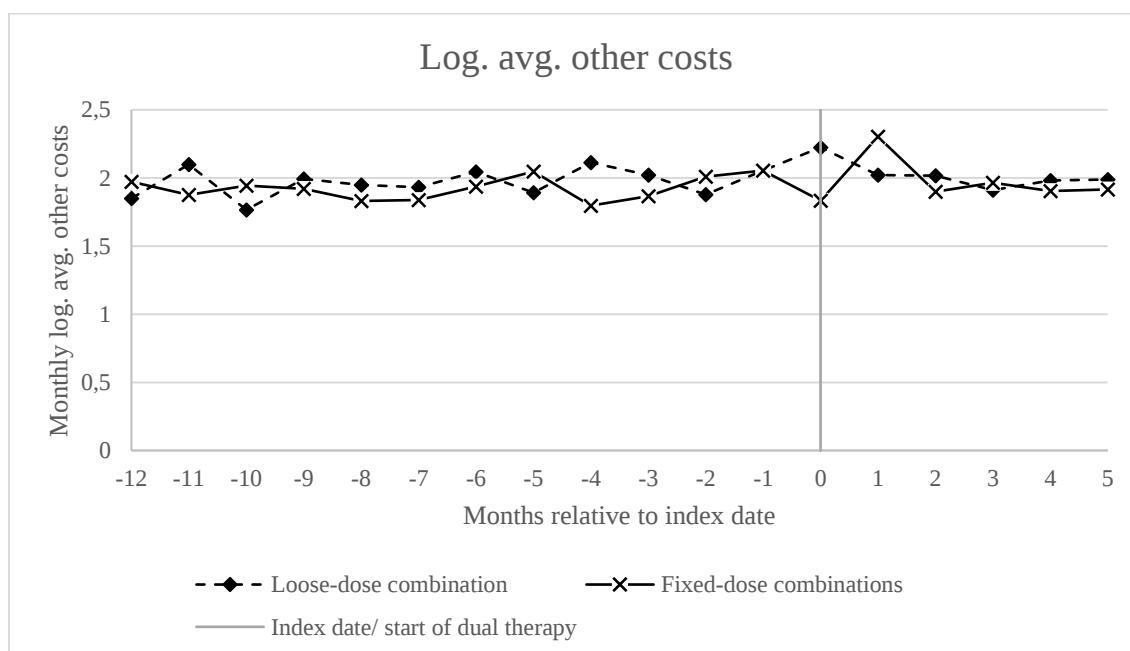
**Supplementary Fig. F1: Common trend graphs (continued)**



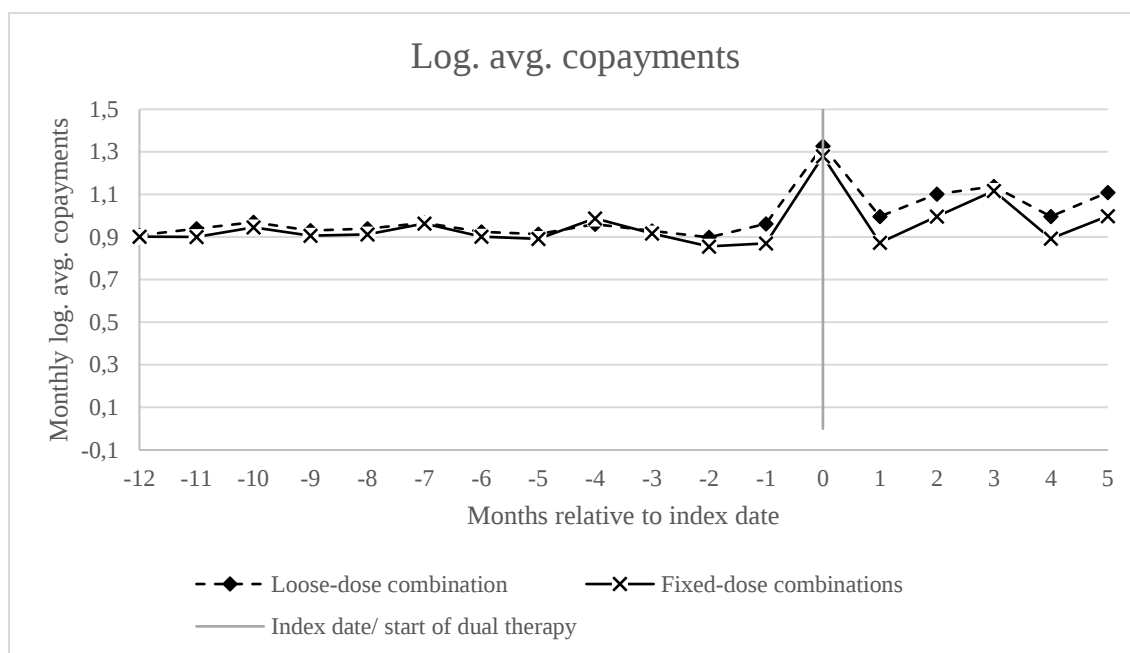
**Supplementary Fig. F1: Common trend graphs (continued)**



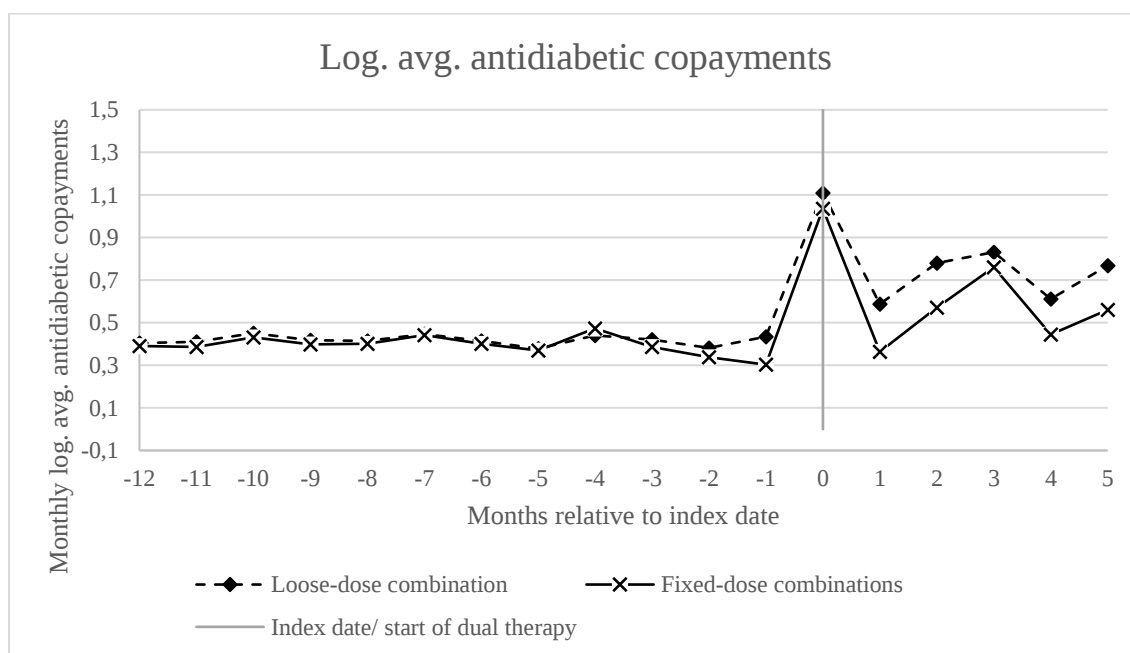
**Supplementary Fig. F1: Common trend graphs (continued)**



**Supplementary Fig. F1: Common trend graphs (continued)**



**Supplementary Fig. F1: Common trend graphs (continued)**



**Supplementary Fig. F1: Common trend graphs (continued)**

**Supplementary Table S2: Results of placebo-in-time Difference-in-differences regression**

| <b>Cost outcomes (log.)</b>               | <b>Average treatment effect on the treated</b> | <b>Standard error</b> |
|-------------------------------------------|------------------------------------------------|-----------------------|
| <i>Payer</i>                              |                                                |                       |
| Pharmaceutical costs                      | -0,06                                          | 0.05                  |
| Of these, due to type 2 diabetes mellitus | -0.06*                                         | 0.03                  |
| Outpatient costs                          | -0,01                                          | 0.04                  |
| Inpatient costs                           | -0.25**                                        | 0.12                  |
| Other costs                               | -0.14                                          | 0.14                  |
| Total costs                               | -0.06                                          | 0.04                  |
| <i>Patients</i>                           |                                                |                       |
| Copayments                                | -0.05*                                         | 0.03                  |
| Of these, due to type 2 diabetes mellitus | -0.06**                                        | 0.03                  |
| <i>Controls</i>                           | <i>yes</i>                                     |                       |

\* p<0.10, \*\* p<0.05, \*\*\*p<0.01

**Supplementary Table S3: Absolute outcome means**

| Cost outcomes <sup>a</sup> | Period           | FDC     | LDC     |
|----------------------------|------------------|---------|---------|
|                            |                  | Mean    | Mean    |
| <i>Payer</i>               |                  |         |         |
| Pharmaceutical costs       | Pre-index period | 618.94  | 670.20  |
|                            | Year 1           | 1016.13 | 1123.17 |
|                            | Year 2           | 1022.67 | 1112.63 |
| Of these, due to T2D       | Pre-index period | 42.32   | 45.35   |
|                            | Year 1           | 455.40  | 475.43  |
|                            | Year 2           | 375.82  | 397.78  |
| Outpatient costs           | Pre-index period | 792.49  | 801.80  |
|                            | Year 1           | 790.16  | 860.79  |
|                            | Year 2           | 768.95  | 818.59  |
| Inpatient costs            | Pre-index period | 781.48  | 831.01  |
|                            | Year 1           | 738.73  | 1146.37 |
|                            | Year 2           | 895.69  | 1174.60 |
| Other costs <sup>b</sup>   | Pre-index period | 1023.36 | 1076.78 |
|                            | Year 1           | 1285.21 | 1377.01 |
|                            | Year 2           | 1432.82 | 1607.65 |
| Total costs                | Pre-index period | 3216.27 | 3379.79 |
|                            | Year 1           | 3830.23 | 4507.34 |
|                            | Year 2           | 4120.13 | 4713.47 |
| <i>Patients</i>            |                  |         |         |
| Copayments                 | Pre-index period | 105.71  | 111.27  |
|                            | Year 1           | 114.53  | 140.05  |
|                            | Year 2           | 95.46   | 120.98  |
| Of these, due to T2D       | Pre-index period | 21.48   | 22.99   |
|                            | Year 1           | 40.25   | 60.38   |
|                            | Year 2           | 31.00   | 49.59   |
| <i>Observations</i>        |                  | 2389    |         |

FDC: Fixed-dose combination, LDC: Loose-dose combination, T2D: Type 2 diabetes mellitus

<sup>a</sup>All costs were winsorized at 99<sup>th</sup> percentiles

<sup>b</sup>Other costs as part of total costs include, for example, aids and appliances