NUMERICAL APPENDIX: EXAMPLE

In Table 1 we show an exemplar population in which 20% of the population is exposed to a negative exposure (say, smoking); the remainder is unexposed. We assume a fixed follow-up period, and no confounding, selection bias, or missing data. We assume an effective smoking cessation intervention exists and has no side effects.

The risk of the outcome is 10% among the exposed, and 5% among the unexposed. Total population risk can be calculated as a simple weighted average of the exposed and unexposed subpopulations, at 6%. An always/never exposure risk difference (a population (or sample) average causal effect) is calculated simply as 10% - 5% = 5%.

If we were to remove all exposure from this population (Table 2), then the entire population of 2000 would be exposed to the background risk of the outcome of 5%; the population attributable risk difference would be the observed total population risk (from above, 6%) minus that background risk experienced by the now-totally unexposed population (5%), for an estimate of 1%.

If we were to remove 25% of the exposure from this population, then the expected resulting population is shown in Table 3, with 300 exposed individuals instead of 400; the 100 newly-unexposed individuals would face a 5% risk of the outcome rather than a 10% risk, and the total population risk in this population would be 5.75%. One generalized intervention risk difference is therefore 6.00% - 5.75% = 0.25%.

Other generalized intervention risk differences could be calculated for removing different amounts of the exposure.

Now suppose that the population under study comprises half low income individuals, and half high income individuals. We assume that overall death rates are higher among low-income individuals than among high-income individuals (0.085 vs. 0.035), and also that the effect of the exposure is larger among low income individuals than among high income individuals (risk difference 0.081 vs. 0.019 after rounding). This is shown in Table 4a. Note that in this

| Total | Outcome | Total | Risk |
|-------|---------|-------|------|
|       | Yes     | No    |      |
| Exposed | 40 | 360 | 400 | 0.10 |
| Unexposed | 80 | 1520 | 1600 | 0.05 |
| Total   | 120 | 1880 | 2000 | 0.06 |

Table 1.

| Total | Outcome | Total | Risk |
|-------|---------|-------|------|
|       | Yes     | No    |      |
| Exposed | 0 | 0 | 0 | NA |
| Unexposed | 100 | 1900 | 2000 | 0.05 |
| Total   | 100 | 1900 | 2000 | 0.05 |

Table 2.

| Total | Outcome | Total | Risk |
|-------|---------|-------|------|
|       | Yes     | No    |      |
| Exposed | 30 | 270 | 300 | 0.1000 |
| Unexposed | 85 | 1615 | 1700 | 0.0500 |
| Total   | 115 | 1885 | 2000 | 0.0575 |

Table 3.

| Low  | Outcome | Total | Risk |
|------|---------|-------|------|
|      | Yes     | No    |      |
| Exposed | 30 | 170 | 200 | 0.150 |
| Unexposed | 55 | 745 | 800 | 0.069 |
| High  | Outcome | Total | Risk |
|      | Yes     | No    |      |
| Exposed | 10 | 190 | 200 | 0.050 |
| Unexposed | 25 | 775 | 800 | 0.031 |
| Total   | 120 | 1880 | 2000 | 0.060 |

Table 4a.
population, the total number of cases remains 120, and thus the total population risk remains $120/2000 = 6\%$. Note also that there is no confounding shown in Table 4a: the Mantel-Haenszel risk difference is $5\%$, equal to the population average risk difference calculated from Table 1.

Now suppose that our intervention removes 40% of exposure among the low income individuals (and thus an additional 80 low income individuals are subject to the risk of the outcome among unexposed low income individuals), and 10% among the high income individuals (likewise in high income individuals). The expected values resulting from this intervention are shown in Table 4b (with some cell values rounded to integers). Since there are equal numbers of exposed individuals in each income stratum, the total exposed individuals in the whole population remains the same as in Table 3 (120+180=300). But due to a greater effect of the exposure in the low income group, the total population risk differs from that in Table 3: approximately 5.66% (table is rounded; total population risk is accurate), rather than 5.75%. This yields a dynamic intervention risk difference of 6.00% - 5.66% = 0.34%.

If we had removed 10% among the low income individuals and 40% among the high income individuals (not shown) the dynamic intervention risk difference would have been approximately 0.16%.

**COMMENT**

We make four brief remarks on this example. First, note that the size of the population average risk difference is much larger than the population attributable, generalized intervention, or dynamic intervention risk differences. This result arises because it not everyone is exposed; only those who are exposed can have their exposure removed. In general, it may be harder to show a large magnitude risk difference in population intervention effects than in exposure effects. Closely related, we recognize that it is difficult to articulate a realistic intervention that would remove all smoking from a population, which is why the population attributable risk difference might be viewed as a bounding condition for possible interventions.

Second, and related, note that the difference between the generalized intervention risk difference and the two dynamic intervention risk differences is very small: the values of the three estimates range from 0.16% to 0.34%. In relative terms, however, the two dynamic intervention risk differences differ by a factor of two, which may have implications for cost-effectiveness.

Third, note that population attributable, generalized intervention, and dynamic intervention effects all depend on observed total population risk, and that therefore all will change under a different ratio of exposed to unexposed individuals in the target population. In contrast, the population average causal risk difference is (in expectation!) independent of the ratio of exposed to unexposed individuals.
Fourth and finally, we note that here we have assumed that any unintended side-effects of our smoking cessation intervention are negligible and so ignorable. In reality, smoking cessation is sometimes associated with unintended consequences (e.g. weight gain) that would bear consideration in both scientific and policy settings.