The impact of including W in addition to Z for adjustment in the cases 2a and 2b

In the case 2a, we compare the bias $|B^{ZW}|$ and $|B^{Z}|$ within an example, where we keep the bias of ξ constant at a plausible value i.e., bias $\alpha_\xi \beta_\xi = 0.16$. We consider three different patterns for this bias which vary the amplification potential of ξ: (1) amplification is small (i.e., $\alpha_\xi \beta_\xi = 0.2 \cdot 0.8 = 0.16$), (2) amplification is medium (i.e., $\alpha_\xi \beta_\xi = 0.4 \cdot 0.4 = 0.16$), (3) amplification is large (i.e., $\alpha_\xi \beta_\xi = 0.8 \cdot 0.2 = 0.16$). We vary the magnitude of the bias of W in relation to the bias of ξ (i.e., $\alpha_W \beta_W = \frac{1}{4}\alpha_\xi \beta_\xi,\ \frac{1}{2}\alpha_\xi \beta_\xi,\ \alpha_\xi \beta_\xi$) and the amplification potential of W (i.e., $\alpha_W = 0.2, 0.4, 0.8$ and $-0.2, -0.4, -0.8$). In addition we allow that $Rel(Z)$ varies. We illustrate $|B^{Z}|$ with dashed lines and $|B^{ZW}|$ with solid lines for all parameter constellations. Note that $|B^{Z}|$ does not vary related to α_W (see Table 2), thus all dashed lines are at the same points. Figure B1 shows the case $sign(\alpha_W \beta_W) = sign(\alpha_\xi \beta_\xi)$ and Figure B2 the case $sign(\alpha_W \beta_W) \neq sign(\alpha_\xi \beta_\xi)$. When the covariates induce bias in the same direction, then mainly $|B^{ZW}| < |B^{Z}|$. Only when the amplification potential of W is large $|B^{ZW}| > |B^{Z}|$ can be observed. This is especially the case when W induces a small bias (i.e., is a near instrument) and/ or when $Rel(Z)$ is small (i.e., in this case more bias can be amplified). When the covariates induce bias in opposite directions, then much more likely $|B^{ZW}| > |B^{Z}|$ can be observed. When $Rel(Z)$ is close to 1, then (nearly) the complete bias is reduced with Z and W. However, as soon as $Rel(Z)$ decreases a substantial bias can remain when adjusting for Z and W, depending on $Rel(Z)$ and the amplification potential of both covariates. Instead when W is not included for adjustment, then the bias of omitting W and the remaining bias of ξ can (partly) off-set each other. The bias off-setting effect increases as $Rel(Z)$ decreases, but is limited by the magnitude of the bias of W. As such the bias is more likely smaller when W is not included for adjustment; especially when $Rel(Z)$ decreases.

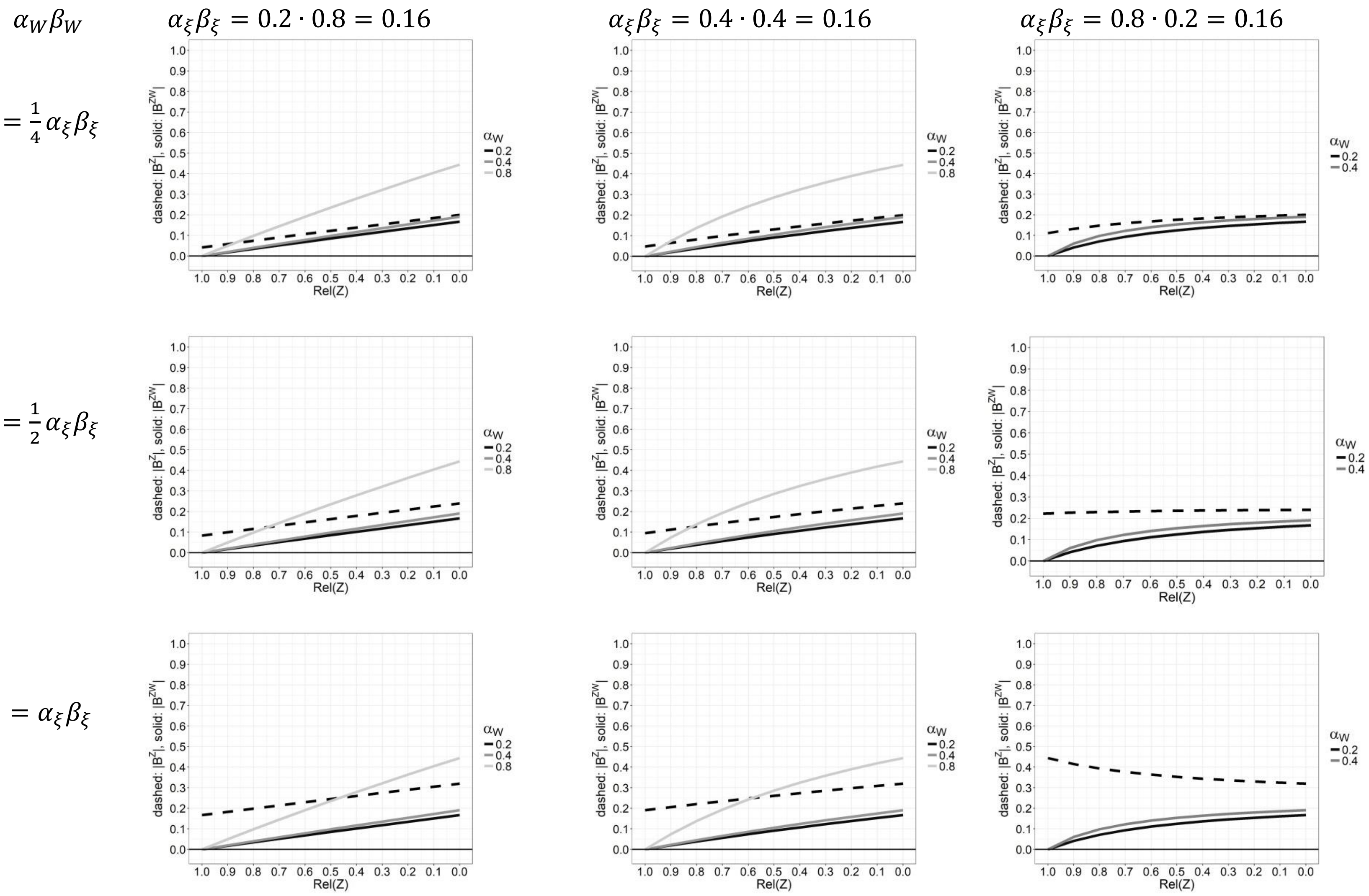


Figure B1. Bias when adjusting only for Z ($|B^Z|$ dashed line) or for Z and W ($|B^{ZW}|$ solid lines) in 2a with $sign(\alpha_\xi \beta_\xi) = sign(\alpha_W \beta_W)$. Note $|B^Z|$ does not vary for different values α_W (see Table 2).

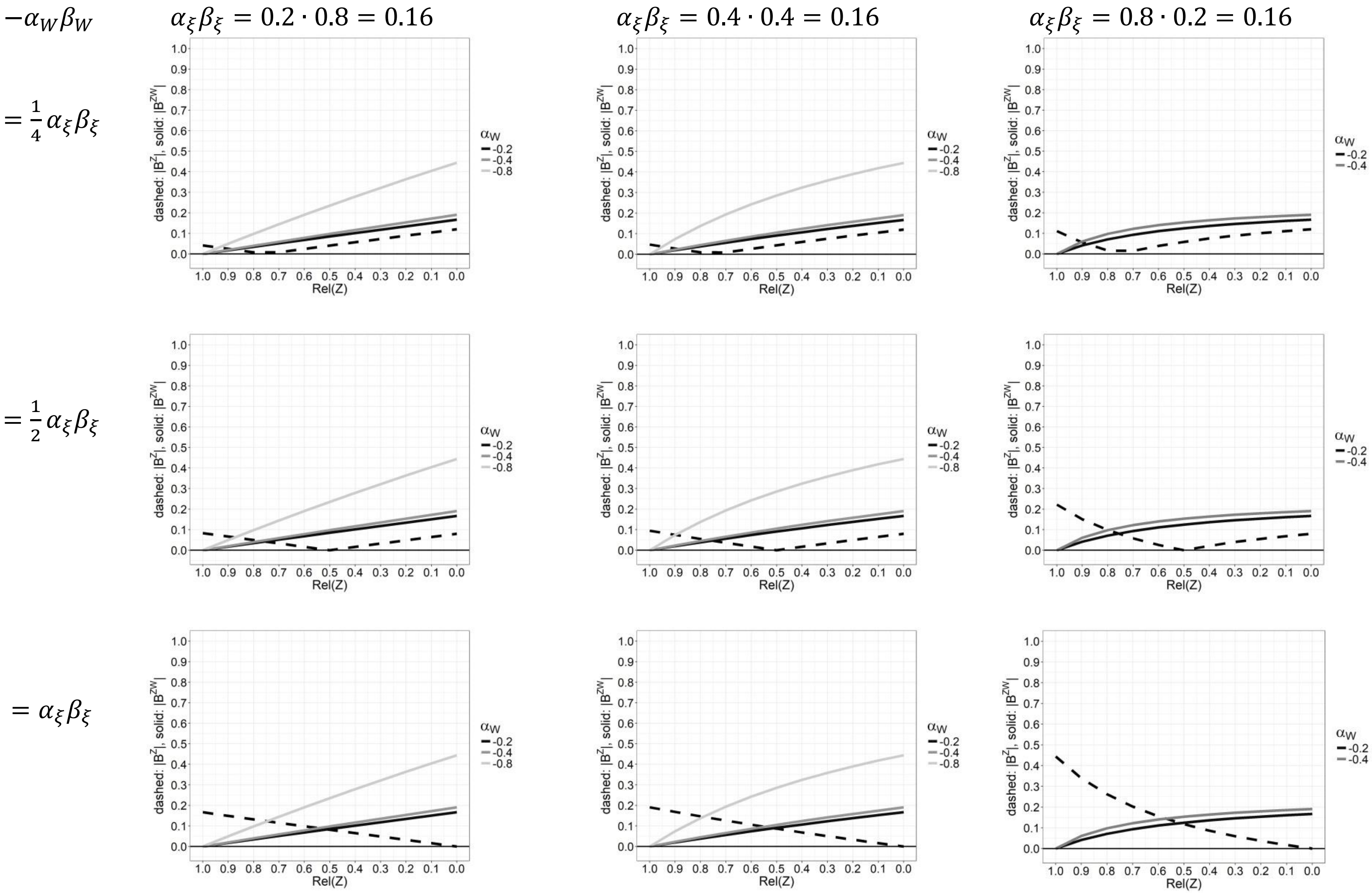


Figure B2. Bias when adjusting only for Z ($|B^Z|$ dashed line) or for Z and W ($|B^{ZW}|$ solid lines) in 2a with $sign(\alpha_\xi\beta_\xi) \neq sign(\alpha_W\beta_W)$. Note $|B^Z|$ does not vary for different values α_W (see Table 2)

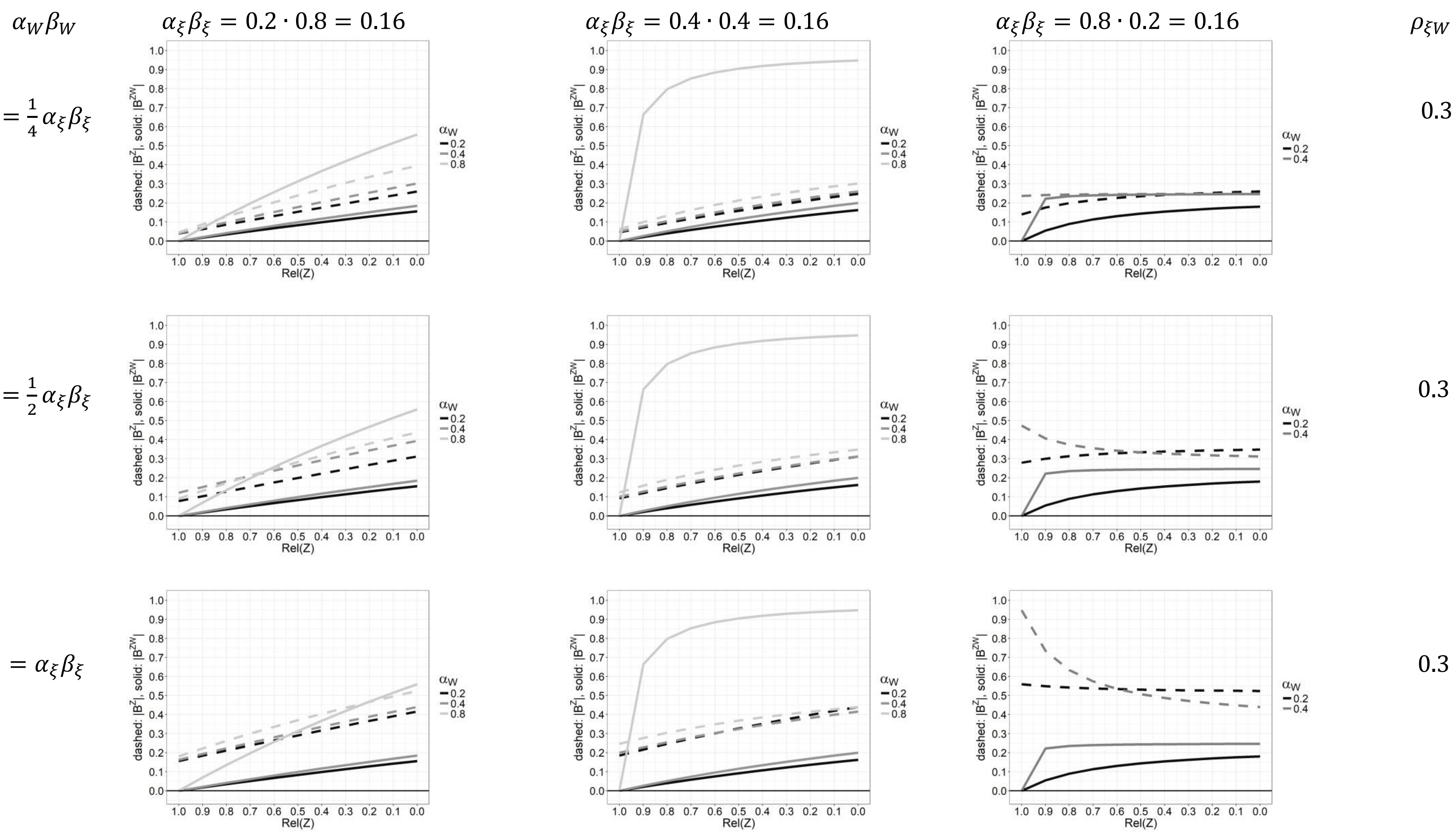
In the case 2b, we consider the same example as above, but include the correlation of the covariates with varying sign and magnitude $\rho_{\xi W} = |0.3|, |0.6|$. The correlation of the covariates increases the complexity immense. Different constellations for the direction of the biases (i.e., $sign(\alpha_\xi \beta_\xi), sign(\alpha_W \beta_W), sign(\alpha_\xi \rho_{\xi W} \beta_W), sign(\alpha_W \rho_{\xi W} \beta_\xi)$) are possible. Figure B3 shows the results when all biases are in the same direction $(\alpha_\xi \beta_\xi) = sign(\alpha_W \beta_W) = sign(\alpha_\xi \rho_{\xi W} \beta_W) = sign(\alpha_W \rho_{\xi W} \beta_\xi)$. Figure B4 shows the case $\left(sign(\alpha_\xi \beta_\xi) = sign(\alpha_W \beta_W)\right) \neq \left(sign(\alpha_\xi \rho_{\xi W} \beta_W) = sign(\alpha_W \rho_{\xi W} \beta_\xi)\right)$, Figure B5 the case $\left(sign(\alpha_\xi \beta_\xi) = sign(\alpha_W \rho_{\xi W} \beta_\xi)\right) \neq \left(sign(\alpha_W \beta_W) = sign(\alpha_\xi \rho_{\xi W} \beta_W)\right)$, and Figure B6 the case $\left(sign(\alpha_\xi \beta_\xi) = sign(\alpha_\xi \rho_{\xi W} \beta_W)\right) \neq \left(sign(\alpha_W \beta_W) = sign(\alpha_W \rho_{\xi W} \beta_\xi)\right)$.

When all biases are in the same direction, then mainly $|B^{ZW}| < |B^Z|$ can be observed, because including W for adjustment can reduce a large amount of bias. Only when W induces a small bias and its amplification potential is large, then including W can result in cases in which $|B^{ZW}| > |B^Z|$. A large amplification potential can increase the bias extremely due to including W even when $Rel(Z)$ is high (0.9).

When $\left(sign(\alpha_\xi \beta_\xi) = sign(\alpha_W \beta_W)\right) \neq \left(sign(\alpha_\xi \rho_{\xi W} \beta_W) = sign(\alpha_W \rho_{\xi W} \beta_\xi)\right)$, see Figure B4, then the correlation reduces the amount of bias in B^Z, thus less bias can be reduced when including W for adjustment. Again $|B^{ZW}| > |B^Z|$ occurs especially when the amplification potential of W is large. However, the difference between $|B^{ZW}|$ and $|B^Z|$ is rather small and only for low $Rel(Z)$ the bias can increases substantially due to a large amplification.

The bias of the covariates is in opposite directions in Figure B5 $\left(sign(\alpha_\xi \beta_\xi) = sign(\alpha_W \rho_{\xi W} \beta_\xi)\right) \neq \left(sign(\alpha_W \beta_W) = sign(\alpha_\xi \rho_{\xi W} \beta_W)\right)$ and Figure B6 $\left(sign(\alpha_\xi \beta_\xi) =\right.$

$sign(\alpha_\xi \rho_{\xi W} \beta_W)\big) \neq \big(sign(\alpha_W \beta_W) = sign(\alpha_W \rho_{\xi W} \beta_\xi)\big)$. Not including W would allow that the biases can (partly) off-set each other, when $Rel(Z)$ decreases. Thus $|B^{ZW}| > |B^Z|$ occurs more often and not only when the amplification potential of W is large. A large amplification potential can increase the bias extremely due to including W even when $Rel(Z)$ is high in $\big(sign(\alpha_\xi \beta_\xi) = sign(\alpha_W \rho_{\xi W} \beta_\xi)\big) \neq \big(sign(\alpha_W \beta_W) = sign(\alpha_\xi \rho_{\xi W} \beta_W)\big)$. The difference between $|B^Z|$ and $|B^{ZW}|$ is rather small in $\big(sign(\alpha_\xi \beta_\xi) = sign(\alpha_\xi \rho_{\xi W} \beta_W)\big) \neq \big(sign(\alpha_W \beta_W) = sign(\alpha_W \rho_{\xi W} \beta_\xi)\big)$.



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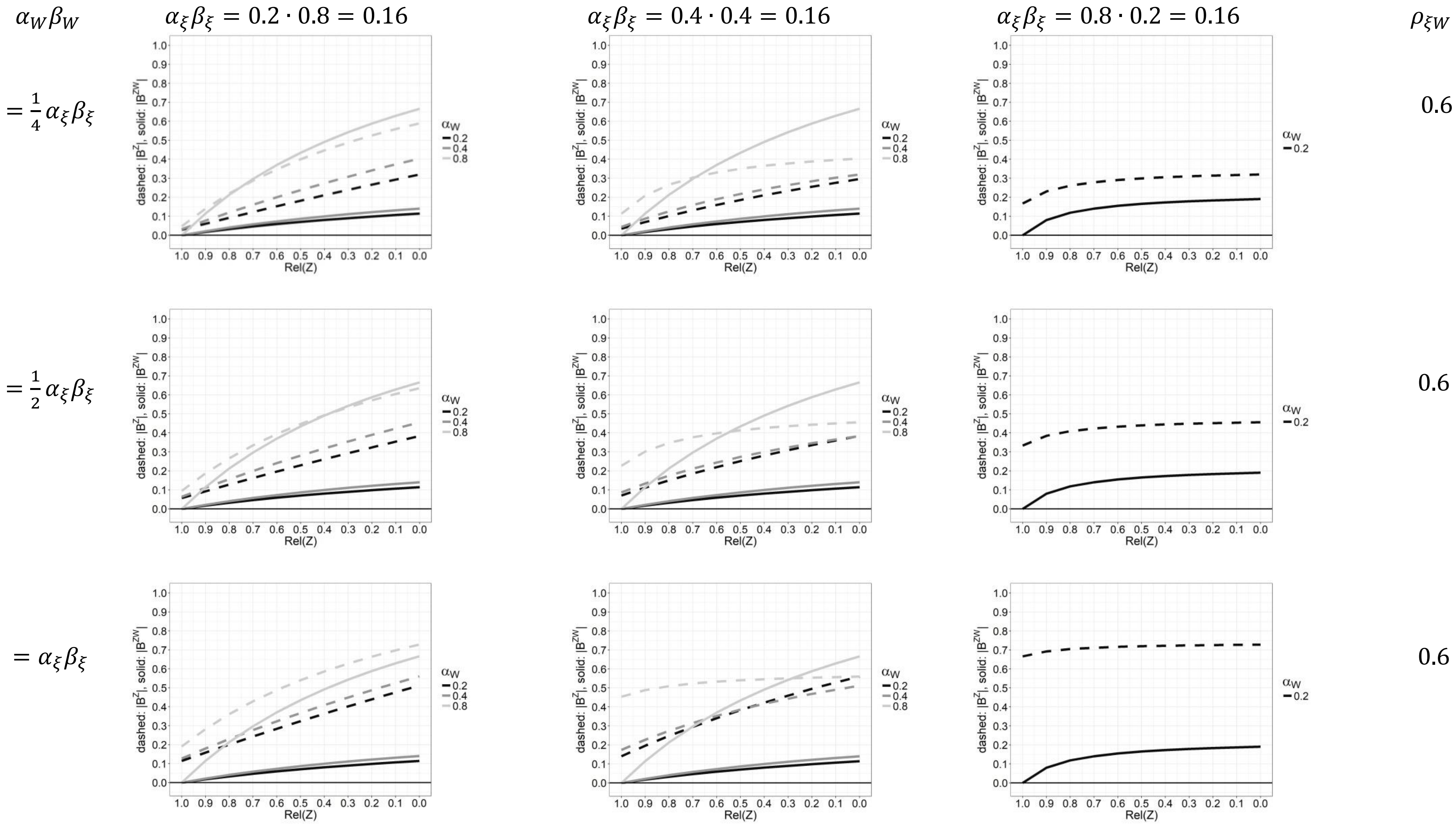
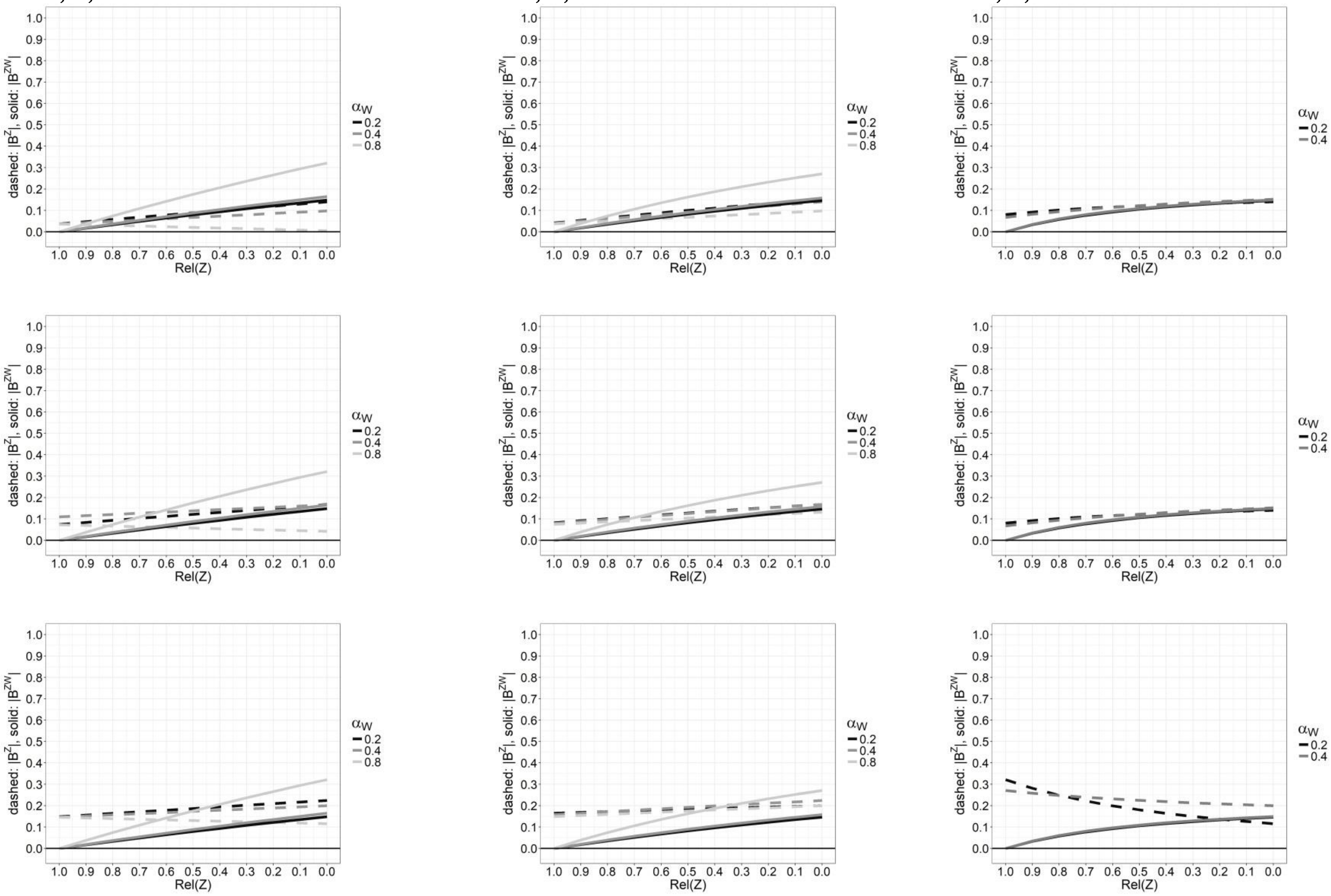


Figure B3. Bias when adjusting only for Z ($|B^Z|$ dashed lines) or for Z and W ($|B^{ZW}|$ solid lines) in 2b when $sign(\alpha_\xi \beta_\xi) = sign(\alpha_W \beta_W) = sign(\alpha_\xi \rho_{\xi W} \beta_W) = sign(\alpha_W \rho_{\xi W} \beta_\xi)$.

$\alpha_W \beta_W$ | $\alpha_\xi \beta_\xi = 0.2 \cdot 0.8 = 0.16$ | $\alpha_\xi \beta_\xi = 0.4 \cdot 0.4 = 0.16$ | $\alpha_\xi \beta_\xi = 0.8 \cdot 0.2 = 0.16$ | $\rho_{\xi W}$



$= \frac{1}{4} \alpha_\xi \beta_\xi$ — -0.3

$= \frac{1}{2} \alpha_\xi \beta_\xi$ — -0.3

$= \alpha_\xi \beta_\xi$ — -0.3

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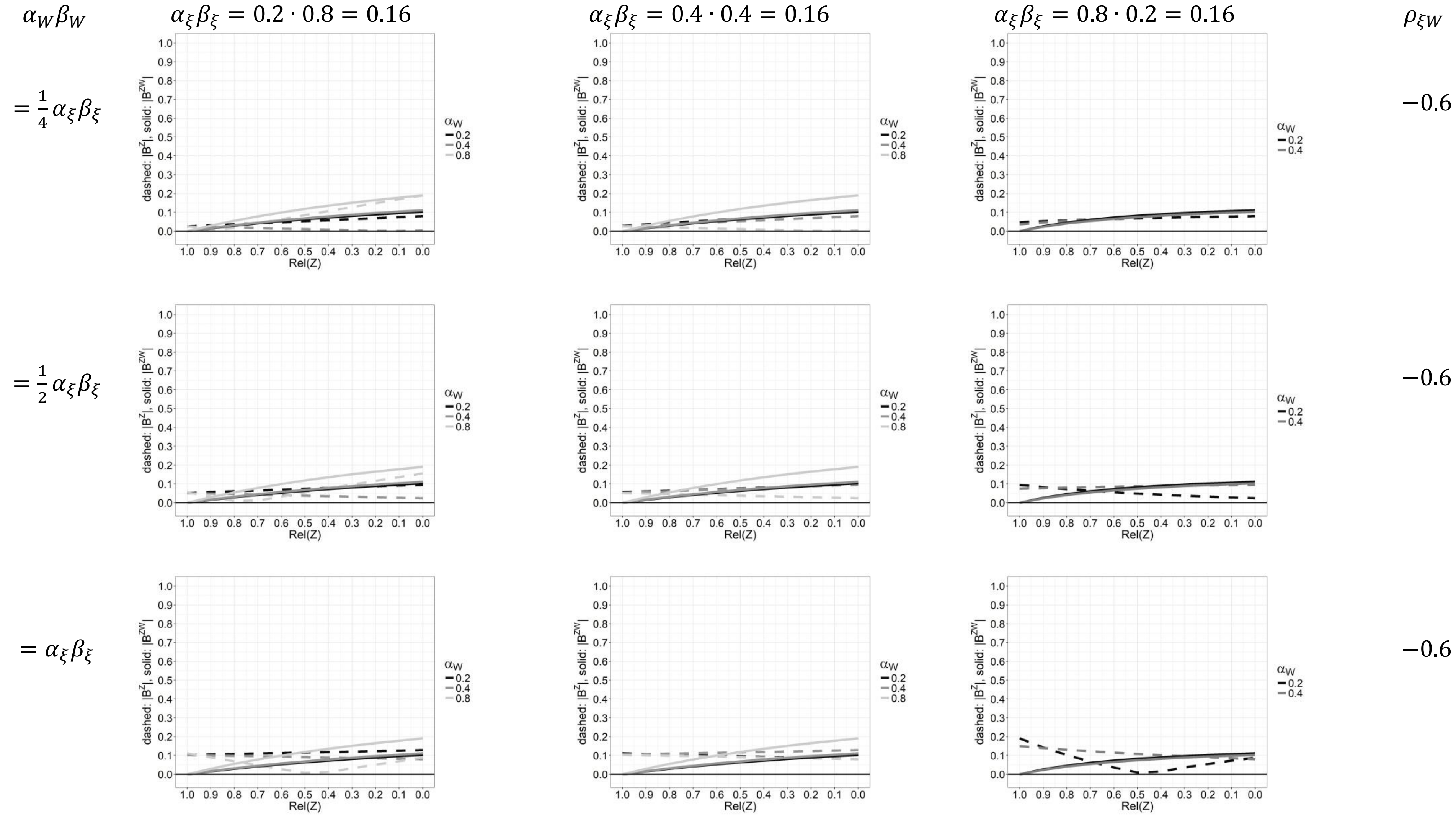
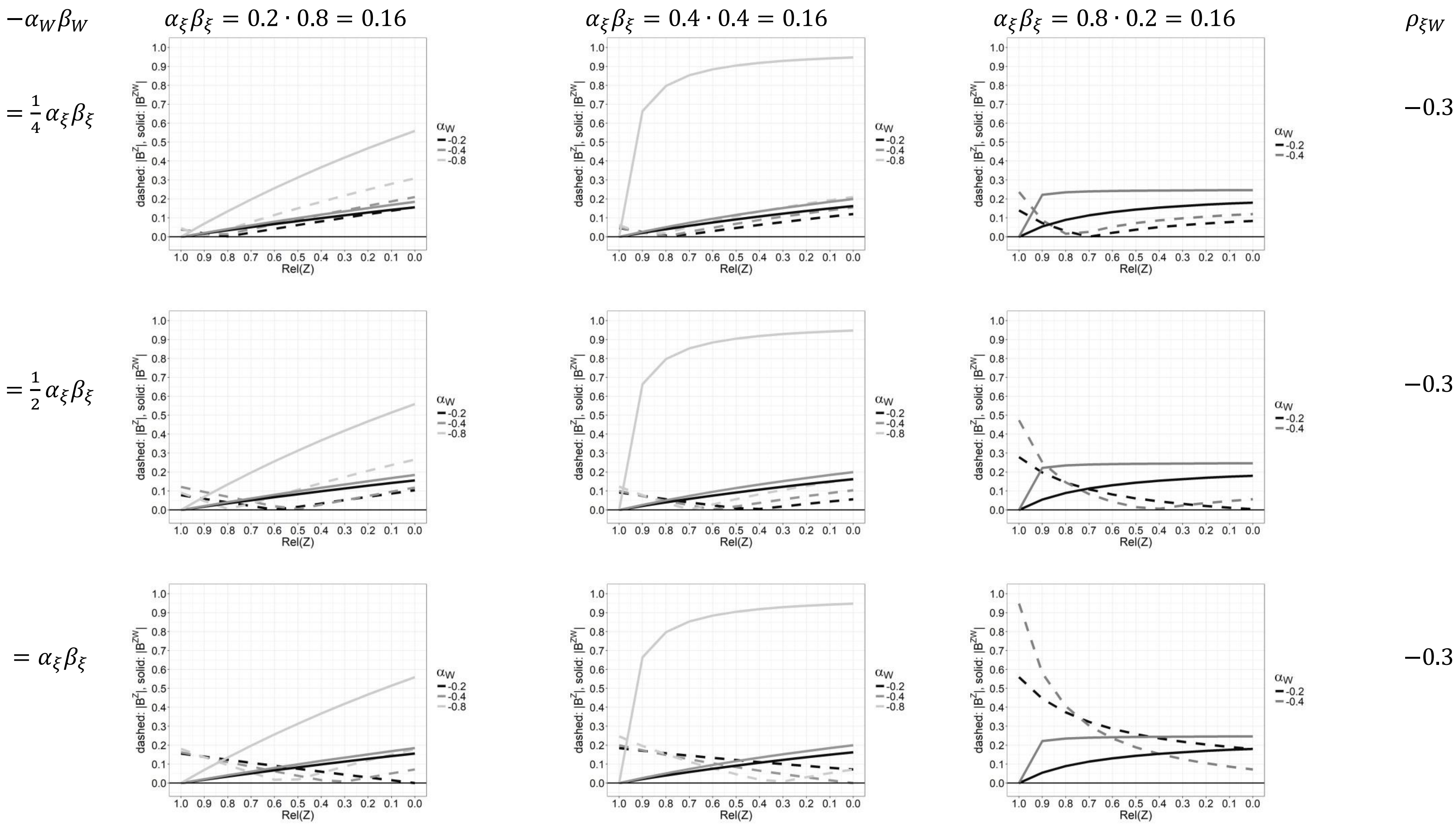


Figure B4. Bias when adjusting only for Z ($|B^Z|$ dashed lines) or for Z and W ($|B^{ZW}|$ solid lines) in 2b when $\left(sign(\alpha_\xi \beta_\xi) = sign(\alpha_W \beta_W)\right) \neq \left(sign(\alpha_\xi \rho_{\xi W} \beta_W) = sign(\alpha_W \rho_{\xi W} \beta_\xi)\right)$.



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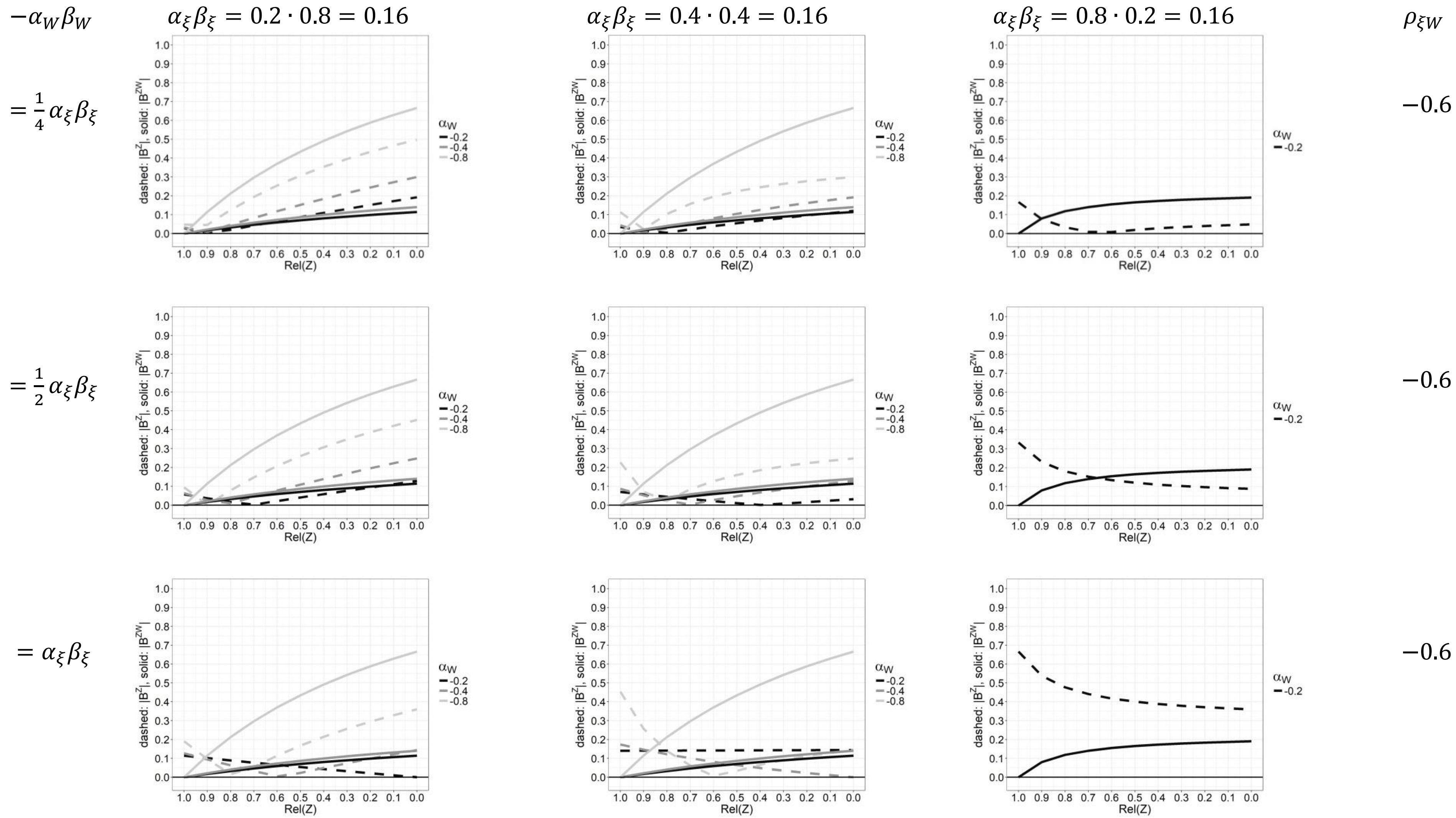
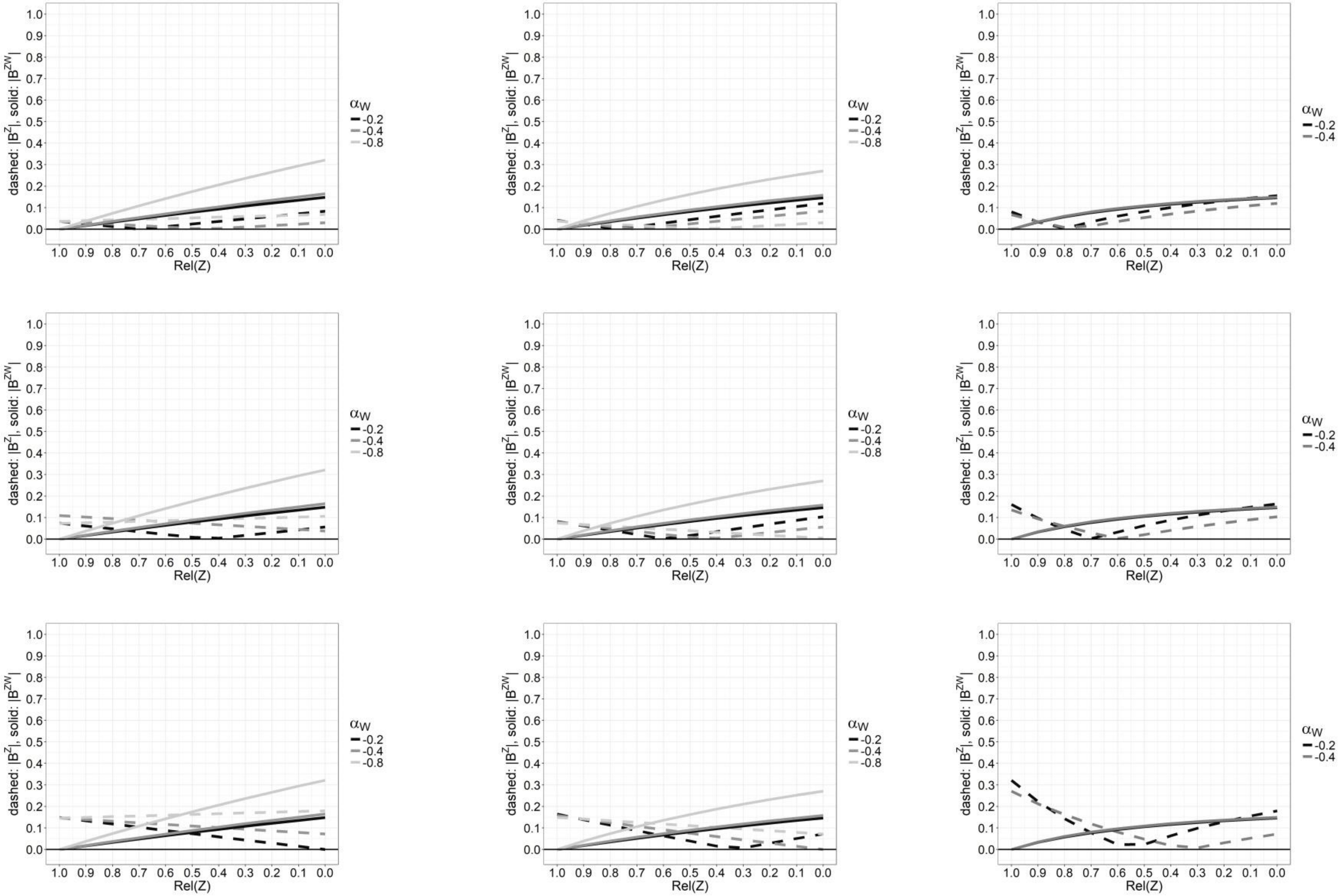


Figure B5. Bias when adjusting only for Z ($|B^Z|$ dashed lines) or for Z and W ($|B^{ZW}|$ solid lines) in 2b when $\left(sign(\alpha_\xi \beta_\xi) = sign(\alpha_W \rho_{\xi W} \beta_\xi)\right) \neq \left(sign(\alpha_W \beta_W) = sign(\alpha_\xi \rho_{\xi W} \beta_W)\right)$

$-\alpha_W \beta_W$	$\alpha_\xi \beta_\xi = 0.2 \cdot 0.8 = 0.16$	$\alpha_\xi \beta_\xi = 0.4 \cdot 0.4 = 0.16$	$\alpha_\xi \beta_\xi = 0.8 \cdot 0.2 = 0.16$	$\rho_{\xi W}$
$= \frac{1}{4} \alpha_\xi \beta_\xi$				0.3
$= \frac{1}{2} \alpha_\xi \beta_\xi$				0.3
$= \alpha_\xi \beta_\xi$				0.3



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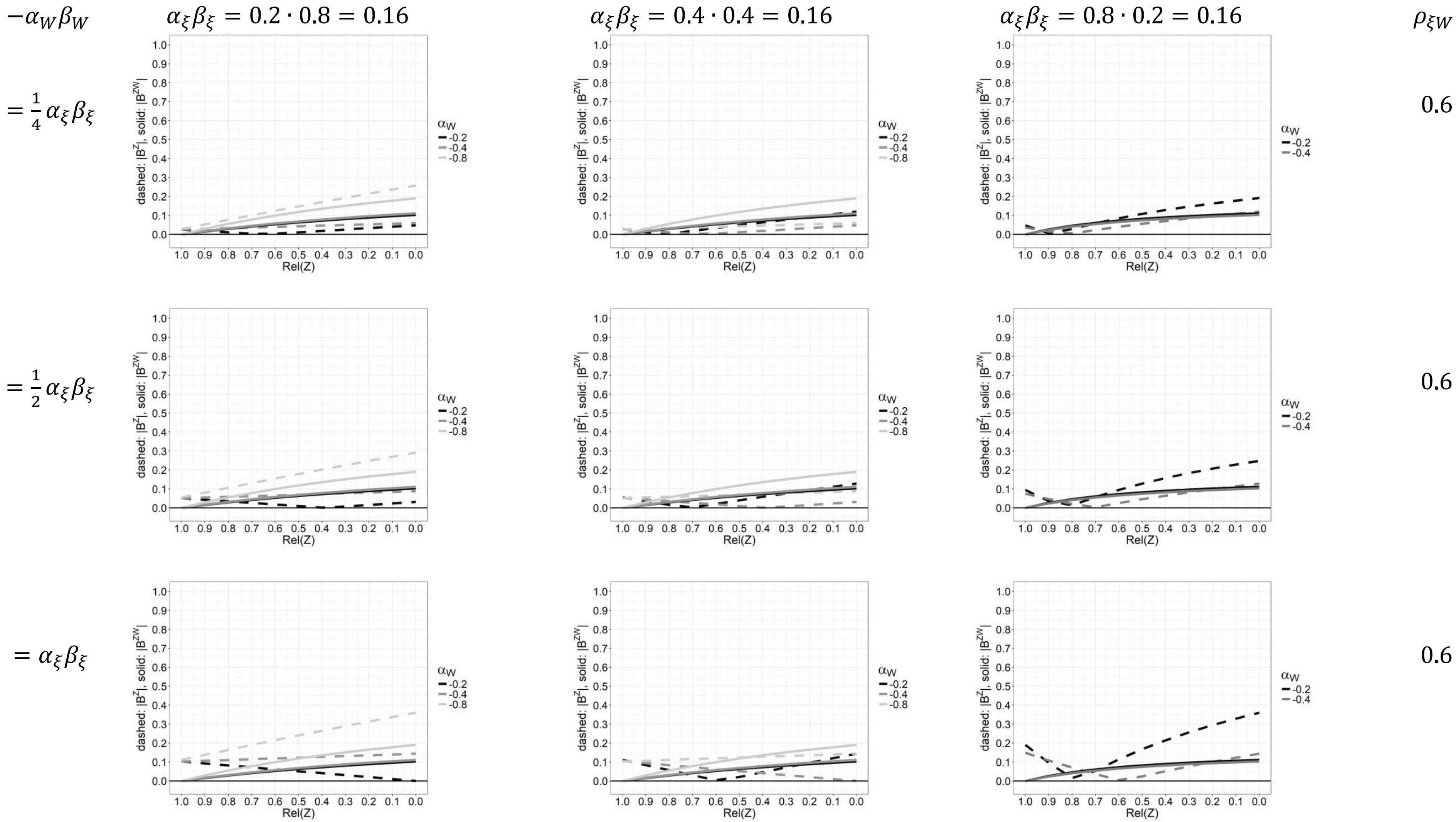

Figure B6. Bias when adjusting only for Z ($|B^Z|$ dashed lines) or for Z and W ($|B^{ZW}|$ solid lines) in 2b when $\left(sign(\alpha_\xi\beta_\xi) = sign(\alpha_\xi\rho_{\xi W}\beta_W)\right) \neq \left(sign(\alpha_W\beta_W) = sign(\alpha_W\rho_{\xi W}\beta_\xi)\right)$