law.

No. of No. of Model triplets microRNAs microRNAs in Srinivasan et al. (2011) Three-way 179 42 hsa-mir-148a, hsa-mir-221, hsa-mir-222 Independent 1715 14 has-mir-221, hsa-mir-148a, hsa-mir-222, hsa-mir-146b, hsa-mir-31 Causal 12267 437 hsa-mir-17-5p, hsa-mir-20a, hsa-mir-106a, hsa-mir-193a, hsa-mir-146b, hsa-mir-200b hsa-mir-31, has-mir-148a, hsa-mir-221, microRNA 2410 14 hsa-mir-146b, hsa-mir-222

Table 14.2 Summary results for the three-way model, the independent model, the causal model, and the microRNA model

can potentially affect patient survival but might be missed by analyses without integration.

For illustrative purposes, we selected 1,000 genes that were most relevant to patient survival in preprocessing the gene expression data for this analysis. However, in practice, this preselection step is not necessary, and all the genes can be screened. The genes supporting the null model, inverse model, microRNA model, and zero effects model will be automatically considered to be irrelevant to patient survival because gene expression is not related to survival or because the model does not reflect the correct biological relationship.

When the number of platforms for integration is more than 2, the number of possible biological relationships increases geometrically. For example, when the number of platforms is 4, the number of possible biological relationships is  $2^4 = 16$ . When the number of platforms is 5, this number increases to  $2^5 = 32$ . In these cases, we need to first determine a subset of biological relationships that are most interested by biomedical researchers and then follow the procedure described at the end of Section 14.3 to obtain the alterations that significantly support each biological relationship.

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