Abstract Design optimization of structural and multidisciplinary systems under uncertainty has been an active area of research due to its evident advantages over deterministic design optimization. In deterministic design optimization, the uncertainties of a structural or multidisciplinary system are taken into account by using safety factors specified in the regulations or design codes. This uncertainty treatment is a subjective and indirect way of dealing with uncertainty. On the other hand, design under uncertainty approaches provide an objective and direct way of dealing with uncertainty. This paper provides a review of the uncertainty treatment practices in design optimization of structural and multidisciplinary systems under uncertainties. To this end, the activities in uncertainty modeling are first reviewed, where theories and methods on uncertainty categorization (or classification), uncertainty handling (or management), and uncertainty characterization are discussed. Second, the tools and techniques developed and used for uncertainty modeling and propagation are discussed under the broad two classes of probabilistic and non-probabilistic approaches. Third, various design optimization methods under uncertainty which incorporate all the techniques covered in uncertainty modeling and analysis are reviewed. In addition to these in-depth reviews on uncertainty modeling, uncertainty analysis, and design optimization under uncertainty, some real-life engineering applications and benchmark test examples are provided in this paper so that readers can develop an appreciation on where and how the discussed techniques can be applied and how to compare them. Finally, concluding remarks are provided, and areas for future research are suggested.