Study design, size, duration: Between January 2017 and October 2020, a total of 206 PGT-M couples applied to Istanbul Memorial Hospital ART Center. Of these couples, multigene PGT-M workups were carried for twelve couples who were carriers of more than one inherited disease. Eight couples were found to be carriers for two different diseases and four couples were carrying three diseases. All biopsies were performed at the blastocyst stage.
Participants/materials, setting, methods: For the 12 couples with multigene PGT-M workups the average female age was 31.0 ± 6.2. Nine of them initiated an ART cycle and the mean number of cumulus-oocyte complexes, metaphaseII oocytes, biopsied blastocysts and transferrable PGT-M embryos were 15 ± 6.9, 13.3 ± 6.3, 5.9 ± 2.0 and 2.9 ± 1.9, respectively. PGT-A was routinely performed for all couples with transferrable PGT-M tested embryos except one couple who refused PGT-A.
Main results and the role of chance: A total of 28 different gene workups were completed for 26 genes. The inheritance mode of the 26 conditions was as follows: 20 autosomal recessive, four autosomal dominant and two X-linked recessive. Out of 12 couples, 9 of them initiated an ART cycle and transferrable embryos were found after PGT-M followed by PGT-A. Eight women had frozen embryo transfers resulting in five healthy babies (3 singletons and 1 twin), two pregnancies still ongoing and one biochemical miscarriage at the time of data collection. The couple who declined PGT-A testing prior to their frozen embryo transfer had anegative bhCG test. Three couples completed their workups but postponed their ART and PGT-M cycle due to Covid-19 pandemic.
Limitations, reasons for caution: The probability of finding at least one transferrable embryo after PGT-M is influenced by the inheritance mode of the disease. Late-onset diseases presumed to be caused by variants of unknown significance and polygenic diseases that are possibly influenced by environmental factors were not included in this study.
Wider implications of the findings: With decreasing costs and improved availability of WES and genetic carrier screening panels, couples, especially consanguineous couples, who were previously shown to have one inherited disease may be offered to be screened for additional undiagnosed inherited diseases that may pose a threat for their offspring.
Trial registration number: Not applicable

P-573 PGT-M for two or more disease carrier patients diagnosed after whole exome sequencing

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Study question: Can whole exome sequencing (WES) before PGT-M identify previously unknown mutations for consanguineous couples having an increased risk of carrying more than one genetic disease?
Summary answer: WES has been successfully applied in combination with PGT-M by identifying new pathogenic mutations in addition to known gene mutations, extending the scope of PGT-M.
What is known already: Most couples ignore their risk of being a carrier of an inherited genetic disease until they have an affected child. Rare, atypical, and undiagnosed autosomal-recessive disorders frequently occur in the offspring of consanguineous couples. Routine single gene diagnostic tests fail to detect any possible gene defects other than the clinically apparent one. Prospective WES or genetic carrier screening testing of consanguineous couples could identify couples who both are carriers of autosomal recessive diseases and thus encourage them to make informed reproductive decisions. Screening tests using NGS technology simultaneously sequence exons and exon-intron boundaries to determine disease carrier status.