Objectives: Classic congenital adrenal hyperplasia (C-CAH) is a rare condition caused by enzyme deficiency in cortisol biosynthesis. The condition is characterised by adrenal insufficiency and androgen excess and is associated with numerous disease- and treatment-related comorbidities that impact the length and quality of a patient’s life. A de novo model was developed to investigate the long-term health effects of modified-release hydrocortisone capsules (Efmody® / MR-HC) compared to the standard glucocorticoid replacement therapies (including immediate-release hydrocortisone, dexamethasone, and prednisolone) currently used to treat patients with C-CAH.

Methods: The model is structured as a series of sub-models reflecting key comorbidities in C-CAH: adrenal crisis, cardiovascular disease, bone health, height (adolescents only), obesity, diabetes and infertility. Effects of both disease, i.e. where cortisol and/or androgen levels are too high or low, and the impact of treatment, i.e. physiological or supraphysiological steroid dosing, on each comorbidity are considered where relevant. The model captures accumulating health outcomes from each sub-model and allows quantification of overall impact on health-related quality of life (HRQoL) and mortality. The population is adolescent (>12 years onwards) and adult patients with C-CAH. The intervention is MR-HC, and comparator is standard glucocorticoid replacement therapies currently used in C-CAH. Model inputs, which were composed of MR-HC clinical trial data, published literature values, and clinical opinion, and the modelling approach were validated with seven European clinical experts.
The model accumulates the health effect, which is measured as life-years (LYs) and quality-adjusted life years (QALYs), over a lifetime time horizon, from the ages of 12 to 100 years old.

**Results:** The model demonstrates that the treatment of C-CAH with standard glucocorticoid replacement therapies known to provide poor hormonal disease control and exposure to supraphysiological steroid dosing long-term have a substantial negative impact on HRQoL and life-expectancy in C-CAH, with modelled outcomes lower than those published for general population. Improved hormonal disease control and physiological steroid dosing with MR-HC compared to standard glucocorticoid replacement therapies result in improvements across the key comorbidities in patients with C-CAH. Quality-adjusted life year (QALY) gains are particularly driven by the reduction in adrenal crises, along with improved growth in the adolescent population and better weight control. Overall, the model demonstrates that long-term treatment of patients with C-CAH with MR-HC, compared to standard glucocorticoid replacement therapies, is expected to extend life by 7.58 years, and results in an additional 3.21 QALYs.

**Conclusion:** The model demonstrates that better hormonal disease control without exposing patients to supraphysiological steroid dosing with MR-HC improves key comorbidities in C-CAH resulting in improvement in both the length and the quality of life of patients with C-CAH.

**Presentation:** Saturday, June 11, 2022 1:00 p.m. - 3:00 p.m.