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Comorbidity Neural Network Model for Personalised Recommendations in Cardiometabolic Risk Factor Management: Towards Early Precision Medicine in Routine Clinical Practice

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Background and Aims
Hypertension and hypercholesterolaemia often develop in tandem to confer a risk of cardiovascular disease that may be more than additive. The present study explored early comorbid therapeutic intervention, i.e., beyond individual disease silos, while minimising data bias to provide clinical decision support tools that are portable across clinics.

Methods
A neural network was created to reproduce UK national clinical guidelines with an accuracy higher than 95%. Relying on real-world evidence from the UK primary care Clinical Practice Research Datalink electronic health record resource, a transfer learning methodology was then applied to achieve recommended risk factor goal attainment after two years. Shapley values derived from game theory were used to define similar digital twin cohorts, and to evaluate individualised recommendations that deviated from national clinical guidelines by rejecting a no-benefit hypothesis retrospectively in a classical proportion test. The methodology was ported to an independent hold-out dataset with anonymized records from six primary care clinics in the South of England.

Results
The adult patient population (n=469,496, mean±SD age 61±11yr; M 56% vs F 44%; primary 84% vs secondary prevention 16%) included 101,255 diagnosed for hypertension and 112,180 for cholesterol management. While a majority of the 52,504 therapeutic decisions in a test set agree with single morbidity guidelines, for 4639 deviations from the guidance, a significant minority was identified for whom alternative therapy was recommended. Rejecting a no-clinical benefit hypothesis at the 95% confidence level in a retrospective analysis, 1367 decisions showed statistically significant better outcomes over guidelines, for example by escalating anti-hypertensive therapies for patients receiving statin therapy (1085) or by complementing anti-hypertensive therapy with a statin (158). Similar findings were obtained when tested in a hold-out dataset with 13,725 decisions for 6531 patients.

Conclusions
The results support the contention that machine learning can identify patient subgroups for whom comorbid intervention deviating from clinical guidelines may be appropriate. A novel aspect of the study is the demonstration of clinically portable and actionable application of machine learning in the context of comorbid cardiometabolic diseases. The results represent practical steps towards personalised precision medicine for cardiovascular comorbidity in routine clinical practice.

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