Examples of Patients with multimorbidity.

Patient ID	Chronic Diseases (ICD-10 Codes)
1	E11, I10, J45
2	E11, I20, K21
3	I10, J45, K21
4	E11, I10, I20

Here, we present a sample table of patients' multimorbidity profiles, with chronic diseases listed using ICD-10 codes. In this illustrative example, the set of four patients corresponds to P as mentioned in Section 4.2.1 of the main text. The distinct set of chronic diseases $\{E11, I10, J45, I20, K21\}$ corresponds to D in the main text, with $|D|$ representing the cardinality of the set D, which is 5 in this example.

For $PatientID = 1$, the set of diseases, denoted as $diseases_1$, is $\{E11, I10, J45\}$. Similarly, for $PatientID = 2$, $diseases_2$ is $\{E11, I20, K21\}$, and so on. Using the sets $diseases_p$, we can determine the occurrences of unique multimorbid conditions. In this example, since each patient's multimorbidity profile is different, each unique multimorbidity occurrence has a frequency of 1, as shown below:

- E11, I10, J45: Frequency = 1
- E11, I20, K21: Frequency = 1
- I10, J45, K21: Frequency = 1
- E11, I10, I20: Frequency = 1

For the disease pair $d_1 = E11$ and $d_2 = I10$, we can derive the unique multimorbidity profiles containing both E11 and I10. The set M_{12} includes $\{E11, I10, J45\}$ and $\{E11, I10, I20\}$. For the specific multimorbidity instance $m = \{E11, I10, J45\}$ within M_{12}, its frequency $O(m) = 1$, as shown in the table above. According to Equation 1 in the main text, $M_P(d_1, d_2)$ can be calculated as follows:

$$M_P(d_1,d_2)=\frac{1}{|M_{12}|}\sum_{m\in M_{12}}O(m)=\frac{1}{2}\times 1=0.5$$

Similarly, for $m=\{E11,I10,J45\}$ within M_{12}, we input E11, I10, and J45 into the hcuppy library in Python to obtain the severity score $E(m)=-1$ of the multimorbidity instance m. According to Equation 2 in the main text, $M_S(d_1,d_2)$ can be calculated as follows:

$$M_S(d_1,d_2)=\frac{1}{|M_{12}|}\sum_{m\in M_{12}}E(m)=\frac{1}{2}\times(-1)=-0.5$$

The calculation of the complexity score $C(m)$ is described in the main text as follows: "For each multimorbidity instance m, determine the multimorbidity complexity score $C(m)$ by calculating the number of different classifications of chronic diseases in m." According to the experimental results of chronic disease identification and classification in Fig.3 in main text, the instance $m=\{E11,I10,J45\}$:

- E11 belongs to group e (Endocrine and metabolic disorders).
- I10 belongs to group b (Cardiovascular, congenital, and respiratory disorders).
- J45 belongs to group b (Cardiovascular, congenital, and respiratory disorders).

Since E11 falls under group e, and both I10 and J45 fall under group b, the multimorbidity instance m spans 2 different classifications. Therefore, the complexity score $C(m)$ is 2. According to Equation 3 in the main text, $M_C(d_1,d_2)$ can be calculated as follows:

$$M_C(d_1,d_2)=\frac{1}{|M_{12}|}\sum_{m\in M_{12}}C(m)=\frac{1}{2}\times 2=1$$

Finally, the mathematical representation of the multimorbidity adjacency matrix element $M(d_1,d_2)$ is shown as follows:

$$M(d_1, d_2) = M_P(d_1, d_2) \times M_S(d_1, d_2) \times M_C(d_1, d_2) = 0.5 \times (-0.5) \times 1 = -0.25$$

This calculation process also highlights the distinct focus (and advantage) of the proposed multimorbidity encapsulation framework compared to traditional methods. For instance, traditional pair-wise disease frequency calculation methods directly count the occurrence of an ICD-10 pair, such as E11 - I10, across all multimorbidity profiles. In contrast, our approach emphasizes the frequency of the multimorbidity profiles themselves.