Chapter 1
Introduction

1.1 Background

Cancer stands as the top cause of death globally and is Indonesia's second most common cause of death. Based on the data provided by Ferlay and others (2024), about 20 million new cancer instances and 9.7 million people died globally in 2022 alone. It is also predicted that by the year 2050, cancer cases will reach 35 million, with approximately 17 million deaths by 2030. The increase in these cases is caused by multifaceted reasons, but lifestyle patterns and exposure to carcinogenic agents can be the major key players as the external factor, while heredity, the balance of hormones, and immunity are internal factors of cancer development (Łukasiewicz et al., 2021). Among the many types of cancer, breast cancer is one of the commonly found cancer types, with 2.2 million cases and sitting in the second position (Ferlay et al., 2022). Conversely, breast cancer is the most prevalent type in Indonesia, followed by lung cancer, with 66,271 and 38,904 cases, respectively, accounting for 25.7% of 408,661 new cancer diagnoses together. In addition to this, the total number of deaths is 242,988 (Ferlay et al., 2022).

Targeted therapy is a revolutionized cancer treatment that uses powerful systemic medications to effectively target and eliminate cancer cells due to its efficient distribution to affected areas (Akhlagi et al., 2020). In addition to this, it has also been shown that targeted therapy provides a more precise treatment than conventional chemotherapy. By working specifically towards protein or molecules associated with the development of cancer, the incidence of affecting healthy cells or tissue is less common, leading to fewer significant side effects than chemotherapy (Choi & Chang, 2023). The administration route of targeted therapy can be intravenously or orally, with cancer patients preferring the oral route for its convenience at-home use (Jacob et al., 2019). An example of oral targeted therapy is CDK4/6 inhibitors (palbociclib, ribociclib, and abemaciclib) that hinder the transition of cancer cells between the G1 to S phases to slow or stop growth by preventing the

phosphorylation of retinoblastoma (Rb) proteins and are commonly used to treat breast cancer. All three types of CDK4/6 inhibitors work similarly, and they differ in the selectivity levels between CDK4 and CDK6, where palbociclib has the same selectivity level for both CDKs, ribociclib has a slightly higher selectivity level for CDK4 than CDK6, and abemaciclib is highly more selective towards CDK4 than CDK6 (Braal et al., 2020). Although the use of oral targeted therapy provides patients with greater autonomy and flexibility, it also puts the obligation of adherence on them, creating special difficulties in guaranteeing the efficacy of therapy (Ciruelos et al., 2019).

The level at which an individual follows a healthcare provider's recommended course of action, whether taking medication, following a nutrition plan, or making other modifications to their lifestyle, is known as patient adherence (World Health Organization, 2003). Self-administered oral antineoplastic medicines may lead to non-adherence due to reduced supervision and education compared to intravenous therapy, resulting in poor outcomes, increased toxic effects, and higher medical expenses. Adherence could be evaluated through different methods, either directly or indirectly. One method of evaluation, namely the medication possession ratio (MPR), determines the ratio of the period a patient has access to their prescription drug. This method is commonly used for chronic illnesses like cancer to assess whether or not patients regularly refill and keep their prescription medications on hand (Kolansinski et al., 2024). The ratio result ranges from 0 to 1, with values closer to 1 indicating better adherence to the regimen, and a result of 0.8 or higher signifying good adherence (Kolansinski et al., 2024). Using the MPR method retrospectively will offer insightful information about adherence trends, underlying causes, and potential approaches to improve adherence rates and progression-free survival (PFS). Although studies conducted in high-income nations demonstrate good adherence to CDK4/6 inhibitors, there is still a dearth of empirical evidence from low- to middle-income nations, such as Indonesia. Due to the novelty of these medications in Indonesia, adherence patterns have not been thoroughly investigated, even at MRCCC Siloam Hospital Semanggi, a preeminent cancer referral facility.

1.2 Objective

This study aims to determine demographic data and evaluate the adherence of breast cancer patients consuming oral CDK4/6 inhibitors at MRCCC Siloam Hospital Semanggi.

1.3 Hypothesis

The adherence of breast cancer patients consuming oral CDK4/6 inhibitors significantly varies across different demographic and clinical subgroups.