UNIVERSITY OF TURKU

Construction of Adverse Events Monitoring View for People Living with HIV Based on AIDS Database

Subject/Department: Future Health and Technology/Nursing Science
Master's thesis

Author(s):
Siyue Ma

Supervisor(s):
Professor Sanna Salantera
Professor Hongzhou Lu

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Abstract

【Background】

Acquired immunodeficiency syndrome (AIDS), is a global malignant infectious disease with extremely high fatality rate caused by human immunodeficiency virus (HIV). Regarding there is still no AIDS vaccine or cure in the world so far, the usage of Highly Active Anti-Retroviral Therapy (HAART) is currently the most effective way to suppress viral replication and also the basic therapy. However, drug resistance and different degrees of adverse events (AE) on PLWHIV could occur and cause major impact on health and quality of life for PLWHIV. Therefore, continuous monitoring and assessment of AE play a key role for PLWHIV. At present, decentralized clinical data are suggested to be a major problem during AE monitoring process, thus digital unified view of AE monitoring is asked for badly from health professionals to simplify the tedious process of clinical data collection. However, current domestic and foreign research still lacks a unified view of AIDS-specific clinical information. Therefore, this study intends to design and construct an AE Monitoring View for PLWHIV who receive HAART based on AIDS database, through which clinicians and nurses are able to be assisted in clinical decision-making, nursing diagnosis as well as timely corresponding intervention measures.

【Objectives】

The Overall objective is to construct an AE Monitoring View for PLWHIV.

There are 3 specific objectives, which are demonstrated respectively:

(1) To explore the demand of AE Monitoring View for PLWHIV among clinicians and nurses,
(2) To construct the framework of AE Monitoring View for PLWHIV,
(3) To develop and perform functional tests on the implemented functions.

【Methods】

The research was comprised of 3 parts:

Part 1: The demand exploration of AE Monitoring View for PLWHIV among clinicians and nurses

The researcher conducted semi-structured interviews to learn about current monitoring process of AE for PLWHIV, current common and rare AE and interventions on AE for PLWHIV, current problems clinicians and nurses would meet with during AE monitoring process, and their usage requirements on AE Monitoring View.

Part 2: The construction of the framework on AE Monitoring View for PLWHIV

The researcher established a research team with clinicians and nurses and technicians to discuss about the framework and drafted a first version based on relevant literature, drug instructions, Common Terminology Criteria for Adverse Events (CTCAE), and interview results. The researchers then sent the version to 14 experts for expert argumentation, until all experts agreed and the final framework version was finalized and moved to the next stage.

Part 3: Testing and application of AE Monitoring View for PLWHIV

Based on the final version of framework previously developed for AE Monitoring View, the researcher developed and internally tested the view in collaboration with technicians from a medical technology company, which the researcher then handed over to the research team with a questionnaire investigated later to conduct internal feasibility pilot-test for usability evaluation. This view is yet unmature and will be put into use after the AIDS Database is fully constructed in the future.

【Results】

Part 1: The demand exploration of AE Monitoring View for PLWHIV among clinicians and nurses

Based on the interview results of 11 clinicians and nurses, the researcher learned about the most common clinical AE in AIDS patients and their monitoring status. In addition, the researcher also summarized the current clinical workers' requirements for electronic information systems on monitoring process of AE.

The demand exploration shows:

1) Current AE monitoring process, including patient self-reports and regular patient review,
2) Common and rare AE for PLWHIV, such as rash, neurological symptoms, gastrointestinal disorders and so on,
3) Common interventions from clinicians and nurses on AE for PLWHIV, for instance, continuous monitoring, conventional conservative treatment and replacement of drug regimen，
4) The problems of current AE monitoring process, including continuity and accuracy,
5) Requirements on AE Monitoring View for PLWHIV, like visualization tool, list of AE with manifestations and interventions.

Part 2: The construction of the framework on AE Monitoring View for PLWHIV

The researcher established a research team of 11 members for frame design and content construction on AE Monitoring View for PLWHIV. After literature study and discussion, the researcher drafted out the preliminary framework of AE Monitoring View for PLWHIV. Meanwhile, through two rounds of Delphi expert consultation methods and collected expert opinions, the

researcher optimized and improved the content of framework, and determined the final version of framework for AE Monitoring View, including 5 levels, which was drug name, system AE belongs to, specific AE, manifestations and corresponding interventions. According to the opinions of experts, the researcher finally deleted the items such as *"allergic reaction"*, *"acidosis"*, *"hypophosphatemia"*, etc., and added items such as *"inattention"* and *"lactic acidosis"*. At the same time, according to the specificity of AIDS and the uniqueness of AE caused by antiviral drugs, the researcher modified and improved the symptoms and corresponding interventions in a targeted manner. For example, most somatic symptoms such as dizziness and headache are mild Symptoms, which do not require intervention, will gradually improve after taking the drug for a period of time. These are slightly different from those described in the CTCAE, thus the researcher has made modifications based on the recommendations made by experts.

Part 3: Testing and application of AE Monitoring View for PLWHIV

The researcher presented the final version over the content framework of the AE Monitoring View for PLWHIV to technicians and collaborated on the development of the Monitoring View, which was internally functionally tested. The actual results were consistent with the expected results, and the research team subsequently conducted a pre-test usability evaluation of the Monitoring View, which indicated a high usability of the AE Monitoring View for PLWHIV.

【Conclusions】

(1) The current state of AE monitoring process and the demands of clinicians and nurses for an AE Monitoring View for PLWHIV were investigated through qualitative interviews,

(2) Based on AIDS database, the content framework of the AE Monitoring View for PLWHIV was determined through two rounds of Delphi expert consultations based on the existing literature and CTCAE criteria as a guideline,

(3) The researcher and the technicians from the medical technology company cooperated to develop and internally test the AE Monitoring View for PLWHIV. After the AIDS Database is successfully built, it will be released to public together.

Key Words: AIDS; special database; adverse event; monitoring view

Abstrakti

Tausta

Immuunikato, Acquired immunodeficiency syndrome (AIDS), on maailmanlaajuinen pahanlaatuinen tartuntatauti, jolla on erittäin korkeat luvut kuolemantapauksien suhteen, jotka aiheuttavat HI-virus. Maailmassa ei ole vielä AIDS-rokotetta tai parannuskeinoa, mutta Highly Active Anti-Retroviral Therapy (HAART) käyttö on tällä hetkellä tehokkain tapa tukahduttaa viruksen replikaatio. HIV-potilailla voi kuitenkin esiintyä lääkeresistenssiä ja erilaisia haittavaikutuksia ja ne voivat aiheuttaa merkittäviä vaikutuksia HIV-potilaiden terveyteen ja elämänlaatuun. Tästä syystä haittatapahtumien jatkuva seuranta ja arviointi ovat avainasemassa HIV-potilailla. Nykyään, suurin ongelma haittatapahtumien seurannassa on ehdotettu olevan hajallaan olevat kliiniset tiedot. Siksi olisikin tärkeää yksinkertaistaa kliinisten tietojen keräämistä. Nykyisestä kansallisesta ja ulkomaisesta tutkimuksesta puuttuu kuitenkin edelleen yhtenäinen näkemys AIDS-spesifisestä kliinisestä tiedosta. Siksi tämän tutkimuksen tarkoituksena on suunnitella ja rakentaa haittatapahtumien seurantajärjestelmä HIV-potilaille, jotka saavat HAART-hoitoa. Haittatapahtumien seurantajärjestelmän avulla voidaan auttaa lääkäreitä ja sairaanhoitajia kliinisessä päätöksenteossa, hoitotyön diagnoosien tekemisessä sekä oikea-aikaisten hoitotoimenpiteiden valinnassa.

Tavoitteet

Tavoitteena on rakentaa haittatapahtumien seurantajärjestelmä HIV-potilaille. Tutkielmassa on kolme osatavoitetta:

(1) Tutkia HIV-potilaiden haittatapahtumien seurantajärjestelmän tarvetta lääkäreiden ja hoitajien näkökulmasta
(2) Rakentaa HIV-potilaiden haittatapahtumien seurantajärjestelmälle viitekehys
(3) Kehittää ja suorittaa toiminnallisia testejä haittatapahtumien seurantajärjestelmälle

Metodit

Tutkimus toteutettiin kolmessa eri vaiheessa:

Vaihe 1: Tarve HIV-potilaiden haittatapahtumien seurantajärjestelmälle lääkäreiden ja sairaanhoitajien näkökulmasta

Tutkija suoritti puolistrukturoidut haastattelut oppiakseen HIV-potilaiden tämänhetkisestä haittatapahtumien seurannasta, oppiakseen HIV-potilaiden yleisistä ja harvinaisista haittatapahtumista, selvittääkseen, mitkä ovat nykyisiä ongelmia haittatapahtumien seurannassa, joita lääkärit ja sairaanhoitajat kohtaavat sekä selvittääkseen millaisia vaatimuksia lääkäreillä ja sairaanhoitajilla olisi haittatapahtumien seurantajärjestelmälle.

Vaihe 2: HIV-potilaiden haittatapahtumien seurantajärjestelmän viitekehyksen rakentaminen

Tutkija perusti tutkimusryhmän lääkäreiden, sairaanhoitajien ja teknikkojen kanssa keskustellakseen viitekehyksestä ja laati ensimmäiseen version, joka perustui kirjallisuuteen, lääkeohjeisiin, Common Terminology Criteria for Adverse Events (CTCAE) -kriteereihin ja haastattelun tuloksiin. Sen jälkeen ensimmäinen versio haittatapahtumien seurantajärjestelmästä lähetettiin 14 asiantuntijalle arvioitavaksi. Kunnes kaikki asiantuntijat olivat yhtä mieltä, lopullinen versio viimeisteltiin ja siirryttiin seuraavaan vaiheeseen.

Vaihe 3: HIV-potilaiden haittavaikutusten seurantajärjestelmän testaus ja soveltaminen

Tutkija kehitti ja testasi edellisessä vaiheessa kehitettyä lopullista versiota haittavaikutusten seurantajärjestelmästä yhteistyössä lääketieteellisen teknologian yrityksen teknikoiden kanssa. Tämän jälkeen tutkimusryhmän jäsenet arvioivat seurantajärjestelmän kyselylomakkeen avulla. Käytettävyyskyselyn tuloksia hyödynnetään tulevaisuudessa, kun AIDS-tietokantaa kehitetään edelleen.

Tulokset

Vaihe 1: Tarve HIV-potilaiden haittavaikutusten seurantajärjestelmälle lääkäreiden ja sairaanhoitajien näkökulmasta

Haastattelun tulosten perusteella (n=11 lääkäriä ja sairaanhoitajaa) tutkija oppi, mitkä ovat AIDS-potilaiden yleisimpiä kliinisiä haittavaikutuksia ja miten niitä seurataan. Lisäksi tutkija kokosi kliinisten työntekijöiden tarpeet ja vaatimukset elektroniseen haittavaikutusten seurantajärjestelmään liittyen.

Tulokset osoittavat:

1) Haittavaikutusten nykyisen seurantaprosessin, mukaan lukien potilaan itseraportit ja säännöllinen potilasarviointi,
2) Yleiset ja harvinaiset haittavaikutukset kuten ihottuman, neurologiset oireet, ruoansulatuskanavan oireet
3) Yleiset hoitokeinot, kuten jatkuva seuranta, tavanomainen konservatiivinen hoito ja lääkehoidon korvaaminen
4) Ongelmat nykyisessä seurantajärjestelmässä, kuten ongelmat jatkuvuudessa ja tarkkuudessa
5) Vaatimukset HIV-potilaiden haittavaikutusten seurantaohjelmalle, kuten visualisointityökalu, luettelo haittavaikutuksista ja niiden hoitokeinoista

Vaihe 2: HIV-potilaiden haittatapahtumien seurantajärjestelmän viitekehyksen rakentaminen

Tutkija perusti 11 henkilön tutkimusryhmän haittavaikutusten seurantajärjestelmän viitekehyksen suunnittelemiseksi ja sisällön rakentamiseksi. Kirjallisuuteen tutustumisen jälkeen, tutkija teki ensimmäisen luonnoksen. Kahden Delphi-asiantuntijapaneelin konsultointikierroksen jälkeen tutkija kehitti ensimmäistä versiota palautteiden perusteella ja lopulta haittavaikutusten seurantajärjestelmän luonnos koostui viidestä eri tasosta, mitkä olivat: lääkkeen nimi, haittavaikutuksen kategoria, haittavaikutus, ilmenemismuodot ja hoitotoimenpiteet. Asiantuntijoiden palautteiden mukaan tutkija poisti lopulta nimikkeet, kuten ”allerginen reaktio”, ”asidoosi”, ”hypofosfatemia” ja lisäsi nimikkeitä, kuten ”tarkkaamattomuus” ja ”maitohappoasidoosi”. Samaan aikaan AIDS:n spesifisyyden ja epävirallisten lääkkeiden aiheuttamien haittavaikutusten ainutlaatuisuuden vuoksi, tutkija muutti ja paransi oireiden ja hoitotoimenpiteiden nimikkeitä kohdennetusti. Esimerkiksi useimmat somaattiset oireet, kuten huimaus ja päänsärky, ovat lieviä oireita, jotka eivät vaadi hoitotoimenpiteitä, paranevat vähitellen lääkkeen ottamisen jälkeen jonkin aikaa. Nämä ovat hieman erilaisia kuin CTCAE:ssä kuvatut, joten tutkija on tehnyt muutoksia asiantuntijoiden suositusten perusteella.

Vaihe 3: HIV-potilaiden haittavaikutusten seurantajärjestelmän testaus ja soveltaminen

Tutkija esitteli teknikoille lopullisen version HIV-potilaiden haittavaikutusten seurantajärjestelmän sisältökehyksestä ja teki yhteistyötä seurantajärjestelmän kehittämisessä, joka testattiin ryhmän sisäisesti. Tulokset olivat yhdenmukaisia odotettujen tulosten kanssa, ja tutkimusryhmä teki vielä myöhemmin seurantajärjestelmän käytettävyystestauksen, joka osoitti, että HIV-potilaiden haittavaikutusten seurantajärjestelmän käytettävyys on korkealla tasolla.

Johtopäätökset

(1) Haittavaikutusten seurantajärjestelmän nykytilaa sekä lääkäreiden ja sairaanhoitajien vaatimuksia seurantajärjestelmään liittyen tutkittiin laadullisten haastattelujen avulla,
(2) AIDS-tietokannan perusteella haittavaikutusten seurantajärjestelmän sisältökehys määritettiin kahdella Delphin asiantuntijakuulemiskierroksella, jotka perustuivat olemassa olevaan kirjallisuuteen ja CTCAE:n kriteereihin,
(3) Tutkija ja lääketieteellisen teknologiayrityksen teknikot yhteistyössä kehittivät ja testasivat HIV-potilaiden haittavaikutusten seurantajärjestelmän. Kun AIDS-tietokanta on rakennettu onnistuneesti, se julkaistaan laajemmalle yleisölle.

Avainsanat: AIDS; tietokanta; haittatapahtuma; seurantajärjestelmä

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1 Introduction

1.1 Research background and significance

Acquired immunodeficiency syndrome (AIDS), is a global malignant infectious disease with extremely high fatality rate caused by human immunodeficiency virus (HIV) [1]. Since the first case of AIDS reported in China in 1985, it has always been one of the most difficult medical problems. Despite the improvement of medical standards in recent years with AIDS epidemic prevention and control work obtained remarkable achievements, the current epidemic situation is still relatively highly severe. By the end of 2021, there was a total of 1140,000 survival people living with HIV (PLWHIV) in China，with 111,000 new cases reported in 2021 [2]. The truth is that expected longevity will not be affected in case PLWHIV receive standardized treatment in time. However, late detection of AIDS is regarded as the main cause of death in China at present. As of the end of 2020, there were still 30% of PLWHIV in China that had not been detected, while 30% of those who had been diagnosed as being infected were found in late-stage infections, which could increase mortality [3]. According to the 2020 national statutory infectious disease report morbidity and death statistics released by the Chinese National Bureau of Disease Control and Prevention, in the year 2020, 62,167 cases of AIDS and 18,819 deaths were reported. AIDS has become the statutory infectious disease with the highest number of reported deaths in China in 2020 [4]. The prevalence of the AIDS epidemic in China mainly presents four characteristics currently: (1) It is at a low epidemic level regarding AIDS epidemic in China in the world as a whole, with dramatic differences in epidemic areas, among which the epidemic situation in some parts is fairly serious; (2) The number of reported surviving HIV/AIDS cases continues to increase with the number of reports of new infections and newly discovered diagnoses being rose up at the same time year by year; (3) PLWHIV had gradually entered the stage of disease, which resulted in an significant increase on the number of AIDS patients, while the number of deaths from all causes has tended to be stable; (4) Sexual contact is regarded as the predominant driver of transmission, in which homosexual transmission among men who have sex with men (MSM) has played an increasingly significant role recently [5-9].

Regarding there is still no AIDS vaccine or cure in the world so far, the usage of Highly Active Anti-Retroviral Therapy (HAART), which is a treatment regimen typically comprised of a combination of three or more antiretroviral drugs, is currently the most effective way to

suppress viral replication and also the basic therapy at present, due to the fact that it can significantly control viral load (how much virus is in the blood), delay the onset of progression to AIDS, and prolong life expectancy of PLWHIV[10]. According to the recommendation of Chinese Guidelines for Diagnosis and Treatment of HIV/AIDS (2018), HAART is mostly composed of two nucleoside reverse transcriptase inhibitors (NRTIs) plus one non-nucleoside reverse transcriptase inhibitors (NNRTIs) or an enhanced protease inhibitor (PIs) plus ritonavir or integrase Inhibitor (INIs) composition [11]. However, drug resistance and different degrees of adverse events (AE), which are also widely known as adverse drug reactions (ADR), on PLWHIV could occur due to the need for lifelong antiviral therapy and poor compliance with medications, including hypersensitivity, myelosuppression, metabolic disorders, gastrointestinal intolerance, drug-induced liver injury, drug-related kidney injury, neurological and psychiatric symptoms [12]. AE prevalence caused by HAART always varies from regions and countries, with the severity and profile of it varies from patients and drug regimen at the same time. According to a study from India, the incidence of AE among PLWHIV who receive HAART globally ranges between 11% and 35.9%, among whom opportunistic infection occurrence rate being as high as 54% [13]. These unexpected and unwanted AE are often soft, but sometimes getting more severe with leading to increased economic burden, a major impact on health and quality of life for PLWHIV in case of being not noticed in time, including but not limited to prolong of hospital stay, a variety of complications and other opportunistic infections happening, and even death [14]. Therefore, continuous monitoring and assessment of AE plays a key role for PLWHIV who are receiving HAART to get all the help they need to minimize the impact of AE.

At present, throughout patient's self-reported symptoms and the observation from health professionals themselves with health records of PLWHIV are still the most common ways to monitor AE among PLWHIV. A study from South Ethiopia reported that an AE monitoring center was established to collect, compile and analyze all the information about AE occurred to PLWHIV who received HAART which was reported by doctors and nurses in the hospital, based on which those unnecessary harm would be avoided as possible throughout risk assessment and clinical intervention [14]. Nevertheless, information on the types and severity of HAART AE is still inadequate in the study area and risk factors for AE have also been controversial. It is reported that gender, age, drug regimens, CD4+ T lymphocyte count, quality of life, and the use of illicit drugs by individuals could all be associated with AE, which means health professionals need to observe the necessary data from different places

such as the patient's medical record and clinical examination report to determine whether the patient has a trend of AE [15]. In addition, clinicians need to synthesize the combination of different clinical indicators in the patient report to determine the probability of the patient's AE or the cause of them in the patient who has already had AE. Decentralized clinical data are suggested to be a major problem during AE monitoring process, which could result in incomplete consideration and extension of diagnosis time, thus digital unified view of AE monitoring is asked for badly from health professionals to simplify the tedious process of clinical data collection in order to make timely adoption of appropriate treatment plans and nursing measures via more efficient monitoring and decision-making.

Special disease database refers to an information software system for centralized management of case information of a single disease, which conducts systematic and standardized management of clinical case information data of a large number of relevant cases with scientific research significance and practical value in order to realize rapid query of past case information of the disease and statistical data analysis, thereby conducting clinical research, giving clinical diagnosis and treatment with providing valuable information or meet the needs of clinical teaching [16]. At present, a huge amount of medical information is generated in the process of clinical AIDS diagnosis and treatment, including clinical data such as clinical features, drug treatments, tests, imaging treatments, and disease outcomes, as well as epidemiological and economic data, which will be of great value for optimizing diagnosis and treatment when being used scientifically and rationally [17]. However, lack of structure and not able to form a standardized data set lead to problems such as heavy workload, low efficiency, high error rate, and difficulty in sharing and using collected data when conducting AIDS research, which result in an urgency to build an integrated AIDS database in the medical big data environment. Clinical information unified view means that clinical medical workers and scientific researchers can consult the patient's medical information through a clear and friendly unified view so that they can have an overall understanding of the patient's medical condition in a short time [18]. A Chinese company has already constructed a clinical information unified view called patient 360 unified view which organized patients' basic information, medical information, health problems, medication information, allergy information, surgery information, inspection reports, past medical history and other information for use of clinicians in the hospital with being provided to health management cloud platform throughout big data platform in order to satisfy patients' requirements for clinical information demands [19]. The unified view of clinical information highly summarizes

the patient's full life cycle data to make the treated data more valuable, meanwhile the data is integrated and labeled to provide individual patient conditions and recovery prediction analysis, which is beneficial to provide assistance to clinicians' decision support and help managers better identify risks with realizing timely intervention and control [20].

However, current domestic and foreign research still lacks a unified view of AIDS-specific clinical information. The complexity of HAART AE monitoring urgently requires highly concentrated patient clinical data to be presented in a unified view to assist health professionals in observation and decision-making to take corresponding intervention measures so that the quality of life for PLWHIV could be improved. Therefore, this study intends to design and construct an AE Monitoring View for PLWHIV who receive HAART based on AIDS database, through which clinicians and nurses are able to independently select clinical indicators and keep them in a unified view. The AE Monitoring View will be displayed in a chronological order in a trend chart to assist health professionals in clinical decision-making, nursing diagnosis as well as timely corresponding intervention measures.

1.2 Literature review

1.2.1 Epidemiology of HIV/AIDS

Human immunodeficiency virus (HIV) is an infection that attacks the body's immune system, which causes acquired immunodeficiency syndrome (AIDS) [21]. Since the turn of 1980s when the first case of AIDS was reported, the world has been experiencing the AIDS epidemic for four decades, which still threatens public health, being regarded as one of the most major public health issues in global. The World Health Organization (WHO) [22] has claimed an estimated 37.7 million (31.6-44.5 million) PLWHIV by the end of 2020, among whom there are a total of 7.1 million (1.2-2.2million) who did not know they have HIV, with 0.7 million (0.5-1.0 million) HIV-related deaths were reported. According to Global HIV Program of WHO [23], the amount of PLWHIV has risen 24% globally relative to 2010 at the end of 2019, and the incidence of new infections over the world has been declined 23% annually relative to 2010, with mortality incidence reducing 39% annually. In addition, new diagnoses rate has decreased by 39% annually relative to 2000, with deaths rate dropping 51% annually. AIDS is also the focus of prevention and treatment of infectious disease in China, as stated at Policy Interpretation Conference held by Chinese National Health Committee, it is still a in a severe situation when meeting with AIDS [24]. By the end of 2021, there was an estimated amount of around 1140,000 survival PLWHIV in China, and 316,000 cases of death

were reported by the end of 2019 [2]. The GBD Compare of Viz Hub [25] indicated that the number of deaths relative to HIV infection in 2019 accounted for 0.3% of the total number of deaths in China, with an increasing mortality of 6.66% per year. Liu et al [26] searched for basic prevalence of HIV/AIDS before they investigated HIV prevalence among 338,432 individuals and pointed out that China was currently in a low prevalence of new HIV infections with incidence rising up slowly, which is similar with study from Lyu et al [27], suggesting that the base number of PLWHIV as well as deaths were continuously increasing slowly in annual. HIV is spread through blood, semen or vaginal secretions and HIV infection could happen by relative risk behaviors, such as having sex, sharing needles, blood transfusions and during pregnancy or delivery or through breast-feeding. Zhang et al [28] revealed the prevalence of HIV among the general population (0.1%), people who inject drugs (PWID) (10.5%), MSM 7.3%, female sex workers (FSWs, 0.2%), and transgender women (14.8%), which suggested a major way to spread by PWID. However, there was a dramatic change in HIV/AIDS epidemic of China during the past few years, with sexual contact becoming the major driver of transmission, and homosexual transmission among MSM became more, resulting in a gradual increasing incidence of HIV among key population, for instance, MSM.

There will be great impacts not only on individuals but society as well once finding out infected with HIV or already stepped into the third stage of AIDS, without getting timely treatment. Adverse outcomes including daily activities hampered, opportunistic infections and mental health problems, could happen and lead to decrease on quality of life, increase of economic burden and even death. Jucá et al [29] observed participants from specified care service center between 2015 and 2016, finding out that there were changes in oral functions to PLWHIV. This research suggested taste losing and compromise of adequate nutrition to PLWHIV due to the disease, which is also found in several other studies [30-32]. Oral health issues related to HIV infection could cause a severe impact on daily lives to PLWHIV, with barriers to access to dental treatment. Apart from taste function, mental health problem is regarded as another major issue caused by HIV infection, among which depression is one of the most common neuropsychiatric complications in PLWHIV [33]. It is reported as an estimated 18.5% incidence of depression among PLWHIV according to the only nationally representative study in the US, with the fact that depressive disorder caused by overwhelmed sorrow, stress on living with chronic disease and lack of support from family and friends, is two to three times more common in PLWHIV versus the general population in global [34]. In a study from Benton et al [35] to young women living with HIV, 80% of women living with HIV

who experience depression were at a level of serious depression, which was indicated in other studies as well [36-38]. In addition, HIV stigma is also documented to be severe among PLWHIV, which is caused by refusal to care for PLWHIV, blaming patients for their HIV status, using harsh language, refusal to touch PLWHIV or using extreme precautions [39]. Ashaba et al [40] conducted the research in an African district with 195,013 participants, and found that HIV stigma is always associated with abuse and neglect from caregivers, bullying by peers, and despair as well, which is similarly reported in the research by Yuvaraj et al [41]. It is obvious that mental health problems are not only highly prevalent but severe among PLWHIV as well which is required for timely therapy in physical and mental health at the same time.

Opportunistic infections (OIs) including bacterial pneumonia, Pneumocystis jiroveci, tuberculosis and so on, could happen in case PLWHIV do not receive treatment timely or stepped into the last stages of HIV, which are severe and threatened, leading to significant morbidity or even mortality. In spite of current most common usage of HAART, which preserves immune function and reduces complications of HIV infection, HIV-1 Associated OIs were suggested to hence [42]. Yen et al [43] investigated 26,258 PLWHIV throughout Taiwan CDC HIV Surveillance Database from between 2,000 and 2014 in order to learn about short and long-term risks of HAART among PLWHIV. This study indicated that 24.4% of PLWHIV who received HAART experienced new onset of OIs, and pointed out that PLWHIV who received HAART were more likely to get OIs, which is also reported in other studies [44,45]. Currently the disease spectrum among PLWHIV has changed gradually due to the widespread development of HAART, while AIDS-related OIs in developed countries has become chronic liver diseases, cardiovascular diseases, non-AIDS-related tumors and hepatitis B/C [46]. Not only those closely related OIs but also chronic complications could impact badly on quality of life among PLWHIV. A recent study claimed that cardiovascular diseases such as, coronary artery diseases, heart failure, hypertension and stroke appear to be more and more common among PLWHIV, with a research result that hypertension might be induced by HAART, reported by Pangmekeh et al [47] through an investigation towards 6,400 PLWHIV from March to June in 2017 on association between HAART and hypertension in PLWHIV in Africa, which was similarly indicated in study by Saito et al [48] via a cross-sectional study targeted at HIV-infected adults in 2015. Liver-related complications are also a significant factor of hospitalizations and deaths in PLWHIV, which was suggested by Katerina et al [49] in a literature review. Moreover, other diseases such as diabetes, dementia and so on could occur complicated to AIDS, which significantly increase mortality [50]. OIs

and other chronic complications would definitely cause tremendous impacts to PLWHIV so that timely treatment and health care are required urgently.

1.2.2 Clinical antiviral treatment of AIDS

1.2.2.1 Choices of drug regimen

Highly Active Anti-Retroviral Therapy (HAART) is currently the most common treatment aiming at PLWHIV, which has enormously decreased the morbidity and mortality relevant to HIV infection. There are a total of more than 30 drugs (including compound preparations) in six major categories globally, which are classified as nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), integrase inhibitors (INSTIs), fusion enzyme inhibitors (FIs) and CCR5 inhibitors [51]. According to the recommendation of Chinese Guidelines for Diagnosis and Treatment of HIV/AIDS (2018), HAART is mostly composed of two nucleoside reverse transcriptase inhibitors (NRTIs) plus one non-nucleoside reverse transcriptase inhibitors (NNRTIs) or an enhanced protease inhibitor (PIs) plus ritonavir or integrase Inhibitor (INIs) composition [11]. In fact, as Sezgin et al [52] indicated in a prospective cohort study with 1,889 PLWHIV participating from 1998 to 2012, since three-drug combination HAART entered into clinical sight, it has been beneficial in improving the prognosis among PLWHIV due to its dramatic effect on sustaining viral load suppression and $CD4^+$ T cell gains, which has led to a result of PLWHIV survival in a range similar to that of HIV-uninfected individuals. Recent studies have discussed about the use of two-drug combination therapy to be a new regimen choice for those who are not able to tolerate three-drug combination regimen or afford the financial burden [53-56]. In spite of the possibility of an excess of toxicity in the medium-term among three-drug combination regimen users, two-drug combination therapy is still not recommended in guidelines not only because of its less obvious efficacy than three-drug combination therapy, but possibility of more residual viral replication which may result in higher immune activation and the development of non-AIDS events as well, This was similarly talked about in the study by Moreno et al [57], who searched the comparison between the two-drug combination therapy and three-drug therapy for PLWHIV through 300 patients.

According to the recommendation of Chinese Guidelines for Diagnosis and Treatment of HIV/AIDS (2018), Common NRTIs include zidovudine (AZT), lamivudine (3TC), abacavir (ABC), tenofovir disoproxil fumarate (TDF), Emtricitabine (FTC), AZT + 3TC, 3TC + TDF, AZT + 3TC + ABC, etc.; NNRTIs are commonly used as Nevirapine (NVP), Efavirenz (EFV), Rilppivrine (RPV), etc.; Common PIs include Atazanavir (ATV), Lopinavir and Ritonavir (LPV/r), etc.; Dolutegravir (DTG) and Raltegravir (RAL) are commonly used in

INSTIs; Common use in FIs include Enfuvirtide (ENF) and Albuvirtide (ABT); And Maraviroc (MVC) is most commonly used in CCR-5 [11]. A foreign study by Alejos et al [58] investigated effectiveness and safety of first-line antiretroviral regimens among PLWHIV in a clinical center from 2004 to 2018 via cohort research method, and found that the most frequently prescribed regimen was ABC/3TC/DTG, and Sun et al [59] suggested in a study investigating blood lipids and risk factors of dyslipidemia among PLWHIV in a hospital of Shenzhen, China, between 2014-2018, that as for adults and adolescents, 2 NRTIs plus 1 NNRTI or boosted PI, that is, TDF or AZT + 3TC + EFV, NVP or LPV/r, are recommended regimens in China currently, with TDF + 3TC + EFV being the most preferred selected first-line regimen, followed by AZT + 3TC + EFV, TDF + 3TC + LPV/r, and AZT + 3TC + LPV/r, which is also founded out in a study by Sun et al [60], This might be caused by the fact that TDF/AZT/3TC/EFV/NVP/LPV/r are free in China right now according to China Health Insurance.

1.2.2.2 Possible adverse events to HAART

1.2.2.2.1 Panorama of adverse events

Adverse events (AE), also known as Adverse drug reactions (ADR), is defined as "An appreciably harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product, which predicts hazard from future administration and warrants prevention or specific treatment, or alteration of the dosage regimen, or withdrawal of the product." [61] Montané et al [62] has reported that AE could result in a high risk of morbidity and mortality, which are responsible for over 6% of hospital admissions and an estimated death rate of 2% in US. Recent studies conducted in developed countries reported a similar mortality due to AE ranged among 0.05% and 3% from global perspective [63, 64], while another study conducted in a developing country suggested 1.8% of death rate and 1.7% in developing and developed countries respectively [65]. It was also indicated by Patton et al [66] that AE could not only impact on patients' quality of daily lives but also prolong hospital stay, rising economic burden, resulting in adverse outcomes. Therefore, it is necessary to assess, diagnose and intervene AE in time.

1.2.2.2.2 Common AE of HAART

1.2.2.2.2.1 Skin reaction

Most studies recently have proved that Skin reaction like rash was the most common AE among PLWHIV who received HAART, especially for PLWHIV who used NVP and EFV [11]. Koochak et al [67] investigated in a Voluntary Counseling and Testing (VCT) center in a hospital of Iran between 2009 and 2010 through a cross sectional study to learn about the

most common AE among PLWHIV and found out skin rash to be the most frequent clinical AE which accounted for 28% among all the participants. Similar result was demonstrated in the research of Gudina et al [68], with the finding that a total of 36.6% of AE was associated to the skin.

1.2.2.2.2.2 Gastrointestinal disorder

Gastrointestinal disorder is also a common AE among PLWHIV which could impact quality of life even to have substantial adverse outcomes. Hall [69] searched articles about digestive system complications relative to HAART and indicated that diarrhea and nausea and vomiting (NV) are still problems which frequently occurred among PLWHIV. Chepkondol et al [70] suggested that diarrhea was a common problem for PLWHIV after investigating prevalence of OIs and AE through a cross-sectional study in 2010 in Kenya. Another case by Riva et al [71] reported a patient experienced nausea, severe epigastric pain radiating to the back, episodes of non-bloody non-bilious vomiting and anorexia after starting BIC/FTC/TAF regimen for 45 days. Similar result was found from a statement of a 39-year-old American man who told that he had nausea/vomiting with abdominal pain after starting HAART for three months, reported by Douse et al [72].

1.2.2.2.2.3 Myelosuppression

According to the guidelines, myelosuppression might happen after receiving AZT, sometimes might also be caused by other regimens [11]. Nakaharai et al [73] reported a case of a 56-year-old Japanese man who experienced myelosuppression after DTG regimen for five months. Currently there are few studies reported myelosuppression associated with HIV-infection and HAART regimens.

1.2.2.2.2.4 Metabolic disorder

It is reported that metabolic disorder is always caused by HAART regimens, especially commonly seen in AZT, EFV and TDF regimens [11]. Noubissi et al [74] conducted a systematic review and suggested in the review that EFV was obvious to increase blood glucose levels which could contribute to the development of diabetes. Another systematic review reported by Masenga et al [75] has shown that HAART therapy might lead to changes in adipose tissue morphology, distribution, and metabolism among PLWHIV, of which the risk would be higher with the age growing. Similar statements were indicated in other studies [76-79].

1.2.2.2.2.5 Drug-induced liver injury

All HAART regimens are reported to lead to liver toxicity varying from transaminitis to frank liver failure [80-83]. Tesfa et al [84] conducted a study with 152 participants to evaluate

liver enzyme among PLWHIV who were treated with HAART compared with who were not in a short term, and found out that around 25% of PLWHIV who took HAART developed mild to moderate liver enzyme elevation which indicated that liver injury could be caused by HAART. Mahajan et al [85] reported in a mixed cohort study among 400 PLWHIV to assess their liver function that all the drugs of HAART would cause different degrees of liver injuries.

1.2.2.2.2.6 Drug-related kidney injury

Drug-related kidney injury could mostly occur when using TDF during HAART [11]. Cattaneo et al [86] indicated in the research that TDF played a significant role in chronic kidney disease, which was similarly reported in other studies [87-89]. Adedeji et al [90] conducted a study among 102 PLWHIV to assess renal toxicity during HAART use, and found that EFV, TDF and 3TC could all impact on renal function in different degrees. Ryom et al [91] also indicated that renal impairment could be caused by several drugs, especially TDF.

1.2.2.2.2.7 Mental and neurological symptoms

Neurological symptoms were reported as another major problem of AE when taking HAART [67]. Adoukonou et al [92] suggested in a study conducted in 2011 among 262 PLWHIV who took HAART that Distal sensory polyneuropathy (DSP) was the most frequent neurological complication among PLWHIV with risk rising up when use HAART continuously, which was similarly reported in another study by Phillips et al [93]. Been et al [94] indicated in a study investigating 352 individuals from 2012 to 2013 that psychological disorders could be associated closely with HAART. Another research by Ren et al [95] found out that sleep quality could be decreased because of anxiety or depression caused by drug regimens throughout cross-sectional method in 2013 in a hospital of China.

1.2.2.3 Risk factors of AE in HAART

Recent studies have suggested that AE among PLWHIV could not only be associated with drug itself but other characteristics such as gender, age, complications and so on [96]. Gebreyohannes et al [97] conducted a cross-sectional study between 2015 and 2016 among PLWHIV to evaluate risk factors impacting AE during HAART use and reported that sociodemographic information including age, gender, education, employment, and marital status, were closely relative to AE when taking HAART. Similar results were reported in another research by Beusekom et al [98]. Pimentel et al [99] investigated 5,177 PLWHIV from 2001 to 2017 age was associated with AE, with aging growing the risk of experiencing AE would be higher, especially meeting with cardiovascular disease. Another study conducted by

Onoya et al [100] found out that alcohol consumption could also cause AE during HAART therapy. In fact, AE in HAART are independently associated with many clinical factors, including frequent changes in HAART regimens, demographic characteristics and other clinical data. AE could be predicted and given timely assessment with decision support, if risk factors are monitored each time follow-up with not only personal records shown in the clinical system but all the expected clinical indices presented as a time line chart at the same time as well [101].

1.2.2.4 AE monitoring, assessment and intervention

Continuous monitoring and assessment on AE for those PLWHIV plays a significant role in minimizing the influence of AE among HAART use. A study conducted in Ethiopia by Tamirat et al [14] has reported a clinical AE monitoring center built to collect and analyze all information about AE when taking HAART to help clinicians and nurses measure the risks and assist them make decisions. Rukmangathen et al [102] used World Health Organization causality assessment scale and Modified Hartwig and Siegel Severity Scale to assess the severity of AE reported as for monitoring. Besides, a center was indicated to specially receive AE reports among PLWHIV in India. Mancano et al [103] discussed about methods to assess and prevention of AE among PLWHIV, suggested that white blood cell count, $CD4^+$ cell count and virus load must be examined, as well as facial expression, mental situation being observed. Horne et al [104] conducted a study via Identity subscale of the Illness Perceptions Questionnaire-Revised (IPQ-R) which was composed of 11 symptoms and Beliefs about Medicines Questionnaire (BMQ) to measure AE among PLWHIV, believing that physical and mental situation were both important during AE monitoring. Different scales and clinical indices as well as symptoms self-report are used in AE monitoring and assessment among clinicians and nurses, on which clinical decision making and nursing intervention will be based. There are ways to help prevent and treat AE. Gebreyohannes et al [97] suggested in their study of intervene those who experienced AE during HAART therapy that pictogram intervention could decrease the risk of getting AE. Similar result was proved in another study by Revol et al [105]. Calva et al [106] pointed out directly that changing to a suitable regimen plan was the most effective way to treat AE, and specific nursing care for each symptom PLWHIV experienced was also necessary. Nasreddine et al [107] reported similar result, for instance, diet education and nursing care were supposed to be used among PLWHIV who suffered from glucose metabolic disorders. Above all, AE monitoring is crucial during HAART treatment, with clinical data, health records, facial observation and self-report at the same time to help health professionals assess risk or severity of AE among PLWHIV. As for

decision and intervention for PLWHIV who already had AE, Change of HAART regimen is the foremost method, with specific nursing intervention such as diet education for metabolic disorders, skin care for skin rash, activity education for renal impairment and so on.

1.2.3 Digitalization development supporting AIDS treatment

1.2.3.1 Current domestic and foreign status of digitalization in AIDS career

With the advent of 5 Generation era and the continuous development of mobile medicine, the prediction, diagnosis and treatment of AIDS and the research of therapeutic drugs have entered a new stage. Currently, researchers are committed to using data mining technology, knowledge base technology, big data management, speech recognition technology and other technologies to assist AIDS diagnosis, trend prediction and decision support therapy from different angles. As for clinicians and nurses, digital health in AIDS has become an expanded universe of potential tools to improve scientificity, accuracy and work efficiency, as well as helping patients awaken awareness of self-management. For instance, Gibson et al [108] reported in a literature review that SMS reminders were commonly used in some developing countries in Africa to remind PLWHIV of taking medicine in time. In addition, digital health records are currently used commonly all over the world not only in AID career but other medical fields as well. Balán et al [109] designed a mobile application called SMART test to help accomplish self and partner testing, with similar applications designed by Biello et al [110] and Rodríguez et al [111]. Chinese studies have also designed information systems and smartphone applications to assist clinicians and nurses as well as patients to implement chronic disease management of AIDS. Guo et al [112] recruited volunteers to conduct a RCT in 2018 to test the usability of a WeChat-based mHealth platform aiming at managing PLWHIV complicated with mental problems. Another m-health application was developed by Yan et al [113] for partner notification to encourage interactive queries among MSM before having sex and even before meeting, which was approved later to reduce the risks of AIDS transmission. Fan et al [114] implemented an AIDS case management information system to help MSM with self-management. Apart from m-health software, technology's processing of AIDS data is also a hot spot among current research. Chen et al [115] conducted a study throughout text mining information technology in order to extract those words which were significant during the year of 2006 to 2013 in different cities of China and the US. Nan et al [116] monitored AIDS epidemics in China using a machine learning method of artificial neural networks (ANNs), which suggested that the technical application of big data was also playing an increasingly key role in the field of AIDS. Above all, it is obvious that different technologies of medical informatics are used in AIDS career, especially applications and data governance. Therefore,

it is necessary to seize the opportunity, keep up with the trend of the times, speed up the construction of AIDS informatization and manage AIDS clinical data in China.

1.2.3.2 Domestic and foreign research status and development prospects of special disease database

With the development of cloud platform and big data technology, medical big data has played an important role in the diagnosis and treatment of many diseases. The construction of special disease database is a new big data platform governance technology in recent years, which refers to an information software system for centralized management of case information of a single disease, conducting systematic and standardized management of clinical case information data of a large number of relevant cases with scientific research significance and practical value in order to realize rapid query of past case information of the disease and statistical data analysis, thereby conducting clinical research, giving clinical diagnosis and treatment with providing valuable information or meet the needs of clinical teaching [16]. In the process of clinical diagnosis and treatment, a large amount of medical information will be generated, including clinical characteristics, drug treatment, inspection, imaging treatment, disease outcome and other clinical data, as well as epidemiological and economic data [117]. However, these data are usually lack of structure and standard data set. In carrying out the research, there are still some problems, such as heavy workload, low efficiency, high error rate and difficult to share the collected data [118]. Therefore, many medical institutions began to try to build a unified database of specific diseases to facilitate the development of clinical care and scientific research.

At present, the research of special disease database has gradually become a hot spot, but due to the recent rise of technology, the research of special disease database is not very mature, researchers are committed to explore the method of data standardization, in order to improve the data governance technology and build a mature special disease database. Bowdish et al [118] reported that clinical data from different information systems were tried to be added into the Adult Cardiac Surgery Database built in 1980s recently, in order to make research more convenient. Rappaport et al [119] suggested that they were trying to add diverse clinical data into the MalaCards, an amalgamated human disease compendium. Actually, there is a lack of foreign literature on the formation of specialized disease database, and most of the relevant literature indicates that the specialized disease database integrating all clinical data is in the exploratory stage. In contrast, there are more researches on special disease database in China, with some databases already being used in clinic. Jia et al [120] have developed a database called PedAM integrating both biomedical resources and clinical data

from health records of patients in order to help users search information directly in an integrated system. Sun et al [121] conducted a study building up a Nasopharyngeal Carcinoma database and kept updating since 2015. Currently there are 39 specialists and researchers applied the database to real-world research with more than 400 research projects. Similar databases have been established in the field of gastric carcinoma, arteriosclerosis obliterans, thymus adenoma and so on [122-124].

Above all, the domestic research on special disease database is becoming more and more active. However, currently there is lack of report on the construction of the special database for AIDS in China. It is conducive to continuously improve the level of AIDS clinical research, individualized treatment, precise treatment, and balance the cost and benefit of treatment, and pre-test the best clinical treatment path, so as to enhance the quality of special medical services for AIDS Through the establishment of standardized, unified, professional authority, open sharing, on-demand expansion, coverage of the whole disease follow-up tracking AIDS special database. At the same time, it supports the high-quality development of biomedicine industry and lays an important foundation for the construction of national clinical medicine research center of AIDS. Therefore, it is significant to establish an AIDS database to provide platform support for high level scientific and technological research and lay an important foundation for the construction of national AIDS clinical center.

1.2.3.3 Research status and prospects of adverse events monitoring view for PLWHIV

The unified view of clinical indicators has existed for a long time, and the most common one is the presentation of basic vital signs on ECG. However, the clinical unified view can only be limited to a single system owing to the lack of structured and standardized data. There is also a lack of relevant research on the presentation of all clinical data in a unified view among domestic and foreign studies. Chen et al [125] realized the clinical data association and integration of various information systems through the construction and application of clinical unified view based on patient indices. A real-time, accurate, clear and friendly unified diagnosis and treatment information interface was presented to the clinical staff from the two dimensions of treatment time and clinical activities, so that the health professionals can quickly and comprehensively understand the patient's medical history and previous diagnosis and treatment process. Besides, they are studying to present the clinical indicators of patients in the form of trend chart, so that clinicians can have an intuitive understanding of the past signs. Liang et al [126] developed a unified View of traditional Chinese medicine (TCM) Entities making the drug information searched intuitively and quickly. As a visualization tool, the unified view can more intuitively reflect the patient's situation than a single text message,

so that health professionals can predict trends and assist them in clinical decision-making. Nevertheless, the existing unified views are embedded in the clinical information system or presented as independent products, only displaying a certain type of clinical data due to the inconsistent data standards of various systems. And the unified view designed based on special disease database in this study can effectively solve the problem of data islands, and present all kinds of clinical information in the form of structured data at the same time.

It is believed that all the wanted clinical indicators presented in the unified view in the form of trend chart with other expected information from other information systems could be realized based on the AIDS database, which would bring great help to improve the efficiency of clinicians and nurses. Therefore, this study is aiming at developing an AE Monitoring View for PLWHIV to make clinicians and nurses assess AE via a more intuitive way. In addition, in order to enrich the function of this monitoring view and make the health professionals experience better, this study decided to add the clinical decision support function. The most common AE among PLWHIV who take HAART and clinical treatment suggestions, nursing diagnosis and nursing intervention suggestions for AE will be put forward through consulting the literature, guidelines and qualitative research. After doctors and nurses evaluate the risk of AE or diagnose PLWHIV who have AE through the trend shown on the unified trend chart, they can click on AE and decision-making suggestions to assist their own judgment and finally make a decision.

1.3 Definitions of key concepts

1.3.1 AIDS

Acquired immunodeficiency syndrome (AIDS), is a malignant infectious disease caused by human immunodeficiency virus (HIV), which is transmitted sexually, via blood transfusions, sharing intravenous needles, and from the mother to a child during the birth process and breastfeeding [128].

1.3.2 People living with HIV (PLWHIV)

It refers to people infected by human immunodeficiency virus (HIV), including HIV-infected persons and AIDS patients. AIDS is the final stage after HIV infection [129]. PLWHIV used in this study specifically refer to the HIV-infected persons who attend the VCT clinic of Shanghai Public Health Clinical Center and participate in the follow-up and PLWHIV who are included in the AIDS database.

1.3.3 The Delphi method

It is also known as the estimate-talk-estimate technique (ETE), which is a systematic and qualitative framework for forecasting the process based on collection of opinions from multiple rounds of questionnaires filled up by a panel of chosen experts in order to arrive at a group consensus [130]. In this study, the researchers set up a research team to construct the AE Monitoring View for PLWHIV, compile the questionnaire and use back-to-back communication to conduct several rounds of inquiries to the members of the expert group, and finally determine the contents for PLWHIV adverse drug reaction monitoring view based on the comprehensive opinions of the experts. The expert group opines their views to an initiator or facilitator who then summarizes the gathered information into an understandable report [131].

1.3.4 Hospital Information System (HIS)

It refers to the use of modern means such as computer software and hardware technology, network communication technology, to comprehensively manage the flow of people, logistics, and finances in the hospital and its various departments; to collect, store, process, and extract data generated during each stage of medical activities, Transmission, aggregation, and processing to generate various information, so as to provide comprehensive and automated management and various service information systems for the overall operation of the hospital [132].

1.3.5 Clinical Information System (CIS)

It is part of a hospital information system which performs the data produced in the various stages of medical activities collection, storage, processing, extraction, transport, processing aggregate and generate a variety of information to support clinical activities of hospital staff, and accumulated rich clinical medicine knowledge; and provide clinical consultation, auxiliary diagnosis and treatment, and auxiliary clinical decision-making to improve medical quality and work efficiency [133].

1.3.6 Special disease database

It refers to an information software system for centralized management of case information of a single disease, which conducts systematic and standardized management of clinical case information data of a large number of relevant cases with scientific research significance and practical value in order to realize rapid query of past case information of the disease and statistical data analysis, thereby conducting clinical research, giving clinical diagnosis and treatment with providing valuable information or meet the needs of clinical teaching [16].

1.3.7 Clinical information unified view

It means that clinical medical workers and scientific researchers can consult the patient's medical information through a clear and friendly unified view, so that they can have an overall understanding of the patient's medical condition in a short time [18]. The monitoring view constructed in this study specifically refers to the view that monitors drug adverse reaction for PLWHIV based on the AIDS database to support clinical medical staff and scientific researchers on decision about drug adverse reaction and therapy and nursing intervention throughout visual data.

1.4 Research purpose

1.4.1 Overall objectives

To construct an AE Monitoring View for PLWHIV.

1.4.2 Specific objectives

1.4.2.1 To investigate the demand to AE Monitoring View for PLWHIV among clinicians and nurses,

1.4.2.2 To construct the framework of AE Monitoring View for PLWHIV,

1.4.2.3 To develop and perform functional tests on the implemented functions.

1.5 Research Content and Technology Roadmap

1.5.1 Research questions

1.5.1.1 What is the demand to AE Monitoring View for PLWHIV among clinicians and nurses?

1.5.1.2 How to construct the framework of AE Monitoring View for PLWHIV for clinicians and nurses?

1.5.1.3 How to develop and test the implemented functions of AE Monitoring View?

1.5.2 Research contents

The research was comprised of 3 parts:

Part 1: The demand exploration of AE Monitoring View for PLWHIV among clinicians and nurses

The researcher conducted semi-structured interviews to learn about current monitoring process of AE for PLWHIV, current common and rare AE and interventions on AE for PLWHIV, current problems clinicians and nurses would meet with during AE monitoring process, and their usage requirements on AE Monitoring View.

Part 2: The construction of the framework on AE Monitoring View for PLWHIV

The researcher established a research team with clinicians and nurses and technicians to discuss about the framework and drafted a first version based on relevant literature, drug instructions, Common Terminology Criteria for Adverse Events (CTCAE), and interview results. The researchers then sent the version to 14 experts for expert argumentation, until all experts agreed and the final framework version was finalized and moved to the next stage.

Part 3: Testing and application of AE Monitoring View for PLWHIV

Based on the final version of framework previously developed for AE Monitoring View, the researcher developed and internally tested the view in collaboration with technicians from a medical technology company, which the researcher then handed over to the research team with a questionnaire investigated later to conduct internal feasibility pilot-test for usability evaluation. This view is yet unmature and will be put into use after the AIDS Database is fully constructed in the future.

1.5.3 Technology Roadmap

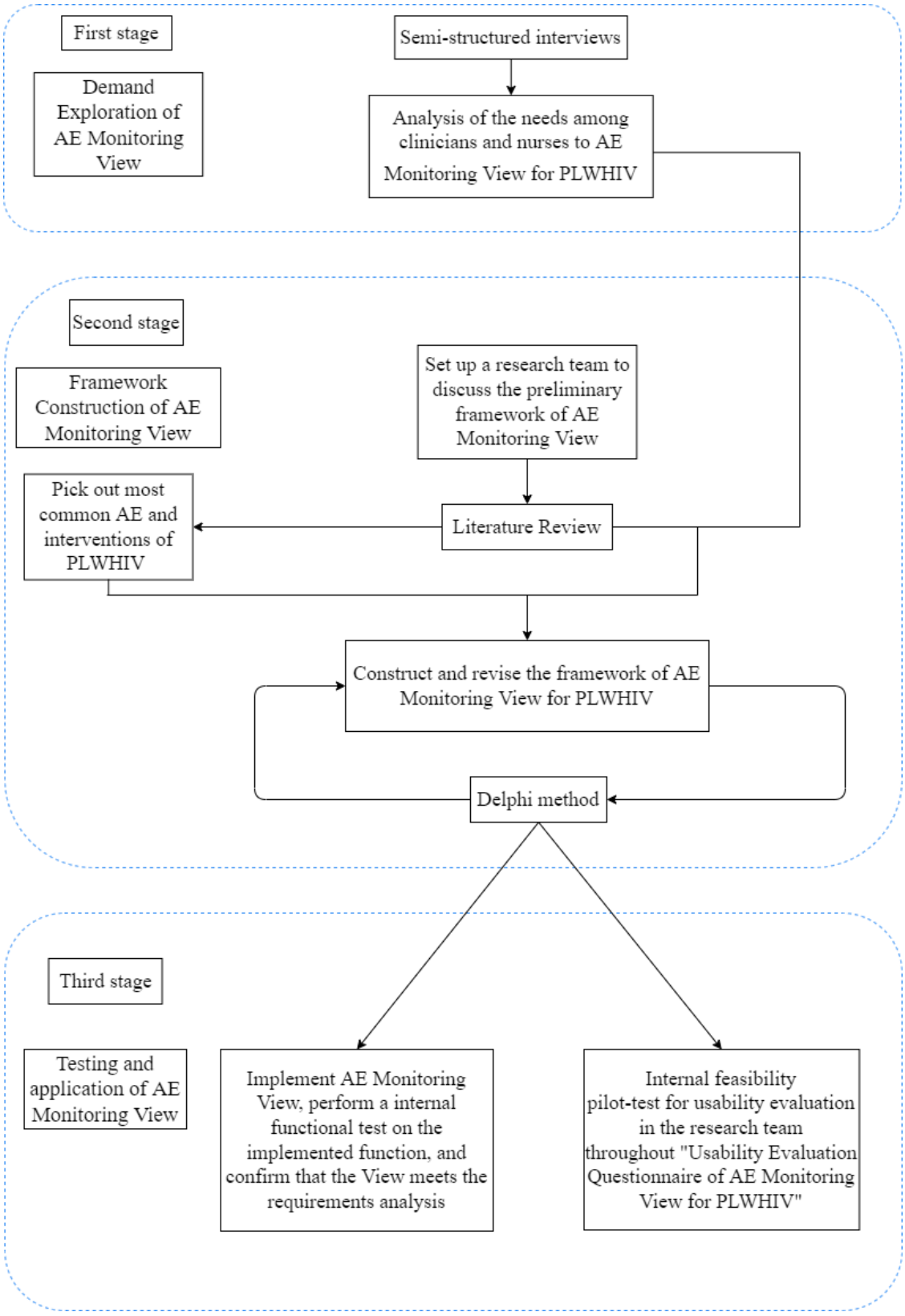


Figure 1-1 Technology Roadmap

2 The demand exploration of AE Monitoring View for PLWHIV among clinicians and nurses

2.1 Research purpose

The researcher conducted semi-structured interviews with clinicians and nurses in the hospital based on qualitative research method to learn about confusions below:

1. The current monitoring process of AE for PLWHIV,
2. The current common and rare AE and interventions on AE for PLWHIV,
3. The current problems clinicians and nurses would meet with during AE monitoring process,
4. The usage requirements for clinicians and nurses on AE Monitoring View for PLWHIV.

2.2 Participants

The most different sample selection strategy in the purposeful sample selection method was adopted in this research. The researcher selected clinicians and nurses who met the criteria engaged in VCT department and HIV/AIDS wards to provide the greatest amount of information for interviews as far as possible.

Inclusion Criteria for clinicians and nurses:

1. Engaged in AIDS-related clinicians and nurses,
2. Worked in AIDS fields for more than 2 years,
3. Voluntary participation in this research.

From August 2021 to September 2021, 11 Clinicians and nurses engaged in VCT department and HIV/AIDS wards in Shanghai Public Health Center were invited to talk about topics above.

2.3 Research methods

2.3.1 Interview outline

The semi-structured interview outline was determined based on the literature reviewed before the start of the research, which was modified according to the effect of pre-interviews on 2-3 clinicians, with finally determining the content of the interview outline (See Appendix IV).

The outline of the interview involved the following:

① What is the current working process on AE monitoring in Shanghai Public Health Clinical Center (SPHC)?
② How do you carry out the clinical monitoring of AE and what is the effect?
③ What do you think are the most common and rare AE among PLWHIV and which should be noticed and found as soon as possible?
④ How do you deal with PLWHIV with AE?
⑤ Do you have any opinions or suggestions on the improvement of AE monitoring methods for PLWHIV?
⑥ What do you think of using IT/digital methods for AE monitoring?
⑦ What are your thoughts and suggestions on presenting clinical data of patients in the form of a unified trend view according to the time axis to monitor AE?

2.3.2 Data collection

This study adopted a semi-structured in-depth interview to collect data. The research started after obtaining the approval of the Ethics Committee of Shanghai Public Health Clinical Center (See Appendix VI).

The researcher explained the purpose, significance, data collection methods and processing methods of the research results to 11 clinicians and nurses before the interview and asked them to fill in the "General Information Questionnaire" so that the researcher could collect general information and retrieve it on site to ensure the accuracy and authenticity of the information (See Appendix II).

The researcher conducted the interview in accordance with the interview outline, with a face-to-face interview lasting 30-60 minutes. The researcher carefully observed the respondent's expressions, movements, and emotional changes, without judging and inducing patients during the interview. The researcher completed each recording and transcription within 24-48 hours after the end of the interview to ensure the timeliness of data analysis.

2.3.3 Data analysis

The researcher used NVivo software as well as the Colaizzi's 7 steps [134] to achieve data analysis. The specific steps are as follows:
① Read all the interview materials carefully, and form a general understanding of the description of the research object,
② Extract meaningful statements that are consistent with the research question,
③ Summarize and refine meaningful statements and code them,
④ Collect the coded opinions, look for common concepts or characteristics, and form themes, subject groups, and categories,

⑤ Link the subject to the research object for a detailed narrative,

⑥ State the essential structure that constitutes the phenomenon,

⑦ Return the final analysis result to the research object, verify the authenticity of the content, and form the final theme.

2.4 Research results

2.4.1 The characteristics of the 11 clinicians and nurses are shown below in Table 2-1.

Table 2-1. Characteristics of clinicians and nurses

No.	Gender	Age	Education background	Professional title	HIV/AIDS working duration
P1	Male	39	PhD	Associate professor	15 years
P2	Female	32	Master	Nurse	5 years
P3	Male	38	PhD	Associate professor	7 years
P4	Male	39	PhD	Attending physician	11 years
P5	Female	31	Master	Nurse	3 years
P6	Male	39	PhD	Attending physician	7 years
P7	Male	40	Bachelor	Attending physician	15 years
P8	Female	39	Bachelor	Attending physician	12 years
P9	Female	43	Bachelor	Supervisor nurse	17 years
P10	Female	39	Bachelor	Nurse	13 years
P11	Female	41	Bachelor	Nurse	15 years

2.4.2 Interview results

2.4.2.1 Current AE monitoring process

At present, there are two most common methods for drug monitoring of HIV-positive patients in hospitals, which are patient self-reports during outpatient follow-up and regular patient review to obtain physiological indicators in the examination report.

2.4.2.1.1 Doctors and case managers jointly monitor patients' AE

At present, most of the HIV-positive patients receiving HAART treatment regularly go to the clinic for review. Some of these patients participate in case management research. They will be followed up by the case manager while attending the doctor's clinic. In fact, the

monitoring of AE for these patients is carried out jointly by case managers (these case managers are composed of specially trained nurses) and doctors who follow up in the outpatient clinic.

P4, "We will let patients come to the clinic regularly, we will ask the patients if there is any discomfort in their body, and the patients will also go to the case manager's clinic to tell them their physical status."

P2, "Our case manager will receive the results of the patient's examination every time, and we will observe whether there are any abnormal indicators and notify the doctor in time. In addition, we will also ask patients if they have had any bad reactions recently when they come for review, and we will also judge whether these are caused by drugs based on our own experience."

2.4.2.1.2 Patient self-reports

Patients' self-reported AE are dominated by specific somatization symptoms, such as dizziness, dreaminess, anxiety, etc. These AE are usually specific symptoms rather than systemic functional impairment.

P6, "We will ask patients if they have any symptoms of discomfort, such as headaches or nausea and vomiting, and we will use our own experience to determine what kind of systemic reactions may be caused by drugs based on these symptoms."

P9, "If the patient has only minor organ damage, many of the AE cannot be observed with the naked eye and the patient will not have uncomfortable symptoms at the early stage of the occurrence. In this case, the patient cannot self-report the adverse reaction."

In addition to some specific symptoms, there are some organ injuries that cannot be obtained by relying solely on patient self-reports at the initial stage of injury.

2.4.2.1.3 Clinical indicators

Organ damages such as liver and kidney injury usually have no clinical symptoms in the early stage of AE. This means that clinical staff can only judge the occurrence of such AE through the physiological indicators of the patient's review.

P1, "Organ AE such as liver injury are not like digestive tract reactions such as diarrhea. These AE will not make the patient feel uncomfortable at all in the early stage."

P9, "We often focus on whether the indicators related to liver and kidney function are abnormal in the inspection report, and we will also check the blood routine, because these indicators are related to the adverse blood reactions such as liver injury, kidney injury or anemia, which patients cannot feel themselves."

It is obvious that some clinical reactions do not have obvious physical symptoms at the initial stage, it is difficult for patients to find out. In this case, clinical medical staff usually observe the patient's physiological indicators to determine whether there is a risk of serious AE.

2.4.2.2 Common and rare AE for PLWHIV

Classified according to the large system, common AE include rash, neurological symptoms, gastrointestinal disorders, drug-induced liver injury, drug-related kidney injury, osteoporosis, myelosuppression, etc. Among them, neurological symptoms, rash, and gastrointestinal disorders have obvious and specific physical manifestations, while liver and kidney injuries have mild clinical symptoms at the initial stage, and physical symptoms are uncommon.

However, there are some AE that are relatively rare, but once they occur and in the middle and late stages, they are likely to lead to irreversible adverse outcomes. Therefore, the precursor signs of such AE should be paid attention to and discovered in time.

2.4.2.2.1 The most common AE are neurological symptoms and rash caused by EFV.

Currently, EFV is commonly used in the domestic first-line treatment program. The AE caused by this drug are the most common and obvious, including rash. Patients may develop symptoms such as skin rash and fever. In addition, the symptoms of the central nervous system are dizziness and dreaminess.

P11, "We often ask patients if they have dizziness, because this is the most common side effect caused by EFV."

P1, "Among the patients I have contacted, many patients develop skin rashes in the early stage of medication. This is a typical drug sensitivity reaction, especially in the first three months of medication, and it will get better after a while."

2.4.2.2.2 Other common AE

Other common AE include gastrointestinal reactions, manifested by varying degrees of nausea, vomiting, and diarrhea. These symptoms generally occur in the early stages of drug treatment and will slowly disappear over time.

P5, "Patients always tell me that they have more diarrhea, sometimes 6-7 stools a day, but most patients with this symptom will get better on their own after a while."

In addition, liver injury and kidney injury are also relatively common. Usually, the abnormality of indicators such as direct bilirubin and indirect bilirubin is related to liver function damage, while the abnormality of glomerular filtration rate indicators is related to kidney function damage.

P11, "We will check the patient's glomerular filtration rate to determine whether there is kidney damage. If it is less than 80%, then it means there is damage and we need to pay attention."

2.4.2.2.3 Rare AE include lactic acidosis, which is the most serious and difficult to cure once it occurs.

Some AE are rare, or the initial symptoms are very difficult to identify, so when they are discovered, they are usually in the middle and late stages, and have very serious clinical manifestations. At the same time, they will be combined with various other infections or complications, which are difficult to cure, and the fatality rate is very high. high.

P7, "I have seen a patient with lactic acidosis. I have not come to our place for a review before. I have a serious discomfort. I came for a checkup. When I looked at the report, the typical blood test index was not good. I judged the lactic acidosis. If you miss the treatment time, you just wait for death."

2.4.2.3 Common interventions from clinicians and nurses on AE for PLWHIV

Common AE are usually caused by the free drug EFV.

At present, for patients with AE, common intervention measures include continuous monitoring, conventional conservative treatment, and replacement of drug regimen. For milder AE, doctors usually choose to strengthen the observation and monitoring of the patient's symptoms; when the symptoms or AE are severe, symptomatic treatment will be given; if the patient cannot tolerate or the conservative treatment fails, clinicians will Choose to change the drug regimen. It should be noted that whether or not to change the drug regimen under non-essential circumstances is more dependent on the patient's wishes, and when necessary, doctors will replace free drugs with self-paid drugs.

2.4.2.3.1 Continuous monitoring

EFV can cause neurological symptoms, psychiatric symptoms, or some gastrointestinal reactions.

P8, "EFV can cause symptoms such as dizziness, dreaming, and insomnia." These symptoms are generally mild and do not have serious consequences.

P5, "Some patients will come to me and tell me that he has a stomachache, or constipation, nausea, etc., but these feelings are not very obvious."

They will naturally get better after a period. The tolerance of different patients to this type of adverse reaction is also different.

P6, "Some patients are well tolerated, maybe he has actually had an adverse reaction, but he can't feel it himself, such as a headache, some people feel the pain is unbearable, and some

people have other diseases and feel that this is fundamental It doesn't feel like, these are all possible."

Therefore, for such AE, doctors usually will not take clear intervention measures for the time being, but will further observe and strengthen monitoring, and continue to pay attention to whether the degree of the patient's AE is aggravated.

2.4.2.3.2 Conventional conservative treatment

For organ damages such as liver and kidney damage, if the patient's physiological indicators suggest mild damage, doctors will generally strengthen monitoring. When a certain threshold is reached, doctors will give priority to conservative treatment and routine use of drugs for symptomatic treatment.

P4, "Some patients may only occasionally high total bilirubin. At this time, we must strengthen observation or look at the previous inspection report. If we judge that the damage is already serious based on experience, then we will use some symptomatic treatment with liver protecting medicine."

P3, "We will find a standard value based on our own experience. Once the standard value is exceeded, I will choose to take medication."

2.4.2.3.3 Replacement of drug regimen

In non-essential circumstances, some patients with better economic conditions will choose to directly change the drug, because the free drug has a higher probability of AE, while the self-funded drug has relatively few or minor AE, so patients with the conditions allow it. Choose to use self-funded drugs. In this case, the doctor will respect the wishes of the patient.

P7, "Some of our patients don't care about money and choose expensive self-funded medicines. The advantage is that the AE will disappear immediately."

However, in fact, most HIV-positive patients have greater financial pressure, and they usually choose to endure some AE that will get better on their own. However, due to physical reasons, the AE of some patients are very slow, or even more and more serious. In this case, it is necessary to change the drug regimen.

P8, "For some people, the rash can't go away and there is no alternative but to change the medication regimen."

2.4.2.4 The problems of current AE monitoring process

At present, the continuity and accuracy of monitoring are the biggest problems in the monitoring of AE, and what kind of intervention measures should be taken for AE also urgently need to be standardized.

P1, "Actually, I often reflect on myself. Sometimes I don't have enough time to ask patients about their symptoms."
P9, "Symptoms such as dizziness and nausea must be missed in the hospital. Even if asked, the patient may not necessarily say it."

Many symptoms can only be discovered through patient self-reports, and these AE are easily overlooked.

The process of reviewing historical inspection reports and indicators by doctors is cumbersome and inefficient, and at the same time it is easy to miss some physiological indicators.

P4, "I may see that one index of the patient is not good this time, and to judge liver damage, then I will also look through his original report to see if the value of this index before him is normal, but I may look through it two or three times more. Otherwise, it will take too much time."

Insufficient reading of the inspection report may lead to inaccurate judgments on the trend of AE.

Clinicians sometimes choose interventions excessively based on experience.

P8, "I sometimes set the threshold based on my own experience and decide whether to treat the symptoms or change the plan."

In the process of monitoring AE, there is no standard for the cut-off value of treatment, which can easily lead to changes in the intervention effect, which has a certain impact on patients.

2.4.2.5 Requirements on AE Monitoring View for PLWHIV

2.4.2.5.1 Visualization tool

Clinical medical workers need a clear view of the dynamic changes of patient physiological indicators. This view helps clinical medical staff to judge whether the patient is at risk of AE, so that intervention measures can be taken as soon as possible and in a timely manner.

P1, "I really hope to have a visualized view so that I can quickly see the changing trend of the patient's various organ functions."
P5, "The trend chart is necessary to save time and quickly find the previous physiological indicators, and the judgments made based on the trend chart will be relatively more accurate."

It can be seen that clinical medical staff need the patient's physiological indicators to be presented in the form of a visual dynamic trend chart, which helps clinical medical staff to

judge the patient's physical condition throughout the course of the disease according to the complete change trend, and make timely countermeasures.

2.4.2.5.2 Complete list of AE and their manifestations

Clinical medical staff is under great pressure, and it is inevitable that the complete adverse drug reaction will be forgotten and missed. Therefore, a complete list is necessary.

P6, "I sometimes forget some AE and don't pay too much attention to it."

P2, "I really need a list that allows me to quickly find the AE I need. I usually can't remember all of them in the clinic."

Therefore, listing a complete list of possible AE of the drug and the symptoms of these AE will help doctors to monitor the occurrence of AE in patients more comprehensively and accurately.

2.4.2.5.3 Recommendations on standard intervention measures for different drug AE based on literature and guidelines

At present, clinical medical workers have the general direction of treatment, and different doctors have different standards for standardized intervention thresholds. Therefore, it is very necessary to present intervention suggestions in the system according to the guidelines.

P1, "I don't even need the complete guideline recommendations, but I hope to give me a standard threshold that tells me what is considered mild, what is considered severe, when I should start the medication, and when I must change the medication regimen."

P4, "It is very necessary to have guidelines-based intervention recommendations, which will help us to make decisions very well."

It can be seen that clinical medical staffs are in great need of guidelines-based adverse drug reaction intervention measures, which will help them to make efficient and accurate clinical decision-making. It is of great significance to the treatment of patients and the monitoring of AE.

2.5 Discussion

Patient self-report and objective data to clinical indicators are currently the most important and direct way to monitor AE for PLWHIV. Rukmangathen et al [102] used World Health Organization causality assessment scale and Modified Hartwig and Siegel Severity Scale to assess the severity of AE reported as for monitoring. Besides, Mancano et al [103] discussed about methods to assess and prevention of AE among PLWHIV, suggested that

white blood cell count, CD4+ cell count and virus load must be examined, as well as facial expression, mental situation being observed.

Domestic and foreign studies have indicated that common AE includes rash, gastrointestinal reaction, metabolic disorders, mental and neurological symptoms, and so on. It is reported that metabolic disorders are always caused by HAART regimens, especially commonly seen in AZT, EFV and TDF regimens [11]. Noubissi et al [74] conducted a systematic review and suggested in the review that EFV was obvious to increase blood glucose levels which could contribute to the development of diabetes. However, the participants in this research suggested that the most common AE are neurological system symptoms and rash caused by EFV, and metabolic disorders are difficult to detect early due to long latency.

At present, for patients with AE, common intervention measures include continuous monitoring, conventional conservative treatment, and replacement of drug regimen. Gebreyohannes et al [97] suggested in their study of intervene those who experienced AE during HAART therapy that pictogram intervention could decrease the risk of getting AE. Similar result was proved in another study by Revol et al [105]. Calva et al [106] pointed out directly that changing to a suitable regimen plan was the most effective way to treat AE, and specific nursing care for each symptom PLWHIV experienced was also necessary. In this research, the clinicians and nurses demonstrated that they tended to observe the symptoms or refer to the indicators first and decide how to cope with the AE due to the observation results.

In fact, clinical medical staffs are in great need of guidelines-based AE intervention measures, which will help them to make efficient and accurate clinical decision-making. Currently, researchers are committed to using data mining technology, knowledge base technology, big data management, speech recognition technology and other technologies to assist AIDS diagnosis, trend prediction and decision support therapy from different angles. Therefore, AE Monitoring View is unstoppable trend. In this research, the researcher and the research team screened the most commonly used drugs in the hospital based on the interview results, and sorted out all possible AE over these drugs according to the needs of clinicians, literature, drug description and CTCAE.

3 The Framework Construction of AE Monitoring View for PLWHIV

3.1 The literature review of the research team for AE Monitoring View for PLWHIV

3.1.1 The establishment of research team for AE Monitoring View for PLWHIV

3.1.1.1 Research purpose

The researcher established a research team for frame design and content construction on AE Monitoring View for PLWHIV.

3.1.1.2 Participants

The researcher used purposive sampling method to select participants including technicians and clinical staffs.

Inclusion criteria for technicians:

1) Familiar with medical information system,

2) Understand basic knowledge about HIV/AIDS,

3) Volunteer to participate in this research.

Inclusion criteria for clinical staffs:

1) Familiar with HIV/AIDS,

2) Familiar with medical information system and have basic knowledge about construction on medical informatics,

3) Volunteer to participate in this research.

3.1.1.3 Research results

11 participants including 2 technicians, 3 clinicians and 6 nursing staffs were finally invited to build up a research team for framework design on AE Monitoring View for PLWHIV.

The average age of the research team is 35.55 (±9.59), and the average working/HIV researching duration is 12.55 (±9.39) years.

The characteristics of the research team members are shown below in Table 3-1.

Table 3-1. Characteristics of research team members (N=11)

No.	Gender	Age	Education background	Working area	Research duration
1	Male	38	PhD	Technician	10
2	Male	37	Master	Technician	15
3	Male	56	PhD	Clinician	30
4	Female	46	Master	Nursing	28
5	Male	31	PhD	Nursing	13
6	Female	37	Master	Clinician	14
7	Male	39	PhD	Clinician	11
8	Female	32	Master	Nursing	10
9	Female	26	Bachelor	Nursing	3
10	Female	25	Bachelor	Nursing	2
11	Female	24	Bachelor	Nursing	2

3.1.1.4 Discussion

In this part, the researcher constructed a research team composed of technicians and clinicians and results showed that the members of the research team were moderate in age and had a long working experience in the field of AIDS, which was enough to prove the high level knowledge of the members of the research team on AIDS, Due to the familiarity with the content of this study, the research team would be a driving force in the progress of the follow-up research process.

3.2.2 The literature study of the research team for AE Monitoring View for PLWHIV

3.2.2.1 Research purpose

To design the framework of the AE Monitoring View, it is crucial to learn about existing adverse events as well as electronic system. Therefore, in this part of the research, the researcher searched the literatures with other members of the research team and discussed for several rounds to determine the first version of the framework of AE Monitoring View for PLWHIV.

3.2.2.2 Research methods

The researcher searched the drug instructions on the official website, and also consulted a large number of relevant literature and guidelines on PubMed, Web of Science and CNKI, sorted out common and rare AE for PLWHIV to determined drugs and their interventions with the whole research team. In addition, the researcher also normalized and

unified the terms of the searched adverse events according to the existing Common Adverse Event Evaluation Criteria (CACTE). Finally, after the joint discussion of the research team, the first version of the adverse events and intervention framework to be submitted to experts for demonstration was constructed.

3.2.2.3 Research results

Based on the demand exploration before in the first phase and literature review with the research team, the first version of the framework of AE Monitoring View for PLWHIV includes 6 levels, which are the name of the drug, the disease system to which the adverse event belongs, the name of the specific adverse event, the degree of occurrence of the adverse event, the clinical manifestations of the patient and the corresponding intervention measures. Table 3-2 shows the general framework of the AE Monitoring View for PLWHIV without details and all the contents of the first version are shown in Figure 3-1.

Table 3-2. The general framework of AE Monitoring View for PLWHIV

Level 1	Level 2	Level 3	Level 4	Level 5	Level 6
Abacavir (ABC) Efavirenz (EFV) Lamivudine (3TC) Tenofovir Disoproxil Fumarate (TDF) Zidovudine (AZT) Lopinavir / Ritonavir (LPV/r) Dolutegravir (DTG) Nevirapine (NVP)	The disease system to which the adverse event belongs.	The name of the specific adverse event.	Grading indicators, including 5 levels.	The clinical manifestations of the patient.	Interventions corresponding to different grades of each adverse event.

药物名称（中文）	药物名称（英文）	药物名称（缩写）	不良反应（系统）	具体不良反应	分级指标	症状表现	干预措施
阿巴卡韦	Abacavir	ABC	免疫系统疾病	过敏反应	Ⅰ级	无	无
					Ⅱ级	无	无
					Ⅲ级	荨麻疹	1. 荨麻疹损害区域小于10%的体表面积：局部治疗或加强监测 2. 荨麻疹损害区域覆盖10-30%的体表面积：口服药物治疗 3. 荨麻疹损害区域大于30%的体表面积：静脉给药治疗 4. 更换药物治疗方案
					Ⅳ级	无	无
					Ⅴ级	无	无
			胃肠道疾病	恶心	Ⅰ级	食欲降低，不伴进食习惯改变	加强监测
					Ⅱ级	经口摄食减少不伴明显的体重下降，脱水或营养不良	更换药物治疗方案
					Ⅲ级	经口摄入能量和水分不足	更换药物治疗方案；需要鼻饲，全肠外营养或者住院
					Ⅳ级	无	无
					Ⅴ级	无	无
				呕吐	Ⅰ级	轻度：轻度呕吐1-2次	加强监测；不需要进行其他干预
					Ⅱ级	中度：呕吐3-5次	门诊静脉补液；需要进行医学干预
					Ⅲ级	重度：呕吐6次以上	更换药物治疗方案；需要鼻饲，全胃肠外营养或住院治疗
					Ⅳ级	危及生命	紧急干预；更换药物治疗方案
					Ⅴ级	死亡	无
				腹泻	Ⅰ级	与基线相比，大便次数增加每天<4次；造瘘口排出物轻度增	加强监测
					Ⅱ级	与基线相比，大便次数增加每天4～6次；造瘘口排出物中度增加；僭防于工具的日常生活活动受限	口服补液；更换药物治疗方案
					Ⅲ级	与基线相比，大便次数增加每天≥7次；与基线相比，造瘘口排出物重度增加；自理性日常生活活动受限	更换药物治疗方案；需要住院治疗
					Ⅳ级	危及生命	需要紧急治疗
					Ⅴ级	死亡	无
			神经系统疾病	眩晕	Ⅰ级	轻度不平稳或有移动感	加强监测
					Ⅱ级	中度不平稳的：影响工具性日常生活活动	减少药物剂量
					Ⅲ级	重度不平稳或有移动感：影响自理性日常生活活动	更换药物治疗方案
					Ⅳ级	无	无
					Ⅴ级	无	无
				头痛	Ⅰ级	轻度疼痛	加强监测
					Ⅱ级	中度疼痛：影响工具性日常生活活动	减少药物剂量
					Ⅲ级	重度疼痛：影响自理性日常生活活动	更换药物治疗方案
					Ⅳ级	无	无
					Ⅴ级	无	无
				嗜睡	Ⅰ级	轻度睡眠需求增加	加强监测
					Ⅱ级	中度睡眠需求增加	减少药物剂量
					Ⅲ级	重度睡眠需求增加	更换药物治疗方案
					Ⅳ级	无	无
					Ⅴ级	无	无
			免疫系统疾病	过敏反应	Ⅰ级	无	无
					Ⅱ级	无	无
					Ⅲ级	荨麻疹	1. 荨麻疹损害区域小于10%的体表面积：局部治疗或加强监测 2. 荨麻疹损害区域覆盖10-30%的体表面积：口服药物治疗 3. 荨麻疹损害区域大于30%的体表面积：静脉给药治疗 4. 更换药物治疗方案
					Ⅳ级	无	无
					Ⅴ级	无	无
			精神疾病	焦虑	Ⅰ级	轻度症状：烦躁不安；紧张	加强监测；减少药物剂量
					Ⅱ级	中度：影响工具性日常生活活动；心动过速	更换药物治疗方案；无需住院
					Ⅲ级	重度症状：影响自理性日常生活活动；呼吸困难	更换药物治疗方案；转精神卫生中心进行专病治疗
					Ⅳ级	危及生命	紧急干预；转院治疗
					Ⅴ级	死亡	无
				抑郁症	Ⅰ级	轻度症状	加强监测；减少药物剂量
					Ⅱ级	中度症状：影响工具性日常生活活动	更换药物治疗方案；无需住院
					Ⅲ级	重度症状：个人自理能力受限	更换药物治疗方案；无需住院
					Ⅳ级	危及生命：患者自己或他人	更换药物治疗方案；转精神卫生中心进行专病治疗
					Ⅴ级	死亡	无
				失眠症	Ⅰ级	轻度睡眠困难，保持睡眠状态或平衡	加强监测
					Ⅱ级	中度睡眠困难，保持睡眠状态或平衡	减少药物剂量
					Ⅲ级	重度睡眠困难，保持睡眠状态或平衡	更换药物治疗方案
					Ⅳ级	无	无
					Ⅴ级	无	无

Figure 3-1. The first version of the framework of AE Monitoring View for PLWHIV (1)

依非韦伦	Efavirenz	EFV	新陈代谢与营养不良	高血脂症	Ⅰ级	高胆固醇血症:应用总胆固醇增高>5.72 mmol·L-1，三酰甘油正常；高三酰甘油血症:血清三酰甘油增高>1.70 mmol·L-1，总胆固醇正常；混合型高脂血症:血清总胆固醇和三酰甘油含量均增高,即总胆固醇>5.72 mmol·L-1,三酰甘油>1.70 mmol·L-1；低高密度脂蛋白血症:血清高密度脂蛋白胆固醇降低<1.2	加强监测；患者需要改变饮食习惯
					Ⅱ级	局限性皮下脂肪萎缩:多见于面部、四肢及臀部；向心性脂肪堆积:多见腹部、胸部、颈部、背部,形成所谓水牛背及脂肪瘤	药物干预，常用药物有他汀类:如洛伐他汀、辛伐他汀、普伐他汀；贝特类:如苯扎贝特、非诺贝特、吉非罗齐；烟酸类:如氯甲吡喏等
					Ⅲ级	胰腺炎	1. 轻度，无症状表现，加强监测 2. 酶升高；仅放射学检查所见，急性胰腺炎合并脐旁乳糜状血或血甘油三酯>11.3 mmol/L，可明确诊断为高脂血症性急性胰腺炎：禁食水≥24 h后的饮食调节；使用降血脂药物及其他辅助降脂手段[小剂量低分子肝素、胰岛素、血脂吸附和（或）血浆置换]控制血脂；推荐尽快将甘油三酯水平降至<5.65 mmol/L 3. 重度疼痛，呕吐：液体治疗、镇痛与营养支持 4. 危及生命，需要紧急治疗：手术治疗
					Ⅳ级	导致危及生命后果	无
					Ⅴ级	死亡	无
				高甘油三酯血症	Ⅰ级	轻度：TG水平150 mg/dL-199mg/dL；1.7mmol/L-2.3mmol/L	积极改善生活方式(包括合理饮食、增加体力运动、控制体重等)；加强监测
					Ⅱ级	中度：TG水平200mg/dL-999mg/dL；2.3mmol/L-11.2mmol/L	积极改善生活方式(包括合理饮食、增加体力运动、控制体重等)；加强监测；更换药物治疗方案；当TG水平≥5.65 mmol/L时,患者发生急性胰腺炎的风险既已显著增加,此时应立即启动降TG的药物(特别是贝特类)治疗
					Ⅲ级	重度：TG水平1000mg/dL-1999mg/dL；11.2mmol/L-22.4mmol/L	药物干预，常用药物有他汀类:如洛伐他汀、辛伐他汀、普伐他汀；贝特类:如苯扎贝特、非诺贝特、吉非罗齐；烟酸类:如氯甲吡喏等
					Ⅳ级	极重度：TG水平≥2000mg/dL；≥22.4mmol/L	患者发生急性胰腺炎的风险将显著增加,应立即应用贝特类、烟酸或n-3脂肪酸类药物单独治疗或与他汀联合治疗；同时需对患者进行更为严格的饮食控制,减少脂肪与简单糖类的摄入
					Ⅴ级	死亡	无
			肝胆疾病	药物性肝损伤	Ⅰ级	轻度肝损伤：ALT、AST < 5.0 ULN，TBIL 正常或 <2.5 ULN；多数患者可适应。可有或无乏力、虚弱、恶心、厌食、右上腹痛、黄疸、瘙痒、皮疹或体质量减轻等症状	继续抗病毒治疗，保肝治疗，临床观察。保肝治疗包括：1）抗炎保肝药物：异甘草酸镁可用于治疗ALT明显升高的急性肝细胞型和混合型DILI；甘草酸制剂也可用于治疗轻－中度肝细胞损伤型和混合型DILI；艾滋病初治病例，HAART后出现总胆红素正常的肝功能异常患者，在不停止HAART的基础上，可采用水飞蓟宾护肝治疗药物性肝损害；2）抗氧化药物：还原型谷胱甘肽常与甘草酸制剂联合应用治疗DILI患者；HAART后DILI患者同时联合使用硫普罗宁，治疗2个月，肝功能恢复时间明显缩短；3）促进胆汁排泄药物：熊去氧胆酸可用于治疗胆汁淤积型肝细胞损伤DILI；腺苷蛋氨酸可用于治疗胆汁淤积型肝细胞损伤DILI；4）改善肝细胞能量代谢：三磷酸腺苷、辅酶A、肌苷和维生素类等可通过改善肝细胞能量代谢，在一定程度上起到保护肝细胞的作用，也可以适当使用维生素B等
					Ⅱ级	中度肝损伤：ALT、AST < 5.0 ULN，TBIL 正常或 <2.5 ULN；；上述症状可有加重	继续抗病毒治疗，保肝治疗，临床观察。保肝治疗包括：1）抗炎保肝药物：异甘草酸镁可用于治疗ALT明显升高的急性肝细胞型和混合型DILI；甘草酸制剂也可用于治疗轻－中度肝细胞损伤型和混合型DILI；艾滋病初治病例，HAART后出现总胆红素正常的肝功能异常患者，在不停止HAART的基础上，可采用水飞蓟宾护肝治疗药物性肝损害；2）抗氧化药物：还原型谷胱甘肽常与甘草酸制剂联合应用治疗DILI患者；HAART后DILI患者同时联合使用硫普罗宁，治疗2个月，肝功能恢复时间明显缩短；3）促进胆汁排泄药物：熊去氧胆酸可用于治疗胆汁淤积型肝细胞损伤DILI；腺苷蛋氨酸可用于治疗胆汁淤积型肝细胞损伤DILI；4）改善肝细胞能量代谢：三磷酸腺苷、辅酶A、肌苷和维生素类等可通过改善肝细胞能量代谢，在一定程度上起到保护肝细胞的作用，也可以适当使用维生素B等
					Ⅲ级	重度肝损伤。5.0 ULN < ALT、AST < 10.0 ULN，2.5 ULN < TBIL < 5.0 ULN；患者症状进一步加重，需要住院治疗，或住院时间延长	可以考虑停用抗病毒药物，保肝治疗。保肝治疗包括：1）抗炎保肝药物：异甘草酸镁可用于治疗ALT明显升高的急性肝细胞型和混合型DILI；甘草酸制剂也可用于治疗轻－中度肝细胞损伤型和混合型DILI；艾滋病初治病例，HAART后出现总胆红素正常的肝功能异常患者，在不停止HAART的基础上，可采用水飞蓟宾护肝治疗药物性肝损害；2）抗氧化药物：还原型谷胱甘肽常与甘草酸制剂联合应用治疗DILI患者；HAART后DILI患者同时联合使用硫普罗宁，治疗2个月，肝功能恢复时间明显缩短；3）促进胆汁排泄药物：熊去氧胆酸可用于治疗胆汁淤积型肝细胞损伤DILI；腺苷蛋氨酸可用于治疗胆汁淤积型肝细胞损伤DILI；4）改善肝细胞能量代谢：三磷酸腺苷、辅酶A、肌苷和维生素类等可通过改善肝细胞能量代谢，在一定程度上起到保护肝细胞的作用，也可以适当使用维生素B等
					Ⅳ级	急性肝衰竭：ALT、AST≥10.0 ULN，TBIL≥5.0 ULN可同时出现腹水或肝性脑病或与药物性肝损伤相关的其他器官功能	暂停用所有抗病毒药物
					Ⅴ级	致命：因药物性肝损伤死亡，或需接受肝移植才能存活	肝移植

Figure 3-2. The first version of the framework of AE Monitoring View for PLWHIV (2)

富马酸替诺福韦二吡呋酯片	Tenofovir Disoproxil Fumarate	TDF	肾脏和泌尿系统疾病	药物相关性肾损伤	Ⅰ级	肾小球滤过率（eGFR）或肌酐清除率(CrCl)小于60mL/min/1.73m2或蛋白尿2+；尿蛋白/肌酐大于0.5	继续抗病毒治疗；加强监测
					Ⅱ级	估计的eGFR或者CrCl 59～30 mL/min/1.73m2	减少药物剂量或增加给药间隔；停用TDF，更换药物治疗方案
					Ⅲ级	估计的eGFR或者CrCl 29～15 mL/min/1.73m2	更换药物治疗方案，住院治疗
					Ⅳ级	估计的eGFR或者CrCl小于15 mL/min/1.73m2	需要透析或肾移植
					Ⅴ级	死亡	无
			胃肠道疾病	恶心	Ⅰ级	食欲降低，不伴进食习惯改变	加强监测
					Ⅱ级	经口摄食减少不伴明显的体重下降，脱水或营养不良	更换药物治疗方案
					Ⅲ级	经口摄入能量和水分不足	更换药物治疗方案；需要鼻饲，全肠外营养或者住院
					Ⅳ级	无	无
					Ⅴ级	无	无
				呕吐	Ⅰ级	轻度：轻度呕吐1-2次	加强监测；不需要进行其他干预
					Ⅱ级	中度：呕吐3-5次	门诊静脉补液；需要进行医学干预
					Ⅲ级	重度：呕吐6次以上	更换药物治疗方案；需要鼻饲，全胃肠外营养或住院治疗
					Ⅳ级	危及生命	紧急干预；更换药物治疗方案
					Ⅴ级	死亡	无
				腹泻	Ⅰ级	与基线相比，大便次数增加每天<4次；进展口排出物轻度增	加强监测
					Ⅱ级	与基线相比，大便次数增加每天4～6次；进展口排出物中度增加；借助于工具的日常生活活动受限	口服补液；更换药物治疗方案
					Ⅲ级	与基线相比，大便次数增加每天≥7次；与基线相比，进展口排出物重度增加；自理性日常生活活动受限	更换药物治疗方案；需要住院治疗
					Ⅳ级	危及生命	需要紧急治疗
					Ⅴ级	死亡	无
			新陈代谢与营养不良	低磷血症	Ⅰ级	只有实验室发现	无需医学干预；加强监测
					Ⅱ级	只有实验室发现	口服替代药物治疗
					Ⅲ级	严重或有意义的医学事件但非立即危及生命	更换药物治疗方案；住院治疗
					Ⅳ级	危及生命	立即停药；紧急干预；住院治疗
					Ⅴ级	死亡	无
				酸中毒	Ⅰ级	pH<正常值，但≥7.3	加强监测
					Ⅱ级	无	加强监测
					Ⅲ级	pH<7.3	更换药物治疗方案；需要住院治疗
					Ⅳ级	危及生命	更换药物治疗方案；需要住院治疗
					Ⅴ级	死亡	无

Figure 3-3. The first version of the framework of AE Monitoring View for PLWHIV (3)

齐多夫定	Zidovudine	AZT	血液和淋巴系统疾病	贫血	Ⅰ级	血红蛋白＜正常值下限～10.0 g/dL；＜正常值下限～6.2mmol/L；＜正常值下限～100 g/L	加强监测血细胞计数（血常规）；无需更换药物治疗方案
					Ⅱ级	血红蛋白＜10.0～8.0 g/dL；＜6.2～4.9 mmol/L；＜100～80	AZT的剂量应延日减少，直至出现骨髓恢复迹象；停药2～4周，促进骨髓恢复
					Ⅲ级	血红蛋白＜8.0 g/dL；＜4.9 mmol/L；＜80 g/L	在调整剂量的同时给予输血治疗；持续监测血细胞计数（血常规）
					Ⅳ级	危及生命	紧急治疗
					Ⅴ级	死亡	无
			胃肠道疾病	恶心	Ⅰ级	食欲降低，不伴进食习惯改变	加强监测
					Ⅱ级	经口摄食减少不伴明显的体重下降，脱水或营养不良	更换药物治疗方案
					Ⅲ级	经口摄入能量和水分不足	更换药物治疗方案；需要鼻饲，全肠外营养或者住院
					Ⅳ级	无	无
					Ⅴ级	无	无
				呕吐	Ⅰ级	轻度：轻度呕吐1-2次	加强监测；不需要进行其他干预
					Ⅱ级	中度：呕吐3-5次	门诊静脉补液；需要进行医学干预
					Ⅲ级	重度：呕吐6次以上	更换药物治疗方案；需要鼻饲，全胃肠外营养或住院治疗
					Ⅳ级	危及生命	紧急干预；更换药物治疗方案
					Ⅴ级	死亡	无
				腹泻	Ⅰ级	与基线相比，大便次数增加每天<4次；造瘘口排出物轻度增	加强监测
					Ⅱ级	与基线相比，大便次数增加每天4～6次；造瘘口排出物中度增加；借助于工具的日常生活活动受限	口服补液；更换药物治疗方案
					Ⅲ级	与基线相比，大便次数增加每天 ≥7次；与基线相比，造瘘口排出物重度增加；自理性日常生活活动受限	更换药物治疗方案；需要住院治疗
					Ⅳ级	危及生命	需要紧急治疗
					Ⅴ级	死亡	无
			医学检查	肌酸磷酸激酶增高	Ⅰ级	＞正常值上限～2.5倍正常值上限	加强监测
					Ⅱ级	>2.5倍正常值上限～5倍正常值上限	考虑有心力衰竭或心功能衰竭：心肌梗死的风险
					Ⅲ级	>5倍正常值上限～10倍正常值上限	减少药物剂量或更换药物治疗方案
					Ⅳ级	>10倍正常值上限	紧急治疗
					Ⅴ级	无	无
			肝脏疾病	药物性肝损伤	Ⅰ级	轻度肝损伤：ALT、AST＜5.0 ULN，TBIL正常或＜2.5 ULN；多数患者可适应。可有或无乏力、虚弱、恶心、厌食、右上腹痛、黄疸、瘙痒、皮疹或体质量减轻等症状	继续抗病毒治疗，保肝治疗，临床观察。保肝治疗包括：1）抗炎保肝药物：异甘草酸镁可用于治疗ALT明显升高的急性肝细胞型和混合型DILI；甘草酸制剂也可用于治疗轻－中度肝细胞损伤型和混合型DILI；艾滋病初治病例，HAART后出现总胆红素正常的肝功能异常患者，在不停止HAART的基础上，可采用水飞蓟宾护肝治疗药物性肝损害；2）抗氧化药物：还原型谷胱甘肽常与甘草酸制剂联合应用治疗DILI患者；HAART后DILI患者同时联合使用硫普罗宁，治疗2个月，肝功能恢复时间明显缩短；3）促进胆汁排泌药物：熊去氧胆酸可用于治疗胆汁淤积型肝细胞损伤DILI；腺苷蛋氨酸可用于治疗胆汁淤积型肝细胞损伤DILI；4）改善肝细胞能量代谢：三磷酸腺苷、辅酶A、肌苷和维生素类等可通过改善肝细胞能量代谢，在一定程度上起到保护肝细胞的作用，也可以适当使用维生素B等
					Ⅱ级	中度肝损伤：ALT、AST＜5.0 ULN，TBIL正常或＜2.5 ULN；；上述症状可有加重	继续抗病毒治疗，保肝治疗，临床观察。保肝治疗包括：1）抗炎保肝药物：异甘草酸镁可用于治疗ALT明显升高的急性肝细胞型和混合型DILI；甘草酸制剂也可用于治疗轻－中度肝细胞损伤型和混合型DILI；艾滋病初治病例，HAART后出现总胆红素正常的肝功能异常患者，在不停止HAART的基础上，可采用水飞蓟宾护肝治疗药物性肝损害；2）抗氧化药物：还原型谷胱甘肽常与甘草酸制剂联合应用治疗DILI患者；HAART后DILI患者同时联合使用硫普罗宁，治疗2个月，肝功能恢复时间明显缩短；3）促进胆汁排泌药物：熊去氧胆酸可用于治疗胆汁淤积型肝细胞损伤DILI；腺苷蛋氨酸可用于治疗胆汁淤积型肝细胞损伤DILI；4）改善肝细胞能量代谢：三磷酸腺苷、辅酶A、肌苷和维生素类等可通过改善肝细胞能量代谢，在一定程度上起到保护肝细胞的作用，也可以适当使用维生素B等
					Ⅲ级	重度肝损伤。5.0 ULN＜ALT、AST＜10.0 ULN，2.5 ULN＜TBIL＜5.0 ULN；患者症状进一步加重，需要住院治疗，或住院时间延长	可以考虑停用抗病毒药物，保肝治疗。保肝治疗包括：1）抗炎保肝药物：异甘草酸镁可用于治疗ALT明显升高的急性肝细胞型和混合型DILI；甘草酸制剂也可用于治疗轻－中度肝细胞损伤型和混合型DILI；艾滋病初治病例，HAART后出现总胆红素正常的肝功能异常患者，在不停止HAART的基础上，可采用水飞蓟宾护肝治疗药物性肝损害；2）抗氧化药物：还原型谷胱甘肽常与甘草酸制剂联合应用治疗DILI患者；HAART后DILI患者同时联合使用硫普罗宁，治疗2个月，肝功能恢复时间明显缩短；3）促进胆汁排泌药物：熊去氧胆酸可用于治疗胆汁淤积型肝细胞损伤DILI；腺苷蛋氨酸可用于治疗胆汁淤积型肝细胞损伤DILI；4）改善肝细胞能量代谢：三磷酸腺苷、辅酶A、肌苷和维生素类等可通过改善肝细胞能量代谢，在一定程度上起到保护肝细胞的作用，也可以适当使用维生素B等
					Ⅳ级	急性肝衰竭：ALT、AST≥10.0 ULN，TBIL≥5.0 ULN可同时出现腹水或肝性脑病或与药物性肝损伤相关的其他器官功能	暂停用所有抗病毒药物
					Ⅴ级	致命：因药物性肝损伤死亡，或需接受肝移植才能存活	肝移植

Figure 3-4. The first version of the framework of AE Monitoring View for PLWHIV (4)

洛匹那韦/利托那韦	Lopinavir / Ritonavir	LPV/r	胃肠道疾病	恶心	Ⅰ级	食欲降低，不伴进食习惯改变	加强监测
					Ⅱ级	经口摄食减少不伴明显的体重下降，轻水或营养不良	更换药物治疗方案
					Ⅲ级	经口摄入能量和水分不足	更换药物治疗方案；需要鼻饲，全肠外营养或者住院
					Ⅳ级	无	无
					Ⅴ级	无	无
				腹泻	Ⅰ级	与基线相比，大便次数增加每天<4次；进展口排出物轻度增	加强监测
					Ⅱ级	与基线相比，大便次数增加每天4~6次；进展口排出物中度增加；借助于工具的日常生活活动受限	口服补液；更换药物治疗方案
					Ⅲ级	与基线相比，大便次数增加每天≥7次；与基线相比，进展口排出物重度增加；自理性日常生活活动受限	更换药物治疗方案；需要住院治疗
					Ⅳ级	危及生命	需要紧急治疗
					Ⅴ级	死亡	无
			新陈代谢与营养不良	高血脂症	Ⅰ级	高胆固醇血症:血清总胆固醇增高>5.72 mmol·L-1，三酰甘油正常；高三酰甘油血症:血清三酰甘油增高>1.70 mmol·L-1，总胆固醇正常；混合型高脂血症:血清总胆固醇和三酰甘油含量均增高,即总胆固醇>5.72 mmol·L-1,三酰甘油>1.70 mmol·L-1；低高密度脂蛋白血症:血清高密度脂蛋白胆固醇降低<1.2	加强监测；患者需要改变饮食习惯
					Ⅱ级	周围性皮下脂肪萎缩:多见于面部、四肢及臀部；向心性脂肪堆积:多见腹部、躯干、颈部、背部,形成所谓水牛背及脂肪瘤	药物干预，常用药物有他汀类:如洛伐他汀、辛伐他汀、普伐他汀；贝特类:如苯扎贝特、非诺贝特、吉非罗齐；烟酸类:如氯甲吡嗪等
					Ⅲ级	胰腺炎	1. 轻度，无症状表现，加强监测 2. 确诊病：仅放射学检查所见，急性胰腺炎合并静脉乳糜状血或血甘油三酯>11.3 mmol/L，可明确诊断为高脂血症性急性胰腺炎：禁食水≥24 h后的饮食调节；使用降血脂药物及其他辅助降脂手段[小剂量低分子肝素、胰岛素、血脂吸附和（或）血浆置换]控制血脂；推荐尽快将甘油三酯水平降至<5.65 mmol/L 3. 重度疼痛，*恶吐：液体治疗、镇痛与营养支持 4. 危及生命，需要紧急治疗：手术治疗
					Ⅳ级	导致危及生命后果	无
					Ⅴ级	死亡	无
			神经系统疾病	头痛	Ⅰ级	轻度疼痛	加强监测
					Ⅱ级	中度疼痛：影响工具性日常生活活动	减少药物剂量
					Ⅲ级	重度疼痛：影响自理性日常生活活动	更换药物治疗方案
					Ⅳ级	无	无
					Ⅴ级	无	无
			肝胆疾病	药物性肝损伤	Ⅰ级	轻度肝损伤：ALT、AST < 5.0 ULN，TBIL 正常或 <2.5 ULN；多数患者可进展。可有或无乏力、虚肺、恶心、厌食、右上腹痛、黄疸、瘙痒、皮疹或体质量减轻等症状	继续抗病毒治疗，保肝治疗，临床观察。保肝治疗包括：1）抗炎保肝药物：异甘草酸镁可用于治疗 ALT 明显升高的急性肝细胞型和混合型DILI；甘草酸制剂也可用于治疗轻 — 中度肝细胞损伤型和混合型 DILI；艾迪病初治病例，HAART 后出现总胆红素正常的肝功能异常患者，在不停止 HAART 的基础上，可采用水飞蓟宾护肝治疗药物性肝损害；2）抗氧化药物：还原型谷胱甘肽常与甘草酸制剂联合应用治疗 DILI 患者；HAART 后 DILI 患者同时联合使用硫普罗宁，治疗 2 个月，肝功能恢复时间明显缩短；3）促进胆汁排泄药物：熊去氧胆酸可用于治疗胆汁淤积型肝细胞损伤 DILI；腺苷蛋氨酸可用于治疗胆汁淤积型肝细胞损伤 DILI；4）改善肝细胞能量代谢：三磷酸腺苷、辅酶A、肌苷和维生素类等可通过改善肝细胞能量代谢，在一定程度上起到保护肝细胞的作用，也可以适当使用维生素B等
					Ⅱ级	中度肝损伤：ALT、AST < 5.0 ULN，TBIL 正常或 <2.5 ULN；；上述症状可有加重	继续抗病毒治疗，保肝治疗，临床观察。保肝治疗包括：1）抗炎保肝药物：异甘草酸镁可用于治疗 ALT 明显升高的急性肝细胞型和混合型DILI；甘草酸制剂也可用于治疗轻 — 中度肝细胞损伤型和混合型 DILI；艾迪病初治病例，HAART 后出现总胆红素正常的肝功能异常患者，在不停止 HAART 的基础上，可采用水飞蓟宾护肝治疗药物性肝损害；2）抗氧化药物：还原型谷胱甘肽常与甘草酸制剂联合应用治疗 DILI 患者；HAART 后 DILI 患者同时联合使用硫普罗宁，治疗 2 个月，肝功能恢复时间明显缩短；3）促进胆汁排泄药物：熊去氧胆酸可用于治疗胆汁淤积型肝细胞损伤 DILI；腺苷蛋氨酸可用于治疗胆汁淤积型肝细胞损伤 DILI；4）改善肝细胞能量代谢：三磷酸腺苷、辅酶A、肌苷和维生素类等可通过改善肝细胞能量代谢，在一定程度上起到保护肝细胞的作用，也可以适当使用维生素B等
					Ⅲ级	重度肝损伤。5.0 ULN < ALT、AST < 10.0 ULN，2.5 ULN < TBIL < 5.0 ULN；患者症状进一步加重，需要住院治疗，或住院时间延长	可以考虑停用抗病毒药物，保肝治疗。保肝治疗包括：1）抗炎保肝药物：异甘草酸镁可用于治疗 ALT 明显升高的急性肝细胞型和混合型DILI；甘草酸制剂也可用于治疗轻 — 中度肝细胞损伤型和混合型 DILI；艾迪病初治病例，HAART 后出现总胆红素正常的肝功能异常患者，在不停止 HAART 的基础上，可采用水飞蓟宾护肝治疗药物性肝损害；2）抗氧化药物：还原型谷胱甘肽常与甘草酸制剂联合应用治疗 DILI 患者；HAART 后 DILI 患者同时联合使用硫普罗宁，治疗 2 个月，肝功能恢复时间明显缩短；3）促进胆汁排泄药物：熊去氧胆酸可用于治疗胆汁淤积型肝细胞损伤 DILI；腺苷蛋氨酸可用于治疗胆汁淤积型肝细胞损伤 DILI；4）改善肝细胞能量代谢：三磷酸腺苷、辅酶A、肌苷和维生素类等可通过改善肝细胞能量代谢，在一定程度上起到保护肝细胞的作用，也可以适当使用维生素B等
					Ⅳ级	急性肝衰竭：ALT、AST≥10.0 ULN，TBIL≥5.0 ULN可同时出现脑水或肝性脑病或与药物性肝损伤相关的其他器官功能衰竭	暂停用所有抗病毒药物
					Ⅴ级	致命：因药物性肝损伤死亡，或需接受肝移植才能存活	肝移植
			精神疾病	失眠症	Ⅰ级	轻度睡眠困难，保持睡眠状态或平醒	加强监测
					Ⅱ级	中度睡眠困难，保持睡眠状态或平醒	减少药物剂量
					Ⅲ级	重度睡眠困难，保持睡眠状态或平醒	更换药物治疗方案
					Ⅳ级	无	无
					Ⅴ级	无	无
				抑郁症	Ⅰ级	轻度症状	加强监测；减少药物剂量
					Ⅱ级	中度症状：影响工具性日常生活活动	更换药物治疗方案；无需住院
					Ⅲ级	重度症状：个人自理能力受限	更换药物治疗方案；无需住院
					Ⅳ级	危及生命：危害自己或他人	更换药物治疗方案；转销神卫生中心进行专病治疗
					Ⅴ级	死亡	无

Figure 3-5. The first version of the framework of AE Monitoring View for PLWHIV (5)

多替拉韦	Dolutegravir	DTG	神经系统疾病	眩晕	I 级	轻度不平稳或有移动感	加强监测
					II 级	中度不平稳时：影响工具性日常生活活动	减少药物剂量
					III 级	重度不平稳或有移动感：影响自理性日常生活活动	更换药物治疗方案
					IV 级	无	无
					V 级	无	无
				头痛	I 级	轻度疼痛	加强监测
					II 级	中度疼痛：影响工具性日常生活活动	减少药物剂量
					III 级	重度疼痛：影响自理性日常生活活动	更换药物治疗方案
					IV 级	无	无
					V 级	无	无
			胃肠道疾病	恶心	I 级	食欲降低，不伴进食习惯改变	加强监测
					II 级	经口摄食减少不伴明显体重下降，脱水或营养不良	更换药物治疗方案
					III 级	经口摄入能量和水分不足	更换药物治疗方案；需要鼻饲，全肠外营养或者住院
					IV 级	无	无
					V 级	无	无
				呕吐	I 级	轻度：呕吐1-2次	加强监测；不需要进行其他干预
					II 级	中度：呕吐3-5次	门诊静脉补液；需要进行医学干预
					III 级	重度：呕吐6次以上	更换药物治疗方案；需要鼻饲，全胃肠外营养或住院治疗
					IV 级	危及生命	紧急干预；更换药物治疗方案
					V 级	死亡	无
				腹泻	I 级	与基线相比，大便次数增加每天<4次；造瘘口排出物轻度增加	加强监测
					II 级	与基线相比，大便次数增加每天 4~6 次；造瘘口排出物中度增加；僧帽于工具的日常生活活动受限	口服补液；更换药物治疗方案
					III 级	与基线相比，大便次数增加每天 >7 次；与基线相比，造瘘口排出物重度增加；自理性日常生活活动受限	更换药物治疗方案；需要住院治疗
					IV 级	危及生命	需要紧急治疗
					V 级	死亡	无
			免疫系统疾病	过敏反应	I 级	无	无
					II 级	无	无
					III 级	荨麻疹	1. 荨麻疹泛发区域小于10%的体表面积：局部治疗或加强监测 2. 荨麻疹泛发区域覆盖10-30%的体表面积：口服药物治疗 3. 荨麻疹泛发区域大于30%的体表面积：静脉输药治疗 4. 更换药物治疗方案
					IV 级	无	无
					V 级	无	无
			肝脏疾病	药物性肝损伤	I 级	轻度肝损伤：ALT、AST < 5.0 ULN，TBIL 正常或 <2.5 ULN；多数患者可进食，可有乏力、虚弱、恶心、厌食、右上腹痛、黄疸、瘙痒、皮疹或体质重或轻等症状	继续抗病毒治疗，保肝治疗，临床观察。保肝治疗包括：1）抗炎保肝药物：异甘草酸镁可用于治疗 ALT 明显升高的急性肝细胞型和混合型DILI；甘草酸制剂也可用于治疗轻 — 中度肝细胞损伤型和混合型 DILI；艾迪洛尔治疗病例，HAART 后出现总胆红素正常的肝功能异常患者，在不停止 HAART 的基础上，可采用水飞蓟宾护肝治疗药物性肝损害；2）抗氧化药物：还原型谷胱甘肽常与甘草酸制剂联合应用治疗 DILI 患者；HAART 后 DILI 患者同时联合使用硫普罗宁，治疗 2 个月，肝功能恢复时间明显缩短；3）促进胆汁排泄药物：熊去氧胆酸可用于治疗胆汁淤积型肝细胞损伤 DILI；腺苷蛋氨酸可用于治疗胆汁淤积型肝细胞损伤 DILI；4）改善肝细胞能量代谢：三磷酸腺苷、辅酶A，肌苷和维生素类等可通过改善肝细胞能量代谢，在一定程度上起到保护肝细胞的作用，也可以适当使用维生素B等
					II 级	中度肝损伤：ALT、AST < 5.0 ULN，TBIL 正常或 <2.5 ULN；；上述症状可有加重	继续抗病毒治疗，保肝治疗，临床观察。保肝治疗包括：1）抗炎保肝药物：异甘草酸镁可用于治疗 ALT 明显升高的急性肝细胞型和混合型DILI；甘草酸制剂也可用于治疗轻 — 中度肝细胞损伤型和混合型 DILI；艾迪洛尔治疗病例，HAART 后出现总胆红素正常的肝功能异常患者，在不停止 HAART 的基础上，可采用水飞蓟宾护肝治疗药物性肝损害；2）抗氧化药物：还原型谷胱甘肽常与甘草酸制剂联合应用治疗 DILI 患者；HAART 后 DILI 患者同时联合使用硫普罗宁，治疗 2 个月，肝功能恢复时间明显缩短；3）促进胆汁排泄药物：熊去氧胆酸可用于治疗胆汁淤积型肝细胞损伤 DILI；腺苷蛋氨酸可用于治疗胆汁淤积型肝细胞损伤 DILI；4）改善肝细胞能量代谢：三磷酸腺苷、辅酶A，肌苷和维生素类等可通过改善肝细胞能量代谢，在一定程度上起到保护肝细胞的作用，也可以适当使用维生素B等
					III 级	重度肝损伤：5.0 ULN < ALT、AST < 10.0 ULN，2.5 ULN < TBIL < 5.0 ULN；患者症状进一步加重，需要住院治疗，或住院时间延长	可以考虑停用抗病毒药物，保肝治疗。保肝治疗包括：1）抗炎保肝药物：异甘草酸镁可用于治疗 ALT 明显升高的急性肝细胞型和混合型DILI；甘草酸制剂也可用于治疗轻 — 中度肝细胞损伤型和混合型 DILI；艾迪洛尔治疗病例，HAART 后出现总胆红素正常的肝功能异常患者，在不停止 HAART 的基础上，可采用水飞蓟宾护肝治疗药物性肝损害；2）抗氧化药物：还原型谷胱甘肽常与甘草酸制剂联合应用治疗 DILI 患者；HAART 后 DILI 患者同时联合使用硫普罗宁，治疗 2 个月，肝功能恢复时间明显缩短；3）促进胆汁排泄药物：熊去氧胆酸可用于治疗胆汁淤积型肝细胞损伤 DILI；腺苷蛋氨酸可用于治疗胆汁淤积型肝细胞损伤 DILI；4）改善肝细胞能量代谢：三磷酸腺苷、辅酶A，肌苷和维生素类等可通过改善肝细胞能量代谢，在一定程度上起到保护肝细胞的作用，也可以适当使用维生素B等
					IV 级	急性肝衰竭：ALT、AST>10.0 ULN，TBIL>5.0 ULN可伴肝出现肝水肿肝性脑病或与药物性肝损伤相关的其他器官功能衰竭	暂停用所有抗病毒药物
					V 级	致命：因药物性肝损伤死亡，或需接受肝移植才能存活	肝移植
拉米夫定	Lamivudine	3TC	神经系统疾病	头痛	I 级	轻度疼痛	加强监测
					II 级	中度疼痛：影响工具性日常生活活动	减少药物剂量
					III 级	重度疼痛：影响自理性日常生活活动	更换药物治疗方案
					IV 级	无	无
					V 级	无	无
			胃肠道疾病	恶心	I 级	食欲降低，不伴进食习惯改变	加强监测
					II 级	经口摄食减少不伴明显的体重下降，脱水或营养不良	更换药物治疗方案
					III 级	经口摄入能量和水分不足	更换药物治疗方案；需要鼻饲，全肠外营养或者住院
					IV 级	无	无
					V 级	无	无
				腹泻	I 级	与基线相比，大便次数增加每天<4次；造瘘口排出物轻度增	加强监测
					II 级	与基线相比，大便次数增加每天 4~6 次；造瘘口排出物中度增加；僧帽于工具的日常生活活动受限	口服补液；更换药物治疗方案
					III 级	与基线相比，大便次数增加每天 >7 次；与基线相比，造瘘口排出物重度增加；自理性日常生活活动受限	更换药物治疗方案；需要住院治疗
					IV 级	危及生命	需要紧急治疗
					V 级	死亡	无

Figure 3-6. The first version of the framework of AE Monitoring View for PLWHIV (6)

奈韦拉平	Nevirapine	NVP	免疫系统疾病	过敏反应	Ⅰ级	无	无
					Ⅱ级	无	无
					Ⅲ级	荨麻疹	1. 荨麻疹损害区域小于10%的体表面积：局部治疗或加强监测
							2. 荨麻疹损害区域覆盖10-30%的体表面积：口服药物治疗
							3. 荨麻疹损害区域大于30%的体表面积：静脉给药治疗
							4. 更换药物治疗方案
					Ⅳ级	无	无
					Ⅴ级	无	无
			肝胆疾病	药物性肝损伤	Ⅰ级	轻度肝损伤：ALT、AST ＜ 5.0 ULN，TBIL 正常或＜2.5 ULN；多数患者可进症。可有或无乏力、虚弱、恶心、厌食、右上腹痛、黄疸、瘙痒、皮疹或体质量减轻等症状	继续抗病毒治疗，保肝治疗，临床观察。保肝治疗包括：1）抗炎保肝药物：异甘草酸镁可用于治疗 ALT 明显升高的急性肝细胞型和混合型DILI；甘草酸制剂也可用于治疗轻－中度肝细胞损伤型和混合型 DILI；艾滋病初治病例，HAART 后出现总胆红素正常的肝功能异常患者，在不停止 HAART 的基础上，可采用水飞蓟宾护肝治疗药物性肝损害；双环醇可以预防奈韦拉平致艾滋病患者 DILI；2）抗氧化药物：还原型谷胱甘肽常与甘草酸制剂联合应用治疗 DILI 患者；HAART 后 DILI 患者同时联合使用硫普罗宁，治疗 2 个月，肝功能恢复时间明显缩短；3）促进胆汁排泌药物：熊去氧胆酸可用于治疗胆汁淤积型肝细胞损伤 DILI；腺苷蛋氨酸可用于治疗胆汁淤积型肝细胞损伤 DILI；4）改善肝细胞能量代谢：三磷酸腺苷、辅酶A、肌苷和维生素类等可通过改善肝细胞能量代谢，在一定程度上起到保护肝细胞的作用，也可以适当使用维生素B等
					Ⅱ级	中度肝损伤：ALT、AST ＜ 5.0 ULN，TBIL 正常或＜2.5 ULN；；上述症状可有加重	继续抗病毒治疗，保肝治疗，临床观察。保肝治疗包括：1）抗炎保肝药物：异甘草酸镁可用于治疗 ALT 明显升高的急性肝细胞型和混合型DILI；甘草酸制剂也可用于治疗轻－中度肝细胞损伤型和混合型 DILI；艾滋病初治病例，HAART 后出现总胆红素正常的肝功能异常患者，在不停止 HAART 的基础上，可采用水飞蓟宾护肝治疗药物性肝损害；双环醇可以预防奈韦拉平致艾滋病患者 DILI；2）抗氧化药物：还原型谷胱甘肽常与甘草酸制剂联合应用治疗 DILI 患者；HAART 后 DILI 患者同时联合使用硫普罗宁，治疗 2 个月，肝功能恢复时间明显缩短；3）促进胆汁排泌药物：熊去氧胆酸可用于治疗胆汁淤积型肝细胞损伤 DILI；腺苷蛋氨酸可用于治疗胆汁淤积型肝细胞损伤 DILI；4）改善肝细胞能量代谢：三磷酸腺苷、辅酶A、肌苷和维生素类等可通过改善肝细胞能量代谢，在一定程度上起到保护肝细胞的作用，也可以适当使用维生素B等
					Ⅲ级	重度肝损伤。5.0 ULN ＜ ALT、AST ＜ 10.0 ULN，2.5 ULN ＜ TBIL ＜ 5.0 ULN；患者症状进一步加重，需要住院治疗，或住院时间延长	可以考虑停用抗病毒药物，保肝治疗。保肝治疗包括：1）抗炎保肝药物：异甘草酸镁可用于治疗 ALT 明显升高的急性肝细胞型和混合型DILI；甘草酸制剂也可用于治疗轻－中度肝细胞损伤型和混合型 DILI；艾滋病初治病例，HAART 后出现总胆红素正常的肝功能异常患者，在不停止 HAART 的基础上，可采用水飞蓟宾护肝治疗药物性肝损害；双环醇可以预防奈韦拉平致艾滋病患者 DILI；2）抗氧化药物：还原型谷胱甘肽常与甘草酸制剂联合应用治疗 DILI 患者；HAART 后 DILI 患者同时联合使用硫普罗宁，治疗 2 个月，肝功能恢复时间明显缩短；3）促进胆汁排泌药物：熊去氧胆酸可用于治疗胆汁淤积型肝细胞损伤 DILI；腺苷蛋氨酸可用于治疗胆汁淤积型肝细胞损伤 DILI；4）改善肝细胞能量代谢：三磷酸腺苷、辅酶A、肌苷和维生素类等可通过改善肝细胞能量代谢，在一定程度上起到保护肝细胞的作用，也可以适当使用维生素B等
					Ⅳ级	急性肝衰竭：ALT、AST≥10.0 ULN，TBIL≥5.0 ULN可同时出现腹水或肝性脑病或与药物性肝损伤相关的其他器官功能衰竭	暂停用所有抗病毒药物
					Ⅴ级	致命：因药物性肝损伤死亡，或需接受肝移植才能存活	肝移植

Figure 3-7. The first version of the framework of AE Monitoring View for PLWHIV (7)

3.2 The construction of final framework of AE Monitoring View for PLWHIV

3.2.1 Research purpose

To revise the first version of the framework on AE Monitoring View for PLWHIV and determine the final framework, the researcher asked the experts in HIV/AIDS filed for suggestions about the contents in the framework, including but not limited in drug name, specific AE, and corresponding interventions. Experts demonstrated conceptual structure and item pools by accepting Delphi consulting methods to guide the optimization of system content.

3.2.2 Participants

14 Clinicians, nurses and educators in the field of HIV/AIDS were invited to form an expert group for correspondence according to informed consent.

Inclusion criteria for clinicians and nurses:

1) Intermediate and above titles,
2) A master's degree or above, or a bachelor degree with a working experience of more than 10 years,
3) Having a high academic level of AIDS,
4) Volunteer to participate in this research.

Inclusion criteria for educators:

1) Associate professor or above,
2) A PhD degree and above, or a master’s degree with a working experience of more than 10 years,
3) Having a high academic level of AIDS,
4) Volunteer to participate in this research.

3.2.3 Research method

3.2.3.1 Research tools

Based on the above-mentioned qualitative interviews and literature analysis, the researcher designer the expert letter inquiry (See Appendix IV). The expert letter inquiry form developed by researcher included:

(1) Foreword: Research background, research purpose and significance, definition of relevant research concepts, introduction and importance of Delphi method, instructions about filling the survey, etc.

(2) Main part: list the content of the initially formed "Recommendation of decision on AE in the AE Monitoring View for PLWHIV" hierarchically and specifically, according to the Likert 5-point metric to divide expert opinion scores, that is, 5=completely appropriate, 4= More appropriate, 3=general, 2=not suitable, 1=completely inappropriate. The researcher asked the consulting experts to score each item based on its scientificity, rationality, and suitability for use. An expert opinion column was set up after each entry in order to facilitate the experts to modify and supplement the content. At the same time, the researchers set up the "Expert Opinion Column" entry in the form for experts to make declarative supplementary comments, and collect expert suggestions to help researchers make comprehensive judgments and further revise the framework.

(3) Expert data survey form: including general social demographic data and research work background data of the expert inquired, including age, education background, title, research field and working years, etc.

(4) Experts' familiarity with this research question, by means of expert self-evaluation. Expert familiarity was divided into 5 levels, followed by very familiar, familiar, general, unfamiliar, and very unfamiliar. The values are assigned 1.0, 0.8, 0.5, 0.2, 0.0 in sequence. Expert judgment basis was divided into 4 categories, which were practical experience, theoretical basis, domestic/foreign literature reference and intuitive feelings. Each category was divided into three levels: large, medium, and small. The four types of basis were assigned as follows: practical experience (assignment of 0.5, 0.4, 0.3); theoretical basis (assignment of 0.3, 0.2, 0.1); domestic and foreign literature reference (assignment of 0.1, 0.1, 0.1); intuitive experience (assignment of 0.1, 0.1, 0.1).

3.2.3.2 Data collection

Two rounds of Delphi expert consultation were completed in the form of face-to-face expert consultation meetings. After the first round of consultation, the researcher assembled and sorted out all the indicator scores and supplementary comments from experts, and revised the content items of the system framework after discussion by the research team. The researcher then used the same method to conduct a second round of expert consultation, and fed back the revised results of the first round of expert consultation to the experts again, inviting the experts to conduct a second evaluation.

3.2.3.3 Data analysis

All data were analyzed using SPSS24.0 software. The general data of the consulted experts were analyzed descriptively by frequency and rate; non-parametric tests were used to calculate the agreement among various experts regarding the choice of each entry the credibility of an expert's opinion as measured by an expert data questionnaire; The positive coefficient, authority coefficient (CR) of experts as well as the level of agreement of expert opinions were calculated.

The recovery rate (%) using the expert consultation form and the ratio of experts referred indicate the positive coefficient of experts, with higher rates indicating greater positivity of experts for this study.

Authority coefficient (CR) was used to indicate the level of authority of an expert. The CR of an expert reflected with the experts' familiarity with and basis of judgment in this study. The expert authority coefficient was reflected by two indicators, the expert judgment coefficient (Ca) and the expert's familiarity coefficient (Cs). The calculation formula is CR=(Ca+Cs)/2, and the general requirement CR > 0.70, the larger CR, the more reliable the correspondence results. CR>0.80 indicated a high degree of authority of experts.

Importance assignment mean standard deviation, item selection rate (the ratio of the number of experts selected at levels 1 and 2 to the total number of experts) and the full score rate (the ratio of the number of experts selected at level 1 to the total number of experts) were used to analyze the agreement of expert opinions. The higher the mean of importance assignment, the selection rate of 4 points and above, and the full score, with the smaller the standard deviation, the higher the concentration of expert opinions.

The coefficient of variation (CV) and the coordination coefficient (Kendall's W) were used to represent the degree of coordination of experts' opinions. CV=S/M, where S and M were the standard deviation and mean of the scores assigned by experts to each item, respectively. The smaller the coefficient of variation, the higher the degree of coordination of experts, and when the CV of all indicators is less than 0.25, it indicated the convergence of expert opinions, and the indicator could be retained. The Kendall's W score range was 0-1 points, the higher the score, the higher the degree of coordination.

3.2.4 Research results

3.2.4.1 The characteristics of experts

There was a total of 14 experts being invited to participate in the face-to-face expert consultation meeting, including 10 clinicians, 2 educators and 2 nurses. All the participants came from SPHC. The average age of the experts was 44.21±6.83 years. Table 3-3 shows the detailed information of the 14 experts.

Table 3-3. The characteristics of the experts (N=14)

Items	Grouping	Frequency	Percentage（%）
Gender	Male	8	57.1
	Female	6	42.9
Age (Years)	30-39	6	42.9
	40-49	4	28.6
	≥50	4	28.6
Education	PhD	11	78.6
background	Master Degree	3	21.4
Technical title	Senior	6	42.9
	Deputy senior	3	21.4
	Intermediate	5	35.7
Research field	Clinical medicine	12	85.7
	Nursing	2	14.3
Current vocation	Clinical medicine	10	71.4
	Medical education	2	14.3
	Clinical nursing	2	14.3
Working duration	5-15	7	50.0
(years)	16-25	5	35.7
	≥26	2	14.3
HIV/AIDS	5-15	8	57.1
duration (years)	16-25	4	28.6
	≥26	2	14.3

3.2.4.2 Results of the first round of Delphi expert consultation

3.2.4.2.1 The recovery rate

A total of 14 consultation letters were distributed, and 14 were actually recovered. The expert inquiry letter recovery rate was 100%, which indicated that the experts were highly motivated.

3.2.4.2.2 Authority coefficient (CR)

Experts' Familiarity Scores with research content is shown in Table 3-4, and experts' judgments on the research content scores are shown in Table 3-5. Table 3-6

shows the authority of this round of expert consultation. The calculation results indicated CR > 0.70, which means a high-level authority of 14 experts.

Table 3-4. Experts' Familiarity Scores with research content

Degree	Very familiar	Familiar	General	Unfamiliar	Very unfamiliar
Score	1.0	0.8	0.5	0.2	0.0

Table 3-5. Experts' judgment on research content Scores

Judgment basis	Degree of influence on expert judgment		
	Large	Medium	Small
Practical experience	0.5	0.4	0.3
Theoretical basis	0.3	0.2	0.1
Domestic/foreign literature reference	0.1	0.1	0.1
Intuitive feelings	0.1	0.1	0.1

Table 3-6. The authority of 14 experts (N=14)

No.	Judgment basis				Judgment coefficient	Familiarity coefficient	Authority coefficient
	A1	A2	A3	A4	Ca	Cs	CR
1	0.5	0.3	0.1	0.1	1.0	1.0	1.0
2	0.5	0.3	0.1	0.1	1.0	1.0	1.0
3	0.5	0.3	0.1	0.1	1.0	1.0	1.0
4	0.5	0.2	0.1	0.1	0.9	1.0	0.95
5	0.5	0.3	0.1	0.1	1.0	1.0	1.0
6	0.4	0.2	0.1	0.1	0.8	0.8	0.8
7	0.3	0.3	0.1	0.1	0.8	0.8	0.8
8	0.5	0.2	0.1	0.1	0.9	0.6	0.75
9	0.3	0.3	0.1	0.1	0.8	1.0	0.9
10	0.5	0.3	0.1	0.1	1.0	0.8	0.9
11	0.5	0.2	0.1	0.1	0.9	0.8	0.85
12	0.3	0.3	0.1	0.1	0.8	1.0	0.9

13	0.5	0.2	0.1	0.1	0.9	1.0	0.95
14	0.5	0.1	0.1	0.1	0.8	1.0	0.9

3.2.4.2.3 Indicator evaluation results

(1) Scoring results of specific AE of first round Delphi expert consultation meeting

According to the scoring results of this round, a total of 36 indicators has a mean value greater than 4 points, 34 indicators have CV<0.25, with CV of items 1, 7, 8, 22, 23, 33, 35, 36, 42, 43, and 44>0.25, which were considered to be deleted. The Kendall's W is 0.506, which means the degree of coordination of experts is acceptable. The specific scoring results are shown below in Table 3-7.

Table 3-7. The specific scoring results of specific AE of first round (N=45)

Item	Mean value (M)	Standard deviation (S)	CV
Abacavir (ABC)			
1.Allergic reaction	2.50	1.61	0.64
2.Nausea	4.79	0.43	0.09
3.Vomiting	4.79	0.58	0.12
4.Diarrhea	4.57	0.85	0.19
Efavirenz (EFV)			
5.Dizziness	4.79	0.58	0.12
6.Headache	4.86	0.36	0.07
7.Drowsiness	2.64	1.50	0.57
8.Allergic reaction	2.14	1.61	0.75
9.Anxiety	4.79	0.43	0.09
10.Depression	4.57	0.51	0.11
11.Insomnia	4.64	0.63	0.14
12.Hyperlipidemia	4.79	0.58	0.12
13.Hypertriglyceridemia	4.86	0.36	0.07
14.Drug-induced liver injury	4.86	0.36	0.07
Lamivudine (3TC)			
15.Headache	4.79	0.80	0.17
16.Nausea	4.79	0.80	0.17

17.Diarrhea	4.71	0.83	0.18
Tenofovir Disoproxil Fumarate (TDF)			
18.Drug-related kidney injury	4.79	0.43	0.09
19.Nausea	4.79	0.58	0.12
20.Vomiting	4.64	0.93	0.20
21.Diarrhea	4.64	1.08	0.23
22.Hypophosphatemia	2.07	1.44	0.70
23.Acidosis	2.29	1.50	0.65
Zidovudine (AZT)			
24.Anemia	4.36	0.63	0.15
25.Nausea	4.86	0.54	0.11
26.Vomiting	4.79	0.80	0.17
27.Diarrhea	4.71	0.83	0.18
28.Increased creatine phosphokinase	4.79	0.58	0.12
29.Drug-induced liver injury	4.71	0.83	0.18
Lopinavir / Ritonavir (LPV/r)			
30.Nausea	4.93	0.27	0.05
31.Diarrhea	4.93	0.27	0.05
32.Hyperlipidemia	5.00	0.00	0.00
33.Headache	2.43	1.51	0.62
34.Drug-related kidney injury	4.64	0.63	0.14
Dolutegravir (DTG)			
35.Insomnia	4.36	1.15	0.26
36.Depression	4.43	1.16	0.26
37.Dizziness	4.86	0.36	0.07
38.Headache	4.93	0.27	0.05
39.Nausea	4.71	0.61	0.13
40.Vomiting	4.64	0.63	0.14
41.Diarrhea	4.64	1.08	0.23
42.Allergic reaction	1.79	0.98	0.54
43.Drug-induced liver injury	1.57	0.94	0.60
Nevirapine (NVP)			

44.Allergic reaction	2.86	1.29	0.45
45.Drug-induced liver injury	4.93	0.27	0.05

(2) Scoring results of manifestations to AE of first round Delphi expert consultation meeting.

According to the scoring results of this round, a total of 18 indicators has been scored, 14 of which has a mean value greater than 4 points, 16 indicators have CV<0.25, with CV of items 2 and 11>0.25, which were considered to be revised in details or deleted. The Kendall's W is 0.763, which means the degree of coordination of experts is acceptable. The specific scoring results are shown below in Table 3-8.

Table 3-8. The scoring results of manifestations to AE of first round (N=18)

Item	Mean value (M)	Standard deviation (S)	CV
1.Allergic reaction: Urticaria.	1.29	0.61	0.47
2.Nausea: Level I: Decreased appetite without changes in eating habits; Level II: Decreased oral food intake without significant weight loss, dehydration, or malnutrition; Level III: Insufficient oral intake of energy and water; Level IV: -; Level V: -.	4.71	0.61	0.13
3.Vomiting: Level I: Mild: mild vomiting 1-2 times; Level II: Moderate: Vomiting 3-5 times; Level III: Severe: Vomiting more than 6 times; Level IV: Life threatening; Level V: Die.	4.86	0.36	0.07
4.Diarrhea: Level I: Increase in stool frequency <4 times per day compared to baseline; mild increase in ostomy discharge; Level II: Compared with baseline, stool frequency increased by 4 to 6 times per day; moderate increase in stomal discharge; limitation of instrumental activities of daily living; Level III: Increased stool frequency by ≥7 per day compared to baseline; severe increase in ostomy discharge compared to baseline; limited self-care activities of daily living; Level IV: Life threatening; Level V: Die.	5.00	0.00	0.00

5.Dizziness: Level I: Mild jitteriness or movement; Level II: Moderately unstable: affects instrumental activities of daily living; Level III: Severe jitteriness or a sense of movement: Interfering with self-care activities of daily living; Level IV: -; Level V: -.	4.43	0.65	0.15
6.Headache: Level I: Mild pain; Level II: Moderate pain: affecting instrumental activities of daily living; Level III: Severe pain: affects self-care activities of daily living; Level IV: -; Level V: -.	5.00	0.00	0.00
7.Drowsiness: Level I: Increased need for light sleep; Level II: Increased need for moderate sleep; Level III: Increased need for severe sleep; Level IV: -; Level V: -.	4.07	0.83	0.20
8.Anxiety: Level I: Mild symptoms: restlessness; nervousness; Level II: Moderate: limiting instrumental activities of daily living; tachycardia; Level III: Severe symptoms: interfere with self-care activities of daily living; dyspnea; Level IV: Life threatening; Level V: Die.	4.21	0.70	0.17
9.Depression: Level I: Mild symptoms; Level II: Moderate symptoms: affecting instrumental activities of daily living; Level III: Severe symptoms: limited personal self-care ability; Level IV: Endangering life: endangering self or others; Level V: Die.	4.50	0.65	0.14
10. Insomnia: Level I: Mild difficulty sleeping, staying asleep or waking up early; Level II: Moderate difficulty sleeping, staying asleep or waking up early; Level III: Severe trouble sleeping, staying asleep or waking up early; Level IV: -; Level V: -.	2.71	0.91	0.34
11. Hyperlipidemia: Level I: Hypercholesterolemia: increased serum total cholesterol >5.72 mmol·L-1, normal triglycerides; hypertriglyceremia: increased serum triglycerides >1.70 mmol·L-1, normal total cholesterol; mixed hyperlipidemia Symptoms: Serum total cholesterol and triacylglycerol levels were increased, that is, total cholesterol>5.72 mmol·L-1, triacylglycerol>1.70 mmol·L-1; low-density lipoproteinemia: serum high-density	5.00	0.00	0.00

lipoprotein cholesterol decreased <1.2 mmol·L-1; Level II: Peripheral subcutaneous lipoatrophy: more common in the face, limbs and buttocks; concentric fat accumulation: more common in the abdomen, chest, neck, back, forming the so-called buffalo back and lipoma; Level III: Pancreatitis; Level IV: Lead to life-threatening consequences; Level V: Die.			
12. Hypertriglyceridemia: Level I: Mild: TG level 150 mg/dL-199 mg/dL; 1.7 mmol/L-2.3 mmol/L; Level II: Moderate: TG level 200mg/dL-999mg/dL; 2.3mmol/L-11.2mmol/L; Level III: Severe: TG level 1000mg/dL-1999mg/dL; 11.2mmol/L-22.4mmol/L; Level IV: Very severe: TG level ≥2000mg/dL; ≥22.4mmol/L; Level V: Die.	5.00	0.00	0.00
13. Drug-induced liver injury: Level I: Mild liver injury: ALT, AST < 5.0 ULN, TBIL normal or < 2.5 ULN; most patients can adapt. With or without symptoms of fatigue, weakness, nausea, anorexia, right upper quadrant pain, jaundice, itching, rash, or weight loss; Level II: Moderate liver injury: ALT, AST < 5.0 ULN, TBIL normal or < 2.5 ULN; the above symptoms may be aggravated; Level III: Severe liver damage. 5.0 ULN ＜ ALT, AST ＜ 10.0 ULN, 2.5 ULN ＜ TBIL ＜ 5.0 ULN; the patient's symptoms further aggravated, requiring hospitalization, or prolonged hospital stay; Level IV: Acute liver failure: ALT, AST≥10.0 ULN, TBIL≥5.0 ULN, ascites or hepatic encephalopathy or other organ failure related to drug-induced liver injury may occur at the same time; Level V: Fatal: Death due to drug-induced liver injury, or require liver transplantation to survive.	5.00	0.00	0.00
14. Drug-related kidney injury: Level I: Glomerular filtration rate (eGFR) or creatinine clearance (CrCl) less than 60mL/min/1.73m2 or proteinuria 2+; urine protein/creatinine greater than 0.5; Level II: Estimated eGFR or CrCl 59-30 mL/min/1.73m2; Level III: Estimated eGFR or CrCl 29 to 15 mL/min/1.73m2; Level IV: Estimated eGFR or CrCl less than 15 mL/min/1.73m2; Level V: Die.	5.00	0.00	0.00

15. Hypophosphatemia: Level I: Only found in the laboratory; Level II: Only found in the laboratory; Level III: Serious or significant medical event but not immediately life-threatening; Level IV: Life threatening; Level V: Die.	3.00	0.68	0.23
16. Acidosis: Level I: pH < normal, but ≥ 7.3; Level II: -; Level III: pH<7.3; Level IV: Life threatening; Level V: Die.	3.50	0.76	0.22
17. Anemia: Level I: Hemoglobin < lower limit of normal to 10.0 g/dL; < lower limit of normal to 6.2 mmol/L; < lower limit of normal to 100 g/L; Level II: Hemoglobin < 10.0-8.0 g/dL; < 6.2-4.9 mmol/L; < 100-80 g/L; Level III: Hemoglobin < 8.0 g/dL; < 4.9 mmol/L; < 80 g/L; Level IV: Life threatening; Level V: Die.	4.71	0.47	0.10
18. Increased creatine phosphokinase: Level I: > The upper limit of the normal value～2.5 times the upper limit of the normal value; Level II: >2.5 times the upper limit of the normal value ~ 5 times the upper limit of the normal value; Level III: >5 times the upper limit of the normal value ~ 10 times the upper limit of the normal value; Level IV: >10 times the upper limit of normal; Level V: -.	5.00	0.00	0.00

(3) Scoring results of interventions to AE of first round Delphi expert consultation meeting

According to the scoring results of this round, a total of 18 indicators has been scored, 14 of which has a mean value greater than 4 points, 16 indicators have CV<0.25, with CV of items 2 and 16>0.25, which were considered to be revised in details or deleted. The Kendall's W is 0.601, which means the degree of coordination of experts is acceptable. The specific scoring results are shown below in Table 3-9.

Table 3-9. The scoring results of interventions to AE of first round (N=18)

Item	Mean	Standard	CV

	value (M)	deviation (S)	
1.Allergic reaction: Urticaria: urticaria lesions less than 10% of body surface area: topical treatment or enhanced monitoring; urticaria lesions covering 10-30% of body surface area: oral medication; urticaria lesions greater than 30% of body surface area: intravenous administration drug treatment.	1.43	0.65	0.45
2.Nausea: Level I: Strengthen monitoring; Level II: Change medication regimen; Level III: Need for nasogastric feeding, total parenteral nutrition; Level IV: -; Level V: -.	4.71	0.47	0.10
3.Vomiting: Level I: Intensified surveillance; no other interventions required; Level II: Outpatient intravenous fluids; medical intervention indicated; Level III: Change in medication regimen; need for nasogastric feeding, total parenteral nutrition, or hospitalization; Level IV: Emergency intervention; changing drug regimens; Level V: -.	4.50	0.76	0.17
4.Diarrhea: Level I: Strengthen monitoring; Level II: Oral rehydration; change medication regimen; Level III: Change in medication regimen; hospitalization required; Level IV: Need urgent treatment; Level V: -.	4.79	0.43	0.09
5.Dizziness: Level I: Strengthen monitoring; Level II: Reduce drug dose; Level III: Change medication regimens; Level IV: -; Level V: -.	4.57	0.51	0.11
6.Headache: Level I: Strengthen monitoring; Level II: Reduce drug dose; Level III: Change medication regimens; Level IV: -; Level V: -.	4.64	0.50	0.11
7.Drowsiness: Level I: Strengthen monitoring; Level II: Reduce drug dose; Level III: Change medication regimens; Level IV: -; Level V: -.	3.43	0.85	0.25
8.Anxiety: Level I: Increase monitoring; reduce drug dose; Level II: Change in medication regimen; no hospitalization required; Level III: Change in medication regimen; transfer to mental health center for	4.64	0.50	0.11

disease-specific treatment; Level IV: Emergency intervention; transfer to hospital; Level V: -.			
9.Depression: Level I: Increase monitoring; reduce drug dose; Level II: Change in medication regimen; no hospitalization required; Level III: Change in medication regimen; transfer to mental health center for disease-specific treatment; Level IV: Emergency intervention; transfer to hospital; Level V: -.	4.71	0.47	0.10
10. Insomnia: Level I: Strengthen monitoring; Level II: Reduce drug dose; Level III: Change medication regimens; Level IV: -; Level V: -.	2.86	0.66	0.23
11. Hyperlipidemia: Level I: Increased monitoring; patients need to change their eating habits; Level II: Drug intervention, commonly used drugs include statins: such as lovastatin, simvastatin, pravastatin; fibrates: such as bezafibrate, fenofibrate, gemfibrozil; niacin: such as Oxymetholide azine etc.; Level III: Pancreatitis: 1. Mild, asymptomatic manifestations, strengthen monitoring; 2. Enzyme elevation; only radiological examinations, acute pancreatitis complicated with venous chylous blood or blood triglyceride >11.3 mmol/L, can be diagnosed as hyperlipidemia acute pancreatitis: fasting water ≥24 Diet adjustment after h; use lipid-lowering drugs and other auxiliary lipid-lowering means [low-dose low-molecular-weight heparin, insulin, lipid adsorption and/or plasma exchange] to control blood lipids; it is recommended to reduce triglyceride levels to <5.65 mmol/ L; 3. Severe pain, vomiting: fluid therapy, analgesia, and nutritional support; 4. Life-threatening treatment requiring urgent treatment: surgery; Level IV: -; Level V: -.	4.79	0.43	0.09
12. Hypertriglyceridemia: Level I: Actively improve lifestyle (including reasonable diet, increase physical exercise, control weight, etc.); strengthen monitoring; Level II: Actively improve life style (including reasonable diet, increase physical activity, control weight, etc.); strengthen monitoring; change drug	4.79	0.43	0.09

treatment regimen; when TG level ≥ 5.65 mmol/L, the risk of acute pancreatitis has been significantly increased, at this time TG-lowering drugs (especially fibrates) should be started immediately; Level III: Drug intervention, commonly used drugs include statins: such as lovastatin, simvastatin, pravastatin; fibrates: such as bezafibrate, fenofibrate, gemfibrozil; niacin: such as Oxymetholide azine etc.; Level IV: The risk of acute pancreatitis in patients will be significantly increased, and fibrates, niacin or n-3 fatty acids should be treated immediately or in combination with statins. Simple sugar intake; Level V: -.			
13. Drug-induced liver injury: Continue antiviral treatment, hepatoprotective treatment, and clinical observation. Hepatoprotective treatments include: 1) Anti-inflammatory and hepatoprotective drugs: Magnesium isoglycyrrhizinate can be used to treat acute hepatocellular and mixed DILI with significantly elevated ALT; glycyrrhizic acid preparations can also be used to treat mild to moderate hepatocyte damage and mixed 0DILI; For newly treated cases of AIDS, patients with abnormal liver function with normal total bilirubin after HAART, on the basis of not stopping HAART, silibinin can be used to protect the liver to treat drug-induced liver damage; 2) Antioxidant drugs: reducing glutathione The combination of sathione and glycyrrhizic acid is often used in the treatment of DILI patients; after HAART, DILI patients were treated with Tiopronin for 2 months, and the recovery time of liver function was significantly shortened; 3) Drugs for promoting bile excretion: ursodeoxycholic acid It can be used to treat DILI of cholestatic hepatocyte injury; Adenosylmethionine can be used to treat DILI of cholestatic hepatocyte injury; 4) Improve hepatocyte energy metabolism: adenosine triphosphate, coenzyme A, inosine and vitamins can improve hepatocyte energy by improving Metabolism, to a certain extent, it can protect liver cells, and vitamin B can also be used appropriately.	4.86	0.36	0.07

14. Drug-related kidney injury: Level I: Continue ART; strengthen surveillance; Level II: Reduce drug dose or increase dosing interval; discontinue TDF, change drug regimen; Level III: Change of medication regimen, hospitalization; Level IV: Need for dialysis or kidney transplant; Level V: -.	4.86	0.36	0.07
15. Hypophosphatemia: Level I: No medical intervention required; increased surveillance; Level II: Oral alternative medicine therapy; Level III: Change of medication regimen; hospitalization; Level IV: Immediate discontinuation; emergency intervention; hospitalization; Level V: -.	2.00	0.96	0.48
16. Acidosis: Level I: Strengthen monitoring; Level II: Strengthen monitoring; Level III: Change in medication regimen; hospitalization required; Level IV: Change in medication regimen; hospitalization required; Level V: -.	4.21	0.70	0.17
17. Anemia: Level I: Increased monitoring of blood counts (routine blood); no need to change drug regimens; Level II: The dose of AZT should be reduced day by day until signs of bone marrow recovery appear; discontinue the drug for 2 to 4 weeks to promote bone marrow recovery; Level III: Administer blood transfusions while adjusting doses; monitor blood counts continuously (rhythm); Level IV: Emergency treatment; Level V: -.	4.14	0.66	0.16
18. Increased creatine phosphokinase: Level I: Strengthen monitoring; Level II: Consider Heart Failure or Cardiac Disorder: Risk of Myocardial Infarction; Level III: Reduce medication doses or change medication regimens; Level IV: Emergency treatment; Level V: -.	4.43	0.65	0.15

(4) Key points of first round Delphi expert consultation meeting

① Experts suggested that the difference between allergic reaction and hypersensitivity reaction must be clarified. The common serious AE of antiviral drugs are hypersensitivity reactions, for which the intervention is also different from allergic reaction,

② Experts demonstrated that the AE of EFV can change the item "somnolence" to "dreams", and add the items "inattention" and "rash"; in addition, because TDF can cause long-term problems such as osteoporosis, it should be added " Decreased bone density" entry; at the same time, "anemia" is caused by myelosuppression, and myelosuppression can also bring other adverse effects, so experts propose to change the "anemia" entry to "myelosuppression". Common AE of AZT should be added to the item "lactic acidosis",

③ Experts suggested that the grading of mental symptoms such as depression, anxiety, and sleep quality needs to be determined by a clear scale. However, after discussing with the technicians, the researcher demonstrated that the grading of the scale could not be realized from technical level in the information system constructed in this research,

④ Experts suggested that the content formulated according to the CTCAE standard be modified to varying degrees according to the actual situation of AIDS. For example, AE caused by some antiviral drugs are mild and do not need to be graded, and the corresponding treatment measures should also be modified, typically including dizziness, Headache and other physical symptoms. These symptoms generally disappear on their own after taking the drug for a period of time, so researchers do not need to rank these symptoms in the symptoms and make corresponding interventions,

⑤ In this part, the researcher listed all possible AE with their corresponding clinical manifestations and interventions. Experts agreed and indicated that common and rare AE should be integrated to cover all PLWHIV with AE. In fact, common AE, despite their high incidence, are often less deadly than rare AE. Rare AE often have insignificant early clinical manifestations, and require clinical staffs to have high sensitivity and continuous monitoring of relevant physiological indicators. Rare AE that are discovered at a later stage usually cause irreversible harm, thus it can be

seenthat it is very necessary to list all possible AE and clearly indicate targeted interventions at different levels.

3.2.4.3 Results of the second round of Delphi expert consultation

3.2.4.3.1 The recovery rate

A total of 14 consultation letters were distributed, and 14 were actually recovered. The expert inquiry letter recovery rate was 100%, which indicated that the experts were highly motivated.

3.2.4.3.2 Authority coefficient (CR)

Experts' Familiarity Scores with research content is shown in Table 3-4 above, and experts' judgments on the research content scores are shown in Table 3-5. Table 3-6 shows the authority of this round of expert consultation. The calculation results indicated CR > 0.70, which means a high-level authority of 14 experts.

3.2.4.3.3 Indicator evaluation results

(1) Scoring results of specific AE of second round Delphi expert consultation meeting

According to the scoring results of this round, all indicators have a mean value greater than 4 points, with CV<0.25. The Kendall's W is 0.059, which means the degree of coordination of experts is acceptable. The specific scoring results are shown below in Table 3-10.

Table 3-10. Specific AE of second round (N=41)

Item	Mean value (M)	Standard deviation (S)	CV
Abacavir (ABC)			
1.Hypersensitivity	4.93	0.27	0.05
2.Nausea	4.93	0.27	0.05
3.Vomiting	5.00	0.00	0.00
4.Diarrhea	4.93	0.27	0.05
Efavirenz (EFV)			
5.Dizziness	5.00	0.00	0.00
6.Headache	5.00	0.00	0.00
7.Nightmares, vivid dreams	5.00	0.00	0.00
8.Inattention	4.93	0.27	0.05
9.Rash	5.00	0.00	0.00

10.Anxiety	5.00	0.00	0.00
11.Depression	5.00	0.00	0.00
12.Insomnia	4.93	0.27	0.05
13.Hyperlipidemia	5.00	0.00	0.00
14.Hypertriglyceridemia	5.00	0.00	0.00
15.Drug-induced liver injury	4.93	0.27	0.05
Lamivudine (3TC)			
16.Headache	5.00	0.00	0.00
17.Nausea	4.86	0.36	0.07
18.Diarrhea	5.00	0.00	0.00
Tenofovir Disoproxil Fumarate (TDF)			
19.Drug-related kidney injury	5.00	0.00	0.00
20.Nausea	4.93	0.27	0.05
21.Vomiting	5.00	0.00	0.00
22.Diarrhea	5.00	0.00	0.00
23.Decreased bone density	5.00	0.00	0.00
Zidovudine (AZT)			
24.Myelosuppression	5.00	0.00	0.00
25.Nausea	4.93	0.27	0.05
26.Vomiting	5.00	0.00	0.00
27.Diarrhea	5.00	0.00	0.00
28.Lactic acidosis	5.00	0.00	0.00
29.Increased creatine phosphokinase	4.86	0.36	0.07
30.Drug-induced liver injury	5.00	0.00	0.00
Lopinavir / Ritonavir (LPV/r)			
31.Nausea	5.00	0.00	0.00
32.Diarrhea	4.93	0.27	0.05
33.Hyperlipidemia	5.00	0.00	0.00
34.Drug-related liver injury	5.00	0.00	0.00
Dolutegravir (DTG)			
35.Dizziness	4.93	0.27	0.05
36.Headache	5.00	0.00	0.00

37.Nausea	5.00	0.00	0.00
38.Vomiting	4.93	0.27	0.05
39.Diarrhea	4.93	0.27	0.05
Nevirapine (NVP)			
40.Rash	4.93	0.27	0.05
41.Drug-induced liver injury	4.93	0.27	0.05

(2) Scoring results of manifestations to AE of second round Delphi expert consultation meeting

According to the scoring results of this round, all indicators have a mean value greater than 4 points, with CV<0.25. The Kendall's W is 0.054, which means the degree of coordination of experts is acceptable. The specific scoring results are shown below in Table 3-11.

Table 3-11. Manifestations to AE of second round (N=20)

Item	Mean value (M)	Standard deviation (S)	CV
1.Hypersensitivity: High fever, diffuse rash, nausea, headache, diarrhea, arthralgia, laryngitis, dyspnea, abnormal liver function within 6 weeks of taking the drug.	4.93	0.27	0.05
2.Nausea: Level I: Decreased appetite; Level II: Decreased oral food intake without significant weight loss, dehydration, or malnutrition; Level III: Insufficient oral intake of energy and water.	5.00	0.00	0.00
3.Vomiting: Mild: vomiting 1-2 times; Moderate: Vomiting 3-5 times; Severe: Vomiting more than 6 times.	5.00	0.00	0.00
4.Diarrhea: Level I: Increase in stool frequency <4 times per day compared to baseline; mild increase in ostomy discharge; Level II: Compared with baseline, stool frequency increased by 4 to 6 times per day; moderate increase in stomal discharge; limitation of instrumental activities of daily living; Level III: Increased stool frequency by ≥7 per day compared to baseline; severe increase in ostomy discharge compared to baseline; limited self-care activities of daily living.	5.00	0.00	0.00
5.Dizziness: From the first medication, the patient reported.	4.86	0.36	0.07
6.Headache: From the first medication, the patient reported.	5.00	0.00	0.00

7.Nightmares, vivid dreams: From the first medication, the patient reported.	4.93	0.27	0.05
8.Inattention: From the first medication, the patient reported.	5.00	0.00	0.00
9.Rash: Grade I/II (mild/moderate): erythema, pruritus, diffuse maculopapular rash, dry scaling; Grade III/IV (severe/potentially life-threatening): blistering, wet scaling, ulceration, mucosal involvement, Suspected SJ syndrome, toxic necrolysis, erythema multivariate, gangrene, exfoliative dermatitis.	4.93	0.27	0.05
10. Anxiety: Patient self-reported; restlessness; nervousness; limiting instrumental activities of daily living; moderate anxiety can lead to tachycardia; severe dyspnea.	5.00	0.00	0.00
11. Depression: Self-reported by the patient; slow behavior, passive life, lazy, unwilling to do things, unwilling to communicate with people around, often sitting alone, or lying in bed all day, living alone, alienating relatives and friends, avoiding social interaction; depressed, sad or unhappy; Severe cases with negative suicidal thoughts or behaviors.	4.93	0.27	0.05
12. Insomnia: Patient self-reported.	5.00	0.00	0.00
13. Hyperlipidemia: Level I: Hypercholesterolemia: increased serum total cholesterol >5.72 mmol·L-1,; hypertriglyceremia: increased serum triglycerides >1.70 mmol·L-1, normal total cholesterol; mixed hyperlipidemia Symptoms: Serum total cholesterol and triacylglycerol levels were increased, that is, total cholesterol>5.72 mmol·L-1, triacylglycerol>1.70 mmol·L-1; low-density lipoproteinemia: serum high-density lipoprotein cholesterol decreased <1.2 mmol·L-1; Level II: Peripheral subcutaneous lipoatrophy: more common in the face, limbs and buttocks; concentric fat accumulation: more common in the abdomen, chest, neck, back, forming the so-called buffalo back and lipoma; Level III: Pancreatitis.	4.93	0.27	0.05
14. Hypertriglyceridemia: Mild: TG level 150 mg/dL-199 mg/dL; 1.7 mmol/L-2.3 mmol/L; Moderate: TG level	5.00	0.00	0.00

200mg/dL-999mg/dL; 2.3mmol/L-11.2mmol/L; Severe: TG level 1000mg/dL-1999mg/dL; 11.2mmol/L-22.4mmol/L; Very severe: TG level ≥2000mg/dL; ≥22.4mmol/L.			
15. Drug-induced liver injury: Mild liver injury: ALT, AST < 5.0 ULN, TBIL normal or < 2.5 ULN; most patients can adapt. With or without symptoms of fatigue, weakness, nausea, anorexia, right upper quadrant pain, jaundice, itching, rash, or weight loss; Moderate liver injury: ALT, AST < 5.0 ULN, TBIL normal or < 2.5 ULN; the above symptoms may be aggravated; Severe liver damage. 5.0 ULN ＜ ALT, AST ＜ 10.0 ULN, 2.5 ULN ＜ TBIL ＜ 5.0 ULN; the patient's symptoms further aggravated, requiring hospitalization, or prolonged hospital stay; Acute liver failure: ALT, AST≥10.0 ULN, TBIL≥5.0 ULN, ascites or hepatic encephalopathy or other organ failure related to drug-induced liver injury may occur at the same time; Fatal: Death due to drug-induced liver injury, or require liver transplantation to survive.	4.93	0.27	0.05
16. Drug-related kidney injury: Level I: Glomerular filtration rate (eGFR) or creatinine clearance (CrCl) less than 60mL/min/1.73m2 or proteinuria 2+; urine protein/creatinine greater than 0.5; Level II: Estimated eGFR or CrCl 59-30 mL/min/1.73m2; Level III: Estimated eGFR or CrCl 29 to 15 mL/min/1.73m2; Level IV: Estimated eGFR or CrCl less than 15 mL/min/1.73m2; Level V: Die.	5.00	0.00	0.00
17. Decreased bone density: Pain in multiple parts of the body and multiple joints.	4.93	0.27	0.05
18. Myelosuppression: Manifested by anemia and/or neutropenia, which is more common in patients with low baseline CD4. Level I: Hb < lower limit of normal value to 10.0 g/dL; < lower limit of normal value to 6.2 mmol/L; < lower limit of normal value to 100 g/L; Level II: Hb < 10.0-8.0 g/dL; < 6.2-4.9 mmol/L; < 100-80 g/L; Level III: Hb < 8.0 g/dL; < 4.9 mmol/L; < 80 g/L.	5.00	0.00	0.00
19. Lactic acidosis: Uncommon, but fatal, manifesting as fatigue, nausea, vomiting, abdominal pain, muscle	4.93	0.27	0.05

pain, and weight loss, often with late shortness of breath and shortness of breath.			
20. Increased creatine phosphokinase: Level I: > The upper limit of the normal value～2.5 times the upper limit of the normal value; Level II: >2.5 times the upper limit of the normal value ~ 5 times the upper limit of the normal value; Level III: >5 times the upper limit of the normal value ~ 10 times the upper limit of the normal value; Level IV: >10 times the upper limit of normal.	5.00	0.00	0.00

(3) Scoring results of interventions to AE of second round Delphi expert consultation meeting

According to the scoring results of this round, all indicators have a mean value greater than 4 points, with CV<0.25. The Kendall's W is 0.062, which means the degree of coordination of experts is acceptable. The specific scoring results are shown below in Table 3-12.

Table 3-12. Interventions to AE of second round (N=20)

Item	Mean value (M)	Standard deviation (S)	CV
1.Hypersensitivity: Immediately discontinue and not re-administer the drug; urgent intervention; hospitalization; supportive care, poor response to corticosteroids and antihistamines, most symptoms resolve within 48 hours of discontinuation.	4.93	0.27	0.05
2.Nausea: Level I: Strengthen monitoring; Level II: Change medication regimen; Level III: Need for nasogastric feeding, total parenteral nutrition.	5.00	0.00	0.00
3.Vomiting: Mild: intensive monitoring, no other intervention required; moderate: outpatient intravenous fluids, medical intervention required; severe: nasogastric feeding, total parenteral nutrition,	5.00	0.00	0.00

or hospitalization required.			
4.Diarrhea: Level I: Strengthen monitoring; Level II: Oral rehydration; change medication regimen; Level III: Change in medication regimen; hospitalization required.	5.00	0.00	0.00
5.Dizziness: Strengthen monitoring; generally disappear in 2-3 weeks, and the drug treatment plan can be replaced in severe cases.	4.93	0.27	0.05
6.Headache: Strengthen monitoring; generally disappear in 2-3 weeks, and the drug treatment plan can be replaced in severe cases.	5.00	0.00	0.00
7.Nightmares, vivid dreams: Strengthen monitoring; generally disappear in 2-3 weeks, and the drug treatment plan can be replaced in severe cases.	5.00	0.00	0.00
8.Inattention: Strengthen monitoring; generally disappear in 2-3 weeks, and the drug treatment plan can be replaced in severe cases.	5.00	0.00	0.00
9.Rash: Grade I/II (mild/moderate): strengthen monitoring, continue antiviral treatment, and administer antihistamines at the same time. Liver function testing should be carried out for moderate rash accompanied by fever, and drug therapy can be changed. LPV/r; Grade III/IV (severe/potentially life-threatening): stop all antiviral therapy, severe rash with fever, liver function tests should be performed.	4.93	0.27	0.05
10. Anxiety: Strengthen monitoring; reduce drug dose; change drug treatment plan; severe cases or those with anxiety disorder judged by self-rating scale test are transferred to mental health center for special disease treatment.	4.93	0.27	0.05
11. Depression: Strengthen monitoring; reduce drug dose; change drug treatment plan; severe cases or those who are judged to be depressed by the self-rating scale test are transferred to mental health	5.00	0.00	0.00

centers for special disease treatment.			
12. Insomnia: Increase monitoring; reduce drug dose; change drug regimen.	4.93	0.27	0.05
13. Hyperlipidemia: Level I—intensified surveillance; patients need dietary changes. Class II - drug intervention, commonly used drugs include statins: such as lovastatin, simvastatin, pravastatin; fibrates: such as bezafibrate, fenofibrate, gemfibrozil; niacin: Such as Oxymethazine and so on. Grade III - mild pancreatitis asymptomatic, enhanced monitoring; elevated enzymes; acute pancreatitis combined with venous chylous blood or blood triglyceride >11.3 mmol/L only found on radiological examination, can be diagnosed as high Lipemic acute pancreatitis: dietary adjustment after fasting for ≥ 24 hours; use of blood lipid-lowering drugs and other auxiliary lipid-lowering means [low-dose low-molecular-weight heparin, insulin, lipid adsorption and/or plasma exchange] to control blood lipids; Recommend reducing triglyceride levels to <5.65 mmol/L as soon as possible; severe pain, vomiting: fluid therapy, analgesia, and nutritional support; life-threatening, urgent intervention indicated: surgery.	5.00	0.00	0.00
14. Hypertriglyceridemia: Mild: Actively improve lifestyle (including reasonable diet, increase physical exercise, control weight, etc.); strengthen monitoring. Moderate: Actively improve lifestyle (including reasonable diet, increase physical activity, control weight, etc.); strengthen monitoring; change drug treatment regimen; when TG level ≥ 5.65 mmol/L, the risk of acute pancreatitis has been significantly increased, at this time, TG-lowering drugs (especially fibrates) should be started immediately. Severe: drug intervention, commonly used drugs include statins: such as lovastatin, simvastatin, pravastatin; fibrates: such as bezafibrate, fenofibrate, gemfibrozil; niacin: such as oxygen Pyrazine, etc. Very severe: The risk of acute pancreatitis will increase significantly, and fibrates, niacin or n-3 fatty acids	4.93	0.27	0.05

should be treated immediately or in combination with statins; Reduce fat and simple sugar intake.			
15. Drug-induced liver injury: Mild/moderate/severe liver injury: continue antiviral therapy, liver protection therapy, clinical observation. Hepatoprotective treatments include: 1) Anti-inflammatory and hepatoprotective drugs: Magnesium isoglycyrrhizinate can be used to treat acute hepatocellular and mixed DILI with significantly elevated ALT; glycyrrhizic acid preparations can also be used to treat mild to moderate hepatocyte damage and mixed DILI; For newly treated cases of AIDS, patients with abnormal liver function with normal total bilirubin after HAART, on the basis of not stopping HAART, silibinin can be used to protect the liver to treat drug-induced liver damage; 2) Antioxidant drugs: reducing glutathione The combination of sathione and glycyrrhizic acid is often used in the treatment of DILI patients; after HAART, DILI patients were treated with Tiopronin for 2 months, and the recovery time of liver function was significantly shortened; 3) Drugs for promoting bile excretion: ursodeoxycholic acid It can be used to treat DILI of cholestatic hepatocyte injury; Adenosylmethionine can be used to treat DILI of cholestatic hepatocyte injury; 4) Improve hepatocyte energy metabolism: adenosine triphosphate, coenzyme A, inosine and vitamins can improve hepatocyte energy by improving Metabolism plays a role in protecting liver cells to a certain extent, and vitamin B can also be used appropriately. Acute liver injury: Withhold all antiviral drugs. Fatal: Liver Transplant.	5.00	0.00	0.00
16. Drug-related kidney injury: Grade I: Continue antiviral treatment; strengthen monitoring. Class II: reduce the drug dose or increase the dosing interval; discontinue TDF, and change the drug treatment regimen. Grade III: Change the drug treatment plan, hospitalization. Class IV: requires dialysis or kidney transplantation.	4.93	0.27	0.05

17. Decreased bone density: Strengthen monitoring; supplement calcium, VitD; reduce weight; crutches; surgical treatment.	5.00	0.00	0.00
18. Myelosuppression: For mild cases, monitoring of blood cell counts (blood routine) should be strengthened; no need to change drug treatment regimens. If Hb or Hct decreased by ≥25% compared with the baseline level, AZT was discontinued for 2 to 4 weeks to promote bone marrow recovery; if the granulocyte count was lower than 750, AZT could be discontinued, and AZT could be replaced with TDF. In severe cases, hospitalization is required, and blood transfusion therapy is given while the dose is adjusted; continuous monitoring of blood counts (blood count).	4.86	0.36	0.07
19. Lactic acidosis: Immediately evaluate the patient and consider discontinuation of all antiviral therapy if the anion gap (AG) is ≥12, and should be discontinued immediately if AG is ≥16. Rehydration, alkali supplementation, a lot of VitB1, B2, L-carnitine, coenzyme Q, VitC, antioxidants. Full clinical recovery takes 4-28 weeks, and antiviral therapy is restarted after the patient has fully recovered. Treatment regimens may include boosted Pis plus NNRTI, and may also include TDF and ABC.	4.86	0.36	0.07
20. Increased creatine phosphokinase: Level I: Enhanced monitoring; Level II: Consider heart failure or cardiac dysfunction: risk of myocardial infarction; Level III: Reduce drug dose or change drug regimens; Level IV: Emergency treatment.	5.00	0.00	0.00

3.2.5 Discussion

The initial version of the content framework was constructed by the researcher based on the existing literature, drug instructions and CTCAE 5.0, combined with the interview results from clinicians and nurses, which means that this framework has scientific and theoretical basis in theory. However, the CTCAE standard has certain defects in the field of AIDS, and there is a certain mismatch in AE of anti-disease drugs. Therefore, the researcher conducted two rounds of expert consultation and carefully revised the criteria items for each dimension based on expert opinions and have been optimized the pages of the framework according to the technicians' comments.

In this section, the researcher further supplemented the possible AE under the advice of experts, and modified the terms to be more standardized and unified. Some expressions, such as *"dizziness"*, have many synonyms in Chinese, which will lead to omissions when looking for patient information of the same AE in the system. In this research, the standardization of all specific AE terms can avoid this problem to the greatest extent, and provide more accurate data for scientific research and future clinical AE monitoring.

In this part, the researcher also found that there is controversy among experts on whether clinical manifestations should be graded, and some experts believe that grading different degrees of clinical features can more effectively solve the problem of patients, it is very necessary. However, more experts believe that theoretical knowledge should be more integrated with AIDS clinical practice. The AE grading standards mentioned in CTCAE are incomplete for PLWHIV, such as "dizziness" and other symptoms. These AE are self-reported symptoms of patients, which is difficult to define the degree due to the lack of quantitative basis, so that it is difficult to judge how to grade and take corresponding treatment, and such symptoms usually disappear after a period of medication, according to domestic PLWHIV In the current state of treatment, most patients with this symptom do not care when the symptoms are mild, and do not even inform the doctor. When the symptoms are more obvious, due to limitations of economic capacity, patients usually choose to endure the symptoms and wait for them to disappear on their own. A small number of patients who cannot tolerate it and can afford it will choose to change the drug treatment regimen, and this is a regimen that fully respects the patient's wishes, so it is usually not recommended as an intervention. Therefore, in the end, the researcher revised the symptom presentation and removed the clinical grading classification for some AE difficult to define the grading.

4 Testing and application of AE Monitoring View

4.1 Research purpose

After the final version of the framework being determined, the researcher worked with technicians who came from a medical technology company to develop and test the AE Monitoring View for PLWHIV based on AIDS database.

4.2 Research methods

4.2.1 Demands confirmation

The researcher discussed with the technicians from medical technology company about the feasibility of the final framework and asked the technicians to retell the requirements in order to assure that they were clear.

4.2.2 System design

The AE Monitoring View can be regarded as a child system based on AIDS database, thus there was a technician who designed the general system pages who also clarified the key version of the AE Monitoring View.

4.2.3 Development of AE Monitoring View for PLWHIV

After interface designed completely, the researcher asked the technicians to wrote and modify the front-end as well as back-end code of the AE Monitoring View for PLWHIV.

4.2.4 Testing of AE Monitoring View for PLWHIV

The technicians from the company and the information department of the hospital would submit the source code after developing the AE Monitoring View for PLWHIV. The researcher then tested the entire system several times, and suggested revisions to unstable partial programs and imperfect codes, which were revised again by technicians until the entire system remained stable. The researcher listed the complete functions and expected results that needed to be tested internally, and tested each interface through the back-end to confirm whether the actual interface results are consistent with the expected results. The researcher considered the development of the view to be successful when the actual results of all functions or interfaces were the same as the expected results.

4.2.5 Application of AE Monitoring View for PLWHIV

4.2.5.1 Research purpose

The AE Monitoring View for PLWHIV constructed in this research is currently in the beta version, which means no user has used this view yet, and it will be released together to SPHC when the entire AIDS database is built in the future. Therefore, the researcher was unable to conduct a formal usability evaluation over the users. After discussion, the researcher finally decided to conduct a feasibility pilot-test within the research team, and use the pilot-test results as the outcome of the feasibility evaluation of this research.

4.2.5.2 Participants

The researcher invited all 11 members of the research team including technicians and clinical staffs to try out the AE Monitoring View for PLWHIV to complete the pilot-test for internal usability evaluation.

4.2.5.3 Research methods

4.2.5.3.1 Research tools: *"Pilot-test Questionnaire of Internal Usability Evaluation to AE Monitoring View for PLWHIV"* Developed by researcher, including convenience, acceptance, stability, fluency and clinical applicability, was adopted. After drafting the items, the researcher submitted them to 5 experts who were familiar with the field of clinical information system evaluation for review and made amendments, and then submit them to experts for review after the amendments until the amendments were unanimously determined. The content validity coefficient (S-CVI) of the questionnaire was 0.94. The reliability of the questionnaire was tested among 11 research team members and the internal consistency Cronbach' alpha was measured to be 0.966 (See Appendix V).

4.2.5.3.2 Data collection: All the questionnaires were completed by the respondents themselves, and the respondents took them back on the spot at once to the researcher after finishing the questionnaires.

4.2.5.3.3 Data analysis: All data were analyzed using SPSS24.0 software. The researcher adopted frequency, percentage, mean, and standard deviation to describe the availability of views. The questionnaire used a 5-point system to evaluate the user's recognition of each item in the questionnaire. A score of 1-5 represents strongly disagree, disagree, relatively agree, agree, and strongly agree. The higher the score, the higher the satisfaction and usability with the AE Monitoring View for PLWHIV.

4.3 Research results

4.3.1 Key technology of development of AE Monitoring View for PLWHIV

The researcher also participated in the technology part of the system development, and used some key technology for testing. The front-end and back-end of the AE Monitoring View for PLWHIV are separated, and the micro-service architecture is adopted for development in this research. There are no restrictions on front-end and back-end development tools, as long as they are JS. In the actual development process, after discussions with researchers and technicians, it was finally decided to use Webstorm and vscode as development tools. Table 4-1 shows the details of the key technology over the development.

Table 4-1. Key technology of the development on AE Monitoring View for PLWHIV

	Front-end	Back-end
Development language	AngularJS8	.net core
Development environment	Linux	Linux
Development tool	Webstorm	vscode
Coding mode	UTF-8	UTF-8

4.3.2 Internal function tests of AE Monitoring View for PLWHIV

The researcher listed all the functions with expected results to test whether there were any bugs or errors during system implementation, as well as judging whether the actual results of the AE Monitoring View for PLWHIV operation was consistent with the expected results. Since the actual results will be shown below as system page display in another part, the list of functions and expected results will be shown below in Table 4-2 as internal function tests results and the actual results will only be presented in this table in the form of whether they are consistent with the expected results.

Table 4-2. Internal function tests results of AE Monitoring View for PLWHIV (N=58)

No.	Step action	Test data	Expected results	Actual results
	[Prerequisites] The login account has a special disease database, Log in to your account to view the overview of the home page.	N/A	Display library overview, diagnostic name, variable information, visualization variables, etc.	Yes
Special disease project				
1	Enter [Project Name] for a new project, fill in the corresponding content, and click [OK]	Common business - special disease project	The project entry shows [Unpublished]	Yes
2	Click on the project entry	N/A	Enter the [Program Design] page, the [Add Form] button is available; the [Publish to Beta] button is unavailable, and the Open Version Control button is not enabled by default	Yes
3	Click New Form, enter the form name input box, enter [form name], click the field selection box, select the selection/sorting criteria, and click [OK]	Patient information	The new form is successfully created, and the [Publish to Beta] button is available	Yes

4	Add two numerical controls, three text controls, one radio control and one grouping control, one multi-select, drop-down radio, drop-down multi-select, cascade, date, upload, and attachment picture controls to the form, click [Save]	Scheme design sample	Form saved successfully	Yes
5	Click the [Back] button of the [Basic Information] form	N/A	Return to project design page	Yes
6	In Scheme Design - Associated Events, click [Event], click [Add Event]; enter the event name, click [OK]; click New Event; click the New Event button, enter the name input box, enter the event name, and click [OK; click the [Follow-up 1] event edit button, enter the time interval from the previous event input box, input; click the maximum allowable time deviation input box, input; click [OK]; tick the form associated with the baseline, click [Save] Revise	Baseline data	The new event window pops up; the event is created successfully; the edit event window pops up; the event information is added successfully	Yes
7	Click [Form] to enter the form scheme	N/A	Pop-up window [Unpublished] -	Yes

	design, click [Publish to beta version]; click [Confirm and release version]; click [Publish official version]; click [OK]		[Beta]; pop-up window [Published successfully], the upper left corner [Unpublished] changes to [V Beta], add the [Release official version] button, the form can be deleted; the pop-up window "Confirm release" To the official version? The version control status cannot be modified after the project is released to the official version"; the project was successfully released to the official version	
8	Click the project name to enter the scientific research project and view the project entry	N/A	Show [official version]	Yes
9	[Premise: Enable the permission to add patients], click [Subject List] in the upper right corner menu; click [Add Subject]; enter the name in the input box; click OK	Patient name sample	Enter the official version of the subject list; the add patient page pops up; the phonetic code ZHSA is automatically generated according to the name, the subject	Yes

			number is 01000001, the automatic number is automatically checked, and the storage date defaults to the current date of the system; the patient is added successfully	
10	Click the [Form] button of the patient just added by the subject, and open another window page to enter the data entry page; click the submit button	Patient sample	Successfully submitted data, only the audit trail is displayed	Yes
11	Click the button behind the control to view the audit trail	N/A	Display audit trail information	Yes
Data warehouse				
12	Click [Special Disease Database Name] → [Data Warehouse]	N/A	Show that the variables and patient data under [Basic Information] are correct	Yes
13	Click the field menu on the left and select [Field]	Diagnose	Show that the variables and patient data under [Diagnosis] are correct	Yes
14	Click the right-hand down expand arrow in	N/A	Pop up to display all the data	Yes

	the pivot table patient data		under the patient	
15	Hover over the data quality graph of [variable name] in the pivot table	Diagnosis name	The data quality pie chart pops up, and the data scale is correct	Yes
16	Click the down arrow in the [Variable Name] header	Diagnosis name	A drop-down box pops up for sorting and filtering, and the filtering items are correct and not lost	Yes
17	Check [Option 1] and [Option 2] in the filter items, and confirm	Fever	The pivot table shows the correct filter results	Yes
Special disease database search				
18	[Database search page] Add conditions, search	Date of birth	1. Match all variables containing 'date of birth' below; 2. Show all patients	Yes
19	On the [Search Results] page, click [Export Data], select a variable, select an export format, and open the export file for viewing.	Basic information and diagnosis; multiple lines per patient/one line per patient, excel	The data can be exported normally; the exported data is consistent with the data searched according to the search criteria; the exported data is multiple lines for one patient/one line for one patient"	Yes

20	On the search result page, click the drop-down box of the [Basic Patient Information] field to switch fields	Inspection	Display the variables and data under the test domain	Yes
21	Move the mouse to any row of data, click the arrow behind to view multiple records of the patient	N/A	Display different records of medical visits	Yes
22	Click [Advanced Filter]	N/A	Go to the advanced filter page	Yes
23	Select variables and logic symbols, run	Test Quantitative Results Include 30 "AND" Test Item Name Include Platelet Count	Filter expression: Test quantitative results contains 30 AND Test item name contains platelet count; Filter out the data that meet the conditions	Yes
24	Click "Export data" in the [Search results] column, select variables, and select the export format; open the export file to view	Test/Complete Blood Platelet Count; one patient line/one patient line, Excel	The data can be exported normally; the exported data is consistent with the data searched by the advanced filtering of the inspection domain; the exported data is one row for one patient/multiple rows for one patient	Yes

25	On the [Search Results] page, click "Add Special Disease Items", select the version of [Special Disease Items], and confirm	Common business - special disease project	Join the special disease project successfully	Yes
26	Add the variables under the visit, and then add the second-level domains as mutual constraints, search for	N/A	Display search results that meet the conditions	Yes
27	Add multiple combinations of conditions and groups to retrieve	N/A	Display search results that meet the conditions	Yes
28	Expand [Search History] on the right, click any search history, click 'Search'	N/A	The search history is populated into the criteria column; patients who meet the criteria are displayed	Yes
Research cockpit				
29	Check whether the corresponding role of the login account has the "Scientific research cockpit: scientific research data overview, data governance center, hospital operation data overview, scientific research project data overview" permission; if not, please set the scientific research cockpit permission	N/A	Permissions are not checked by default	Yes

	first			
30	Click the "Scientific Cockpit" button	N/A	The newly opened page of the browser displays the "Scientific Cockpit" module	Yes
31	Click "Research Data Overview" in the left navigation bar	N/A	The right page jumps to "Research Data Overview"	Yes
32	Check whether the data display on the interface controls is correct	N/A	The overview page of scientific research data mainly displays the overview of patients & medical records [gender, age of last visit, type of visit, medical insurance category, department of visit, time of visit, hospital (displayed by Fuzhou Bank)], patient distribution map (not displayed by Fuzhou Bank, available at Configuration in the database), Disease & Surgery Overview", "Rare Disease Overview (displayed by Fuzhou Bank), and	Yes

			the data charts are displayed correctly	
33	Click on the "Surgery" option in the "Disease & Surgery Overview" module	N/A	Chart updated to show 10 surgeries, age group and sex ratio of surgical patients	Yes
34	Click on the "Disease" option in the "Disease & Surgery Overview" module	N/A	Chart update showing 10 diseases, age group and sex ratio of disease patients	Yes
35	Click the toggle option under Disease in the Disease & Surgery Overview module	N/A	Chart update showing 11 designated diseases designated diseases (type 1 diabetes, type 2 diabetes, chronic bronchitis, chronic obstructive pulmonary disease, osteoporosis, coronary heart disease, stroke, hypertension, asthma, atrial fibrillation, Parkinson's disease) , and the age group of patients with the disease, sex ratio	Yes
36	Click "Data Governance Center" in the left	N/A	The right page jumps to "Data	Yes

	navigation bar		Governance Center"	
37	Check whether the data display on the interface controls is correct	N/A	Display correctly	Yes
38	Switch the "Time Control" timeline in the "Data Integration Overview" module, day, week, month	(2015-10-06) - (2019-01-26)	Chart data is updated according to time period and interval	Yes
39	Toggle between different types of data above the chart in the "Data Integration Overview" module	N/A	The chart is updated according to the data type	Yes
40	Click "Research Project Data Overview" in the left navigation bar	N/A	The right page jumps to "Research Project Data Overview"	Yes
41	Check the cumulative number of entry fields	N/A	Display the number of fields, entered, not entered and proportion of prospective research projects, the data is correct	Yes
42	Switch the time axis date, day, week, month of the cumulative number of input fields	(2019-01-25) - (2019-01-26)	Chart data is updated according to time period and interval	Yes
43	Check item list	N/A	Displays project status, published, unpublished, donut charts, content	Yes

			and scale	
44	Check the contents of each field in the item list	N/A	Display the project name, the number of people in the group, the field, the project status, the project type, the creator, the creation time	Yes
45	Check realm type	N/A	Tips show counts and proportions for each field	Yes
46	Click "Hospital Operation Data Overview" in the left navigation bar	N/A	The right page jumps to "Overview of hospital operation data"	Yes
47	Switch the timeline of the timeline control, day, week and month	(2017-08-08) - (2019-01-26)	The data is updated according to the time period and interval	Yes
48	Check whether the data display on the interface controls is correct	N/A	Display outpatient and emergency visits, total outpatient and emergency expenses, inpatient visits, number of surgeries, average hospitalization costs, average hospitalization days, and the year-on-year and month-on-month ratios of each field	Yes

49	Check the data trend of each tab data display	N/A	The trend graph switches according to time, and the display is normal	Yes
Search export data validation				
50	Search patient_id, visit_id of patients who meet the conditions	Select DISTINCT patient_id from resdata.dm where patient_id in (select patient_id from diag.patient_diagnose where diag_sycode_set ?& array['91534']); Select DISTINCT visit_id from resdata.dm where visit_id in (select visit_id from diag.patient_diagnose where diag_sycode_set ?& array['91534']);	Data retrieval and Excel table export successfully	Yes
51	Search for the basic information of patients	The total number of patients = the number of rows of basic patient information in excel	Data retrieval and Excel table export successfully	Yes
52	How to query the number of diagnoses	Select "count"(*) from resdata.dg where visit_id in (select visit_id from diag.patient_diagnose where	Data retrieval and Excel table export successfully	Yes

		diag_sycode_set ?& array['91534'])		
53	How to query the number of operations	Select "count"(*) from resdata.pr where visit_id in (select visit_id from diag.patient_diagnose where diag_sycode_set ?& array['91534'])	Data retrieval and Excel table export successfully	Yes
54	Query method of medication quantity	Select "count"(*) from resdata.cm where visit_id in (select visit_id from diag.patient_diagnose where diag_sycode_set ?& array['91534'])	Data retrieval and Excel table export successfully	Yes
55	WBC count query method	Select ""count""(*) from resdata.lb where visit_id in (select visit_id from diag.patient_diagnose where diag_sycode_set ?& array['91534']) and test_item_code='5089'	Data retrieval and Excel table export successfully	Yes
Data query				
56	Click [Advanced Filter] → [Switch Advanced Mode] → Add Condition→[Run]	Drug names, specific AE, system of disease, grading and interventions	Show data that meets the filter criteria	Yes
57	Click [Clear] below the filter expression	Drug names, specific AE, system of disease, grading and interventions	Filters cleared successfully	Yes
58	On the top right [Export Data], select	Drug names, specific AE, system of	The data is exported successfully	Yes

[Export Current Query]	disease, grading and interventions	and the data is correct

3 System page display of AE Monitoring View for PLWHIV

The AE Monitoring View for PLWHIV is a child system of AIDS database, and the 16 figures below shows the actual results of the functions and different pages of the Monitoring View.

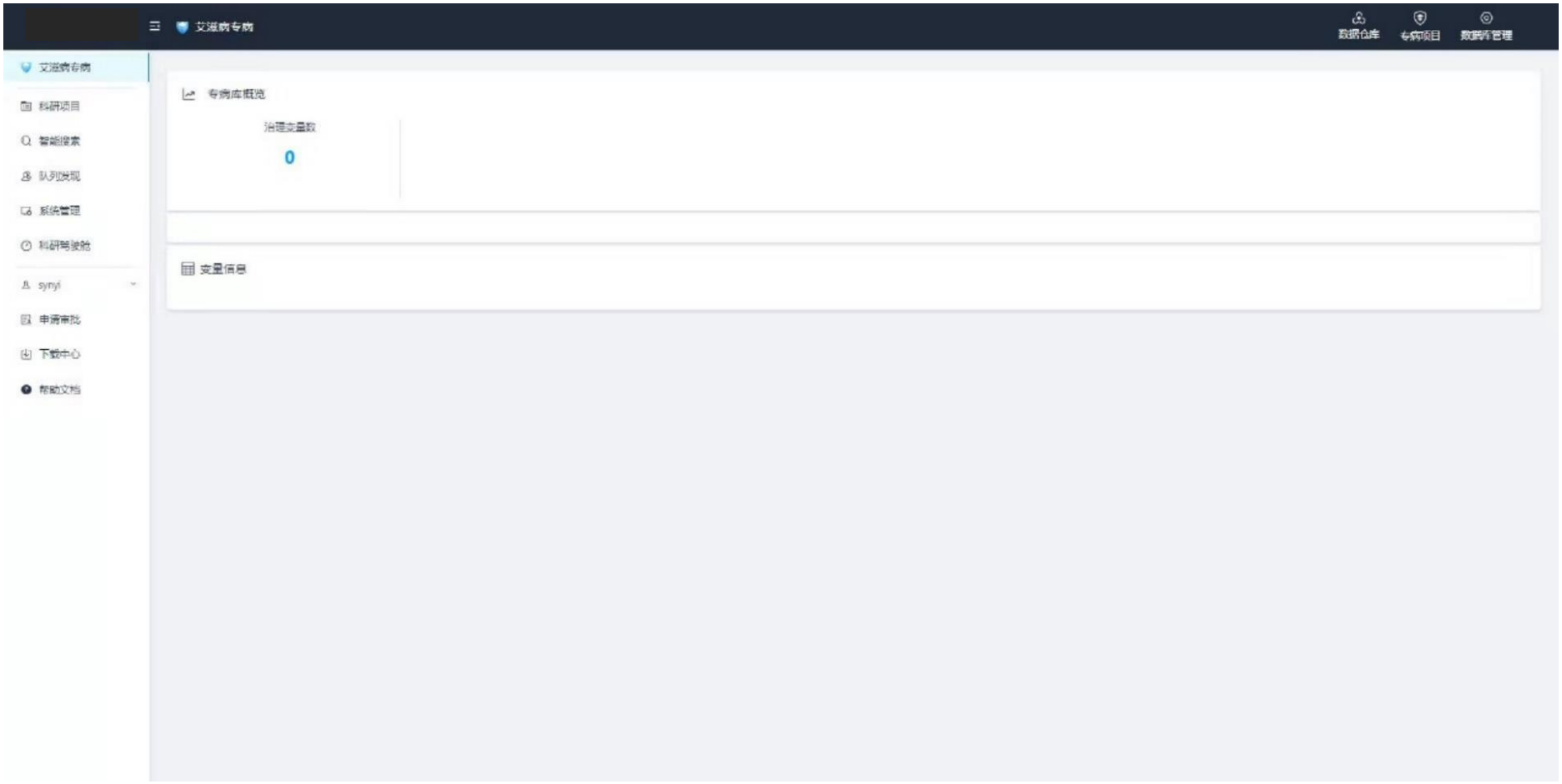


Figure 4-1. Home page of the AIDS database (1)

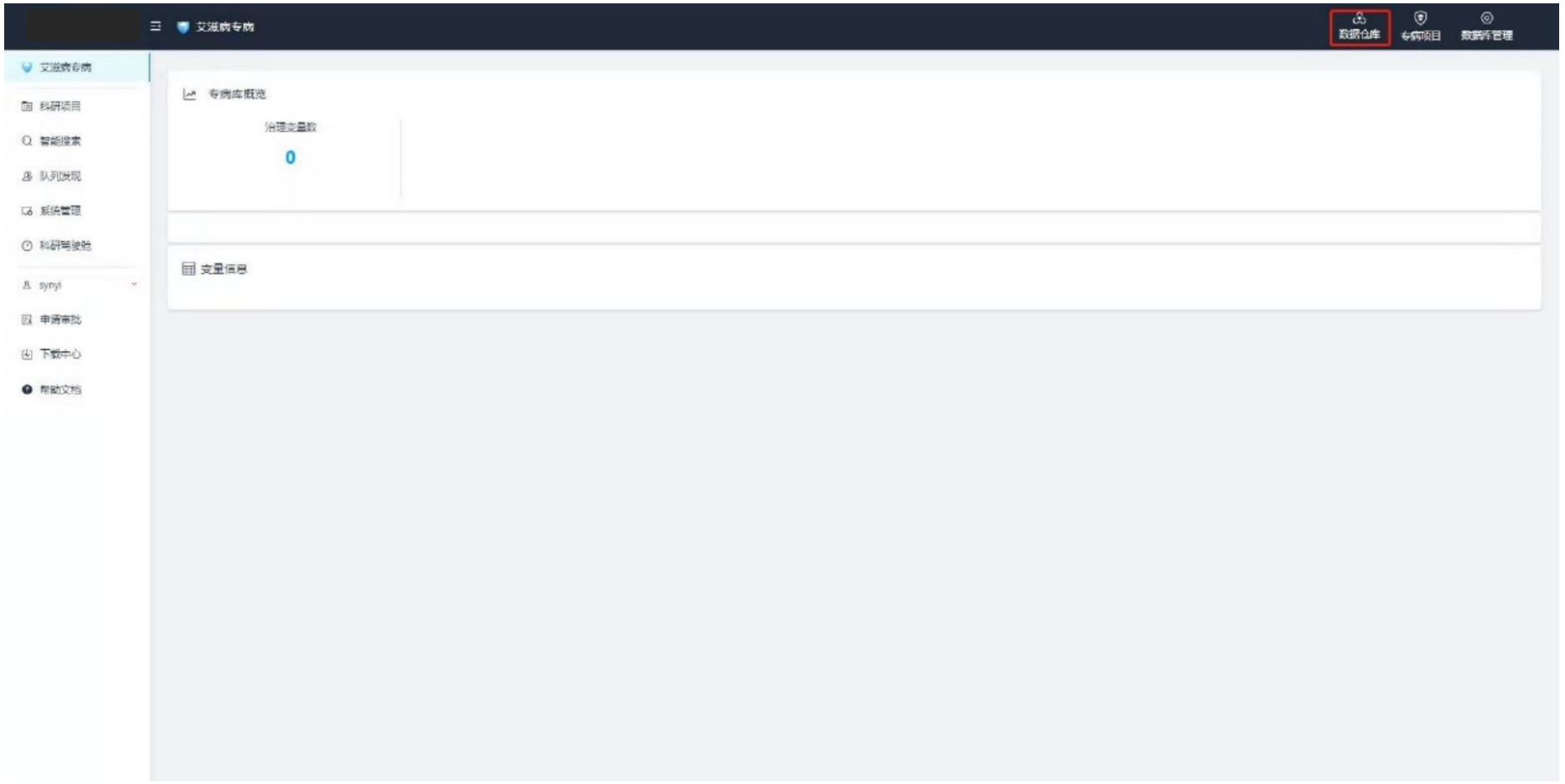


Figure 4-2. Home page of the AIDS database (2)

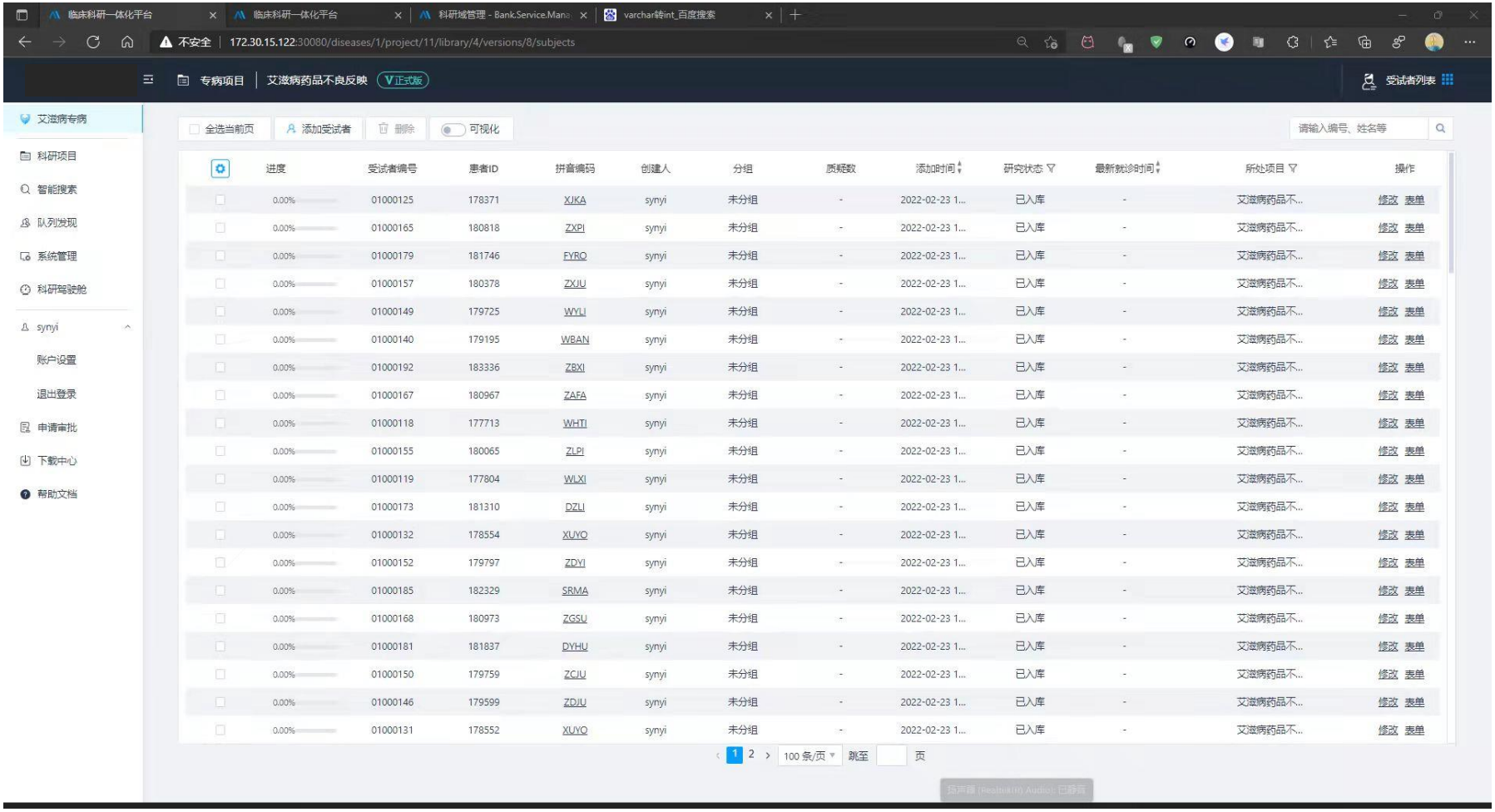


Figure 4-3. Home page of the AIDS database (3)

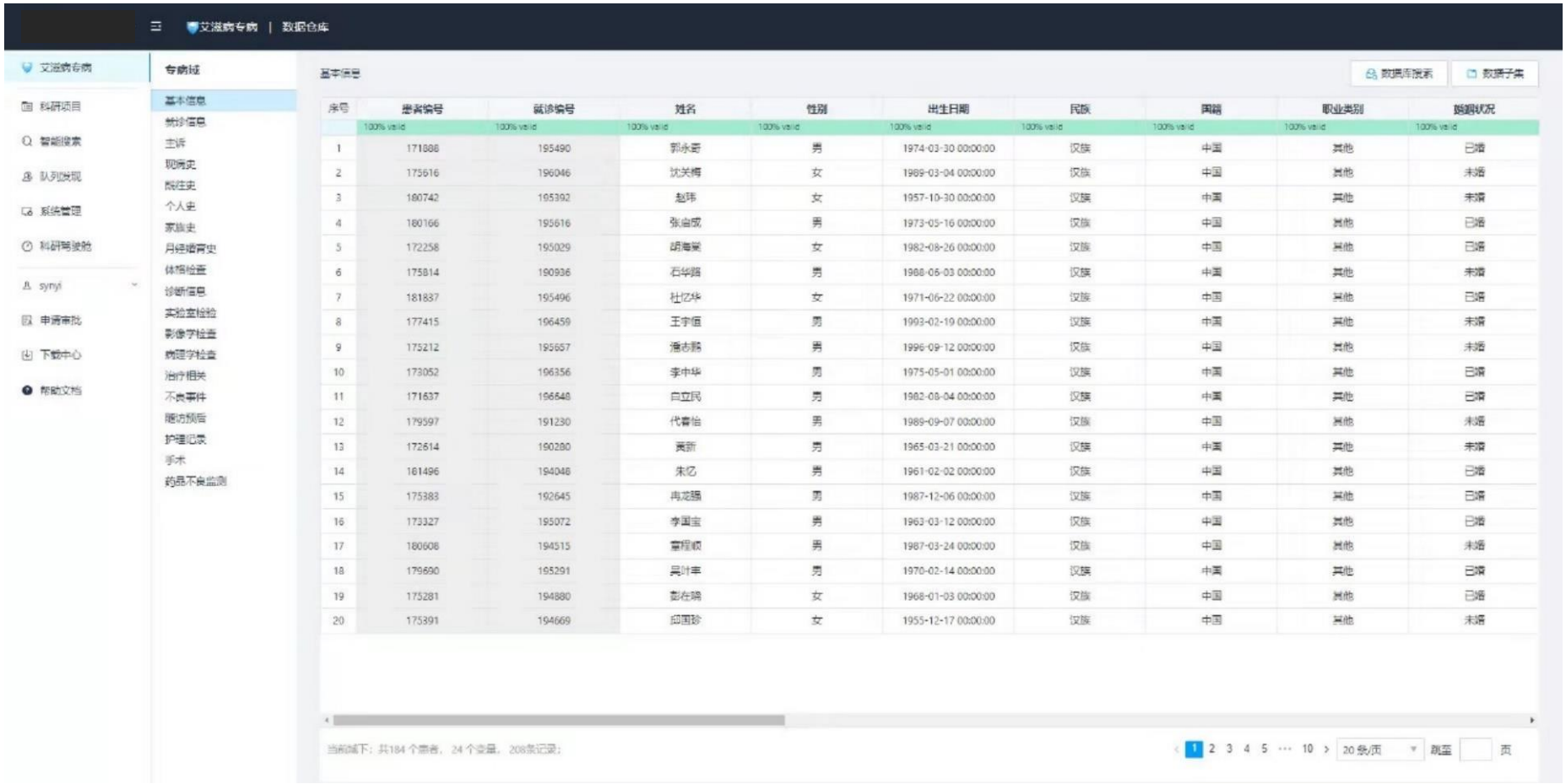


Figure 4-4. General basic information of PLWHIV

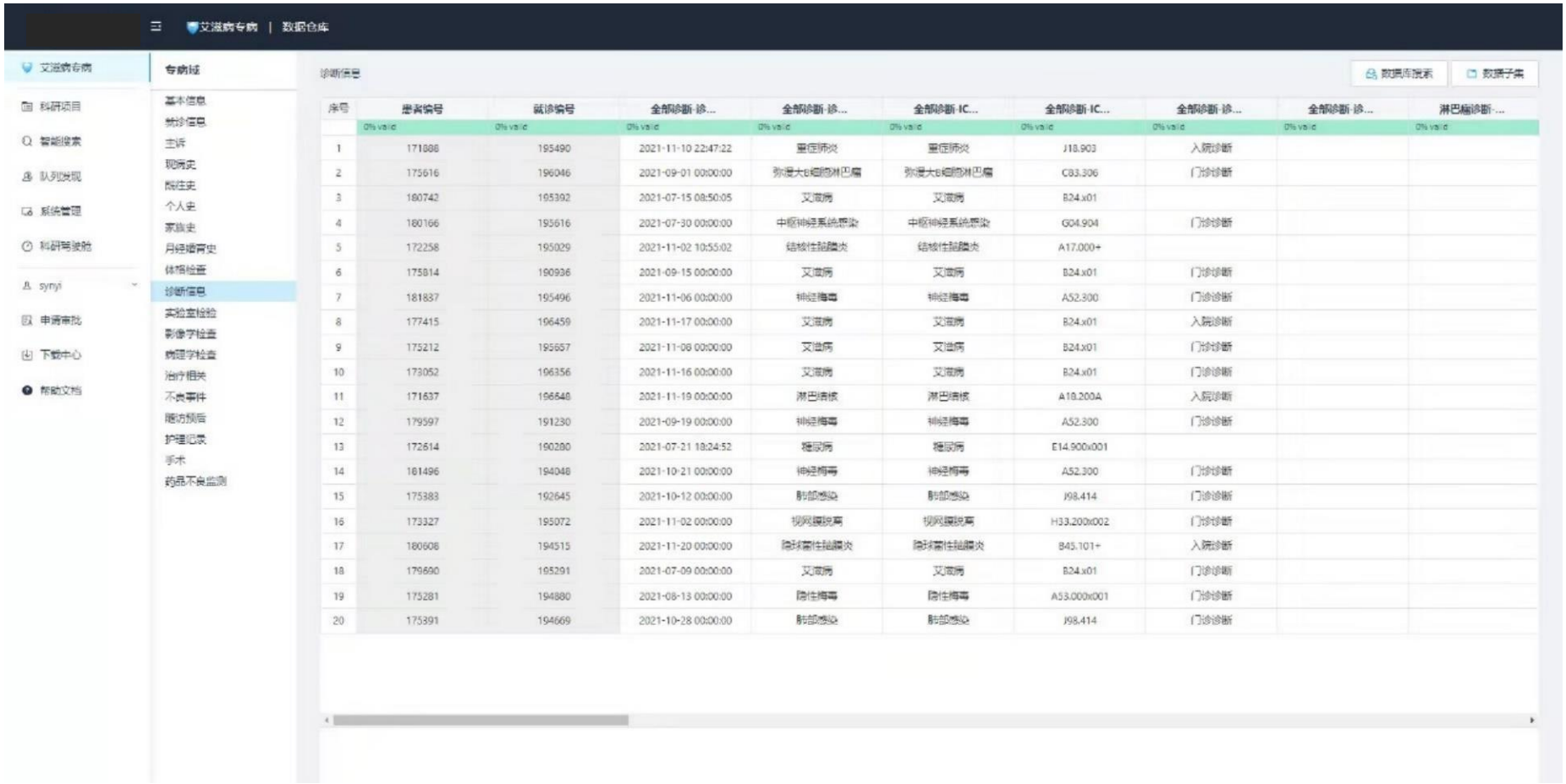


Figure 4-5. Diagnosis page of PLWHIV in AIDS database

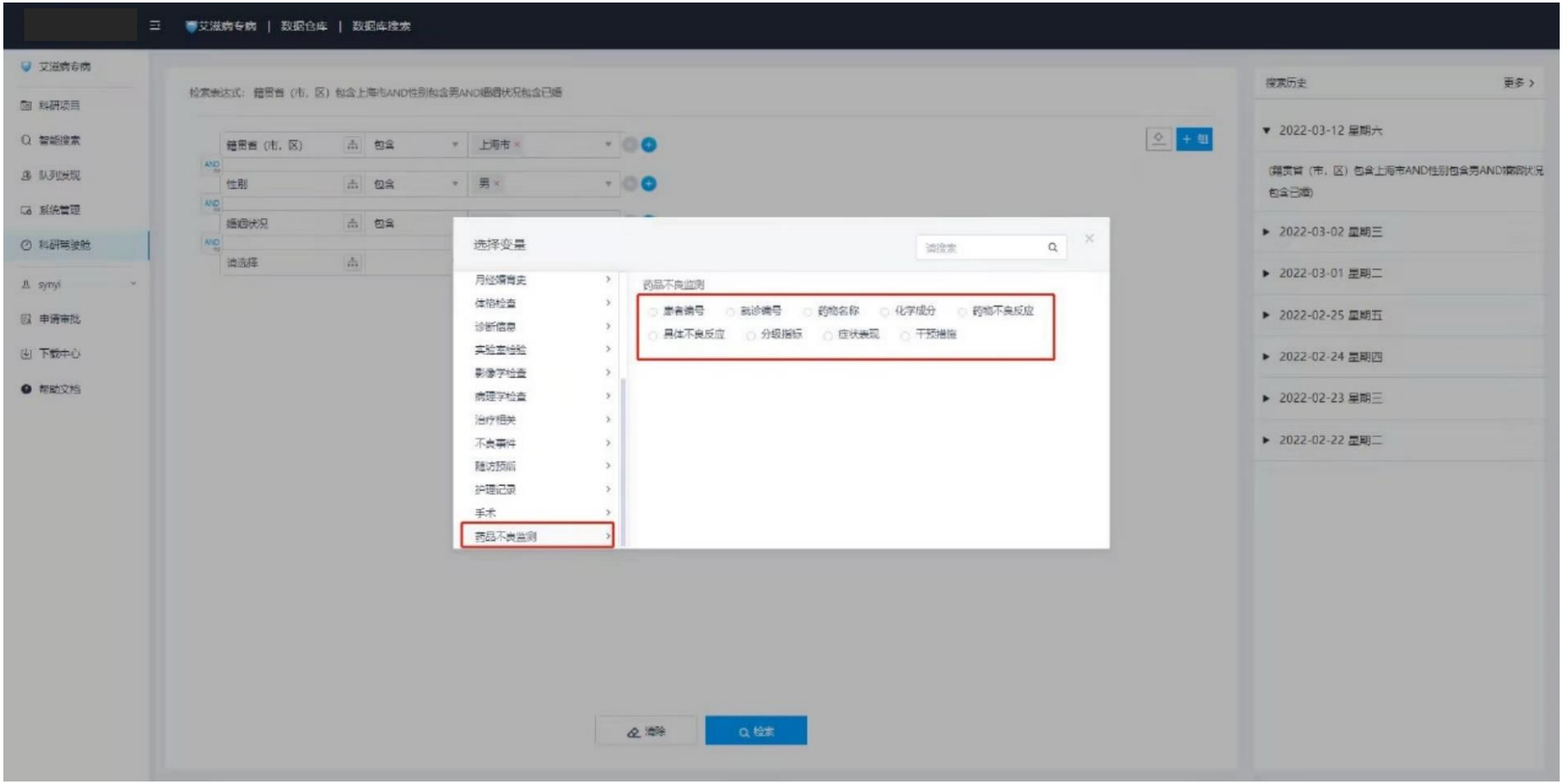


Figure 4-6. Database search interface for different dimensions of search engine functions in the AE Monitoring View

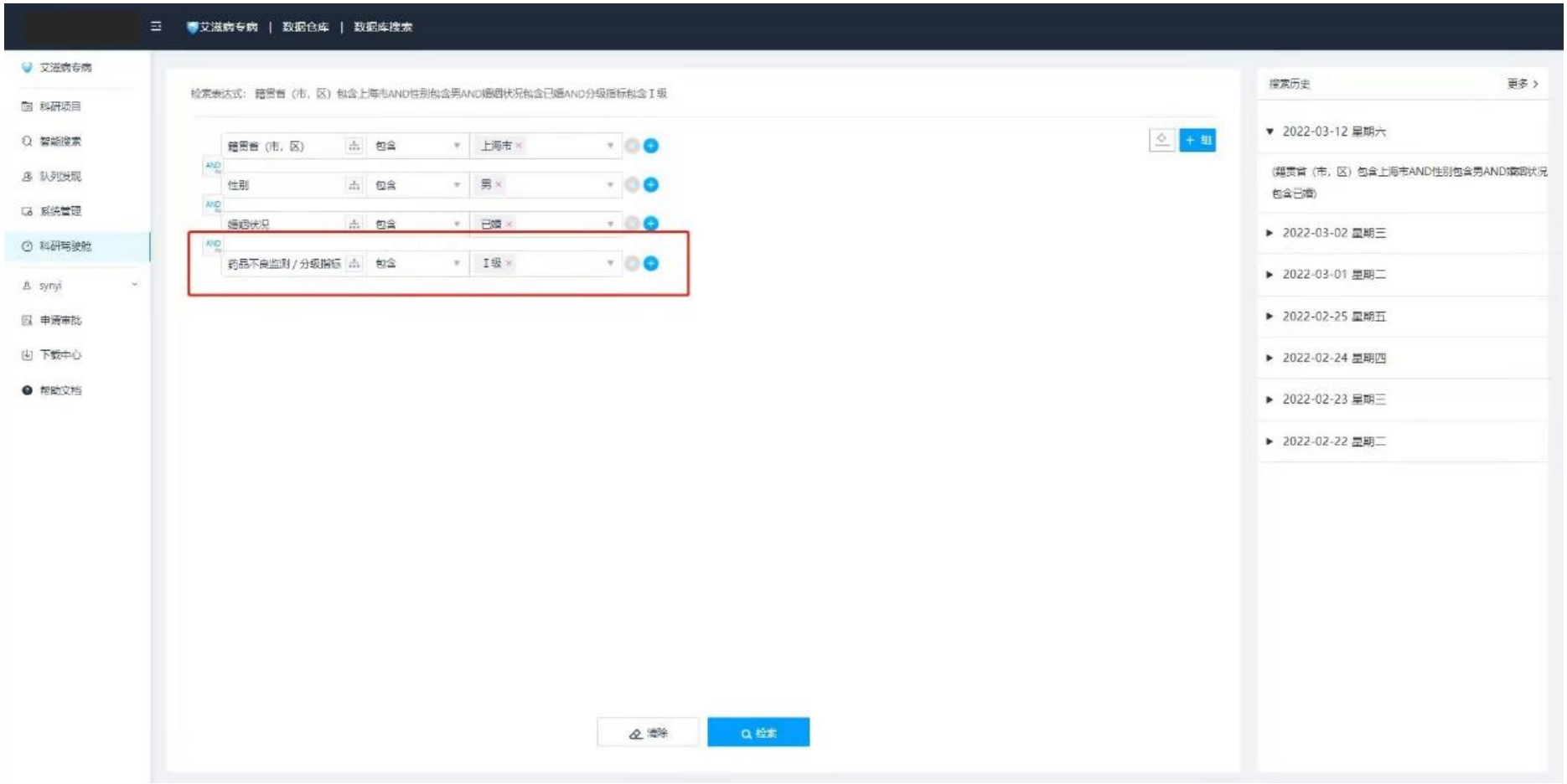


Figure 4-7. Search engine interface

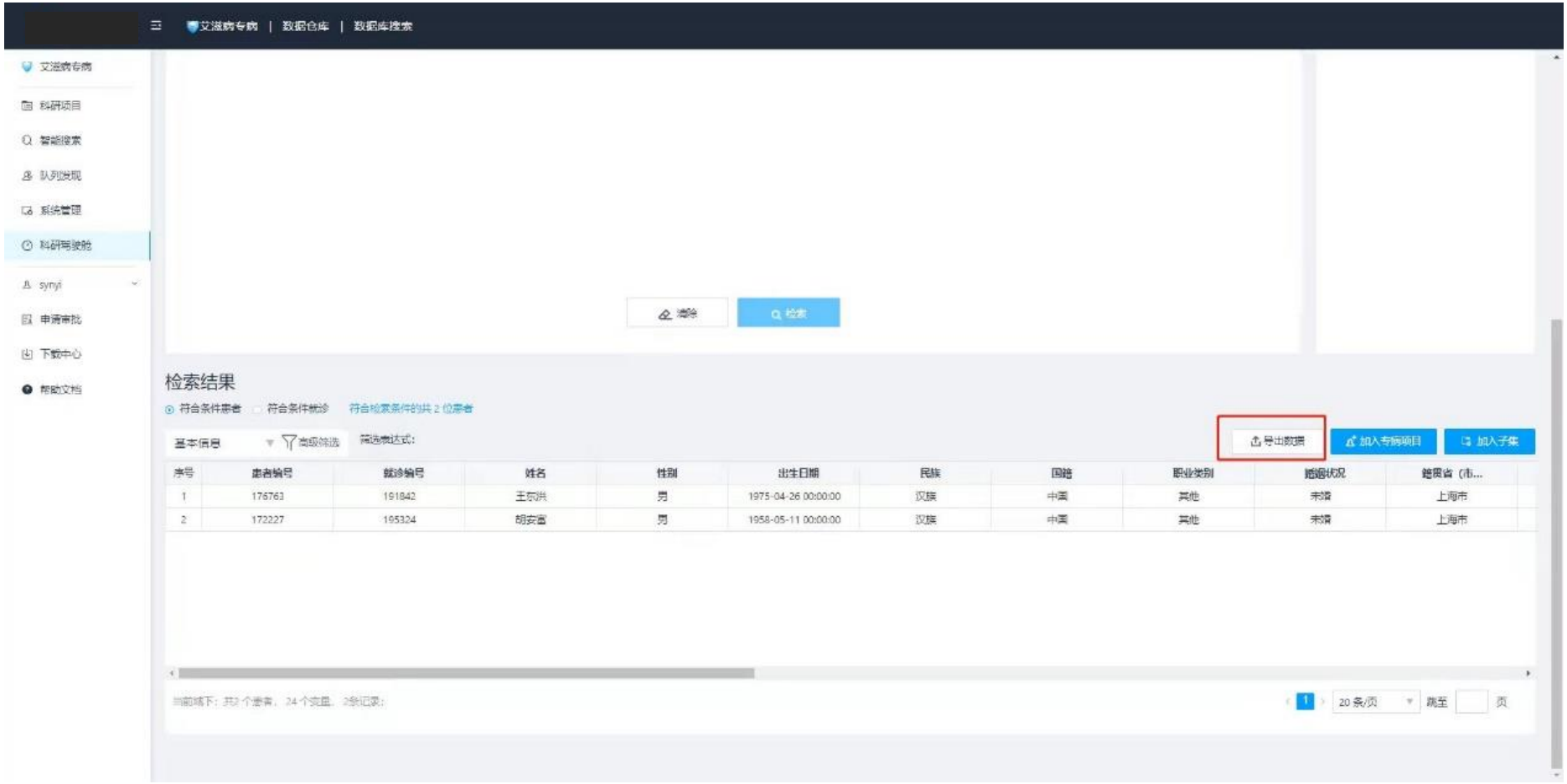


Figure 4-8. Search result interface

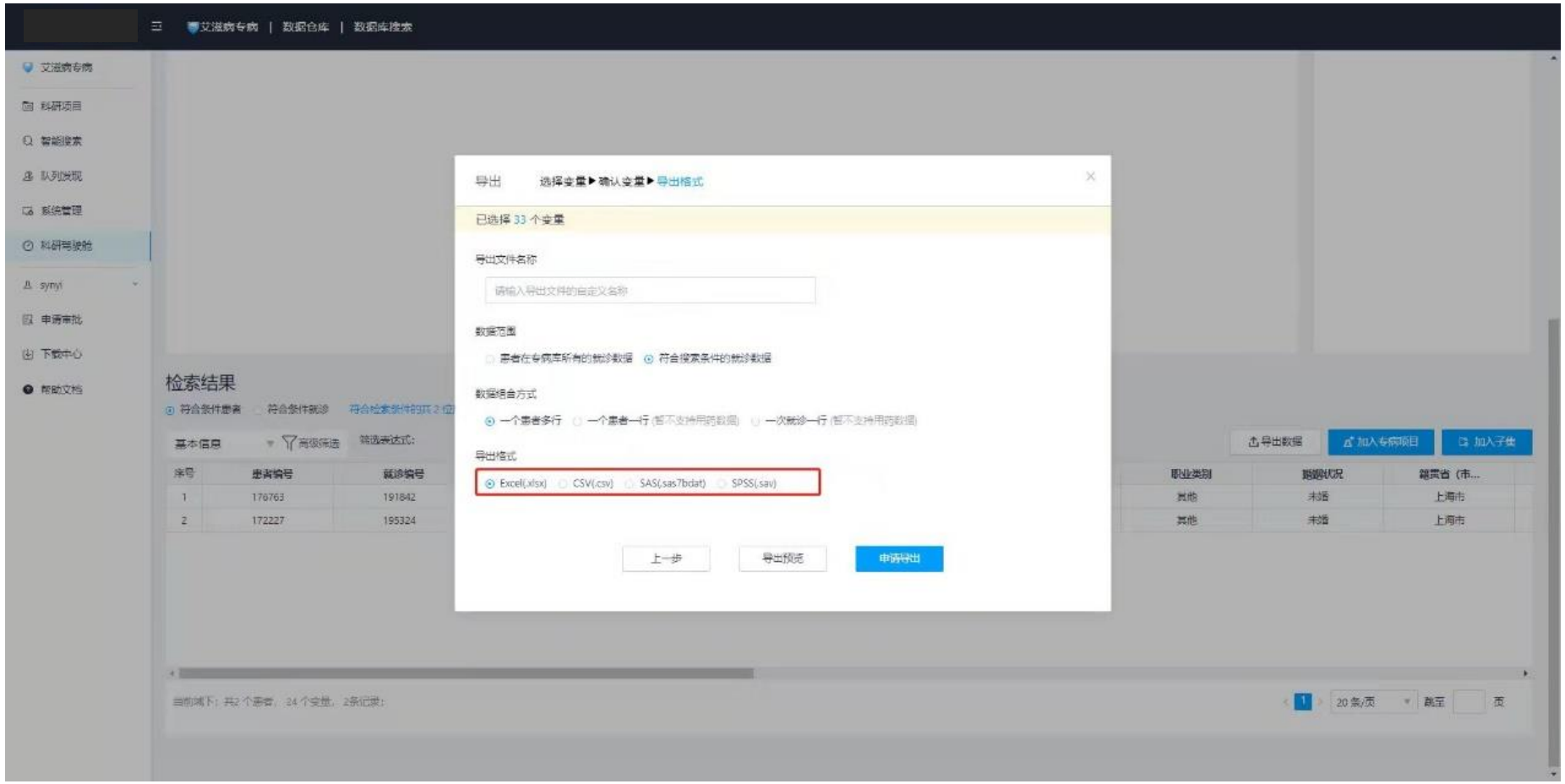


Figure 4-9. Data export interface

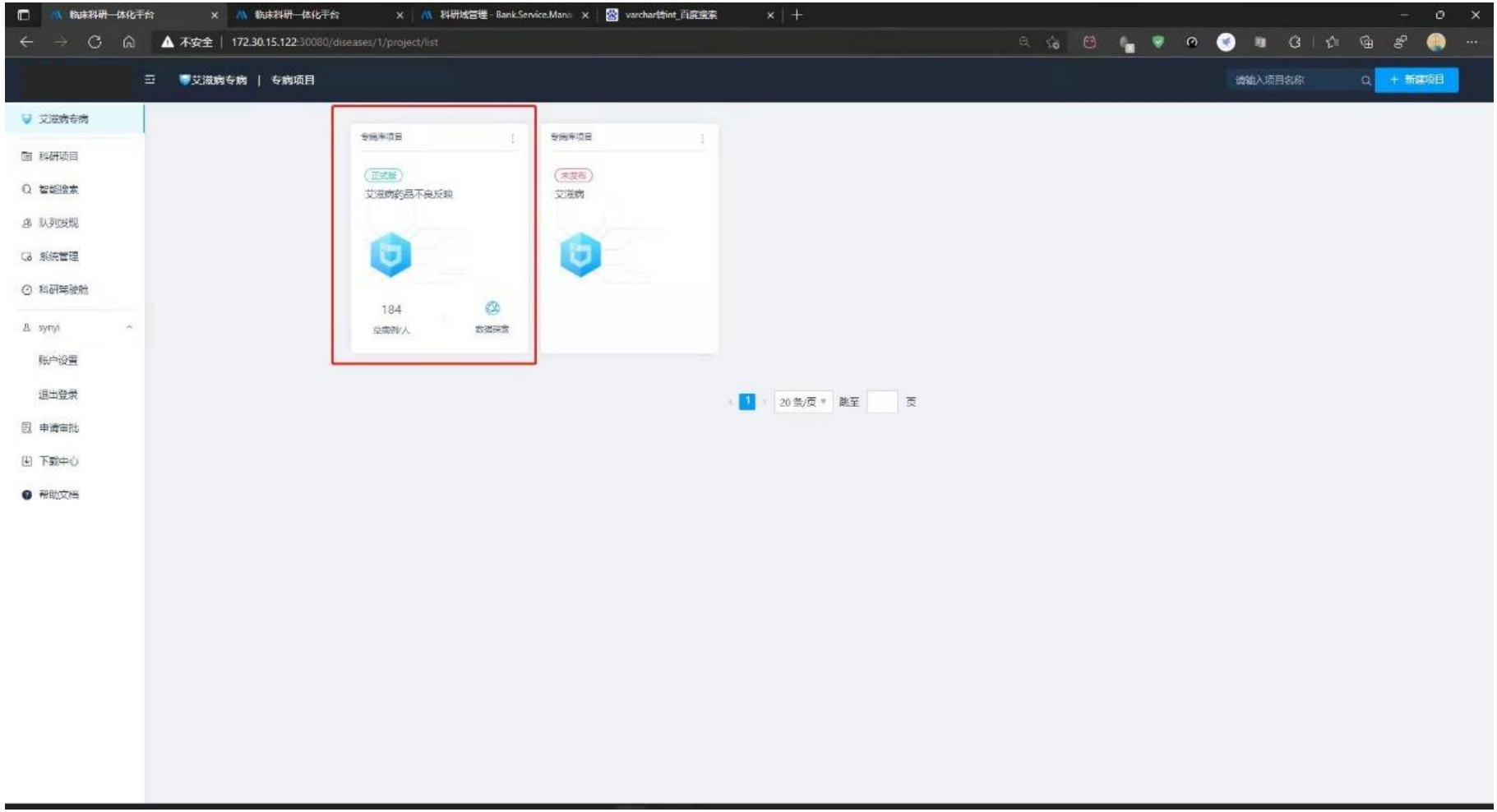


Figure 4-10. Visual part of AE Monitoring View

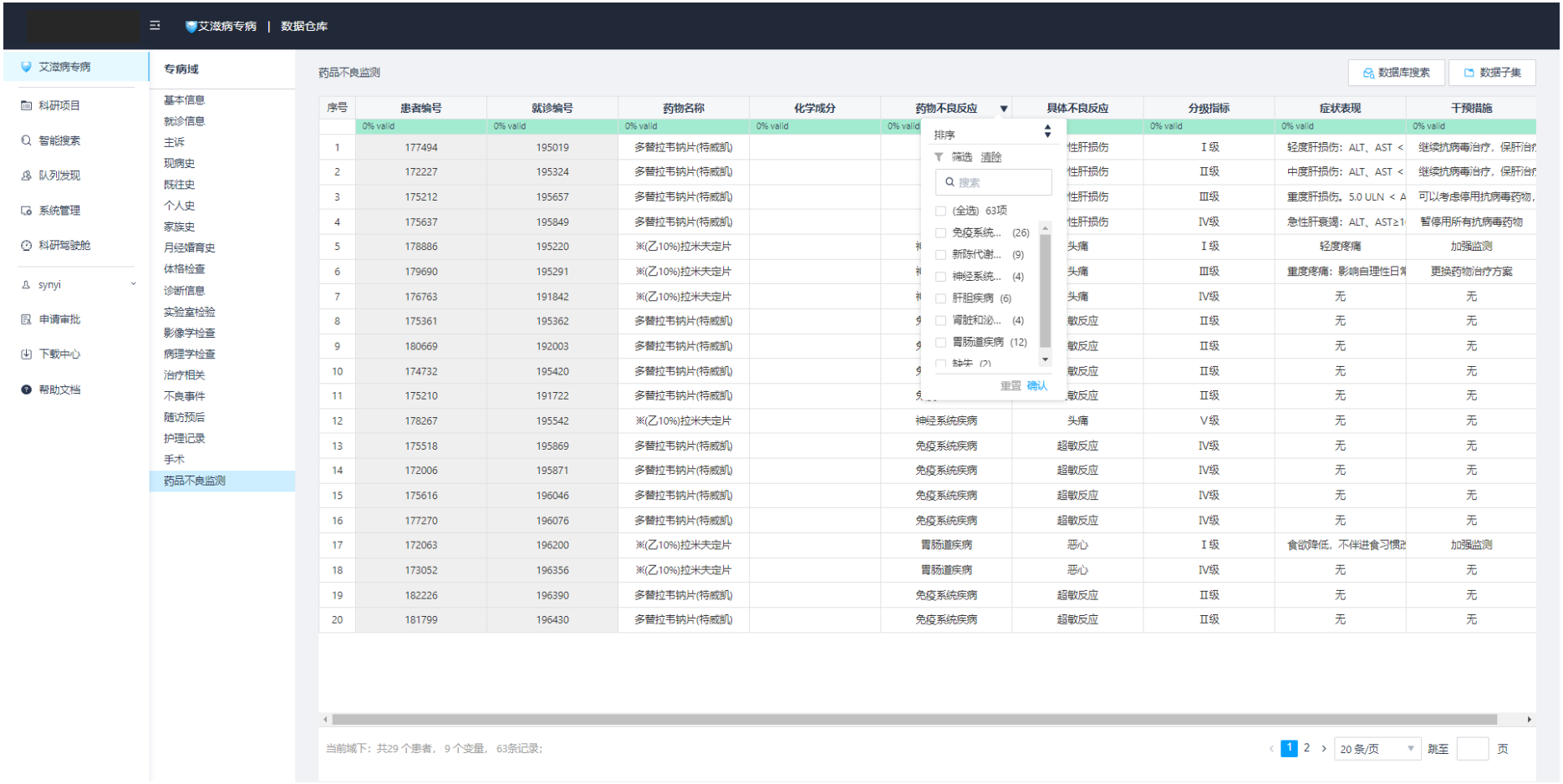


Figure 4-11. Main interface of AE Monitoring View for PLWHIV (1)

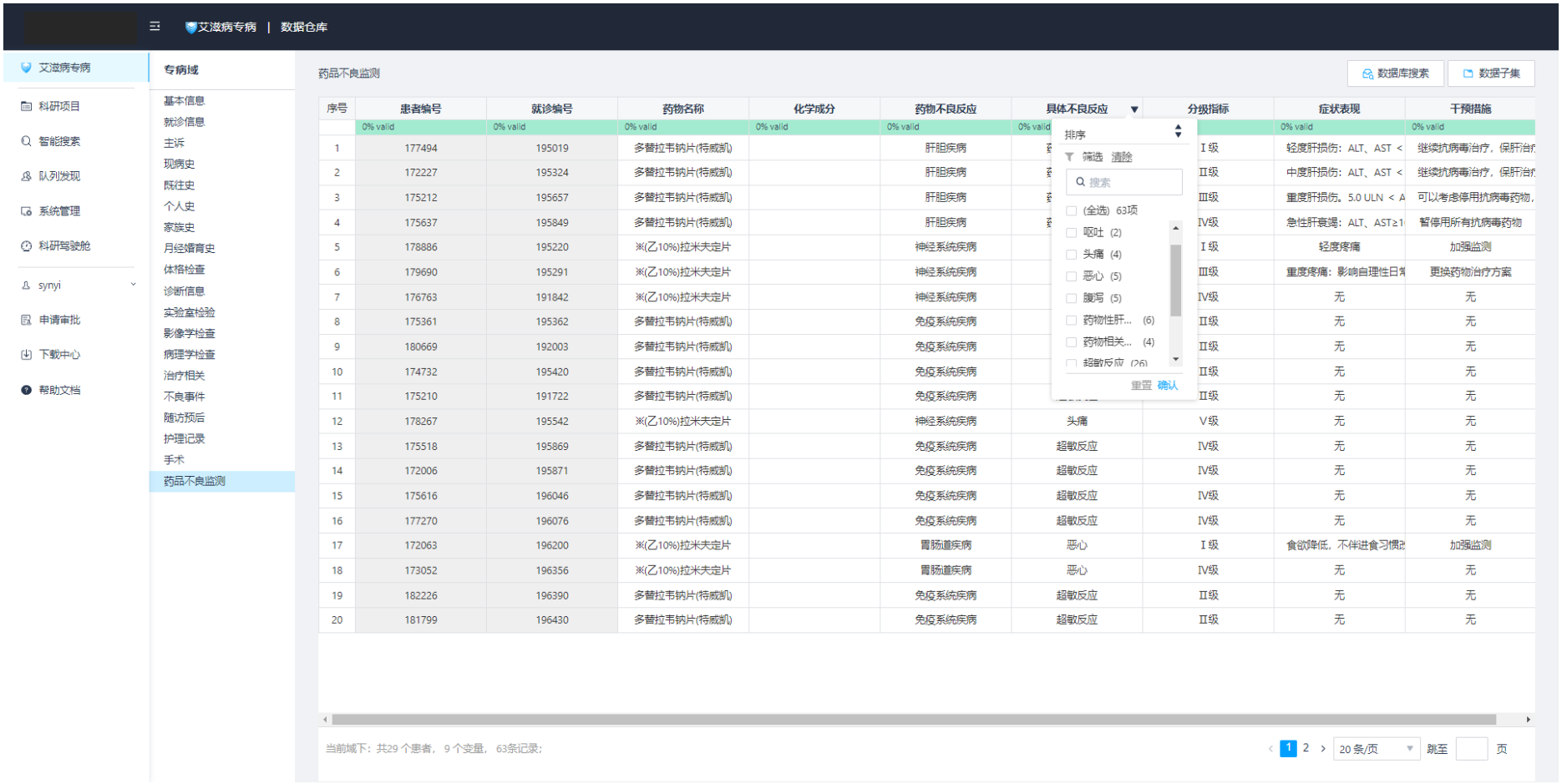


Figure 4-12. Main interface of AE Monitoring View for PLWHIV (2)

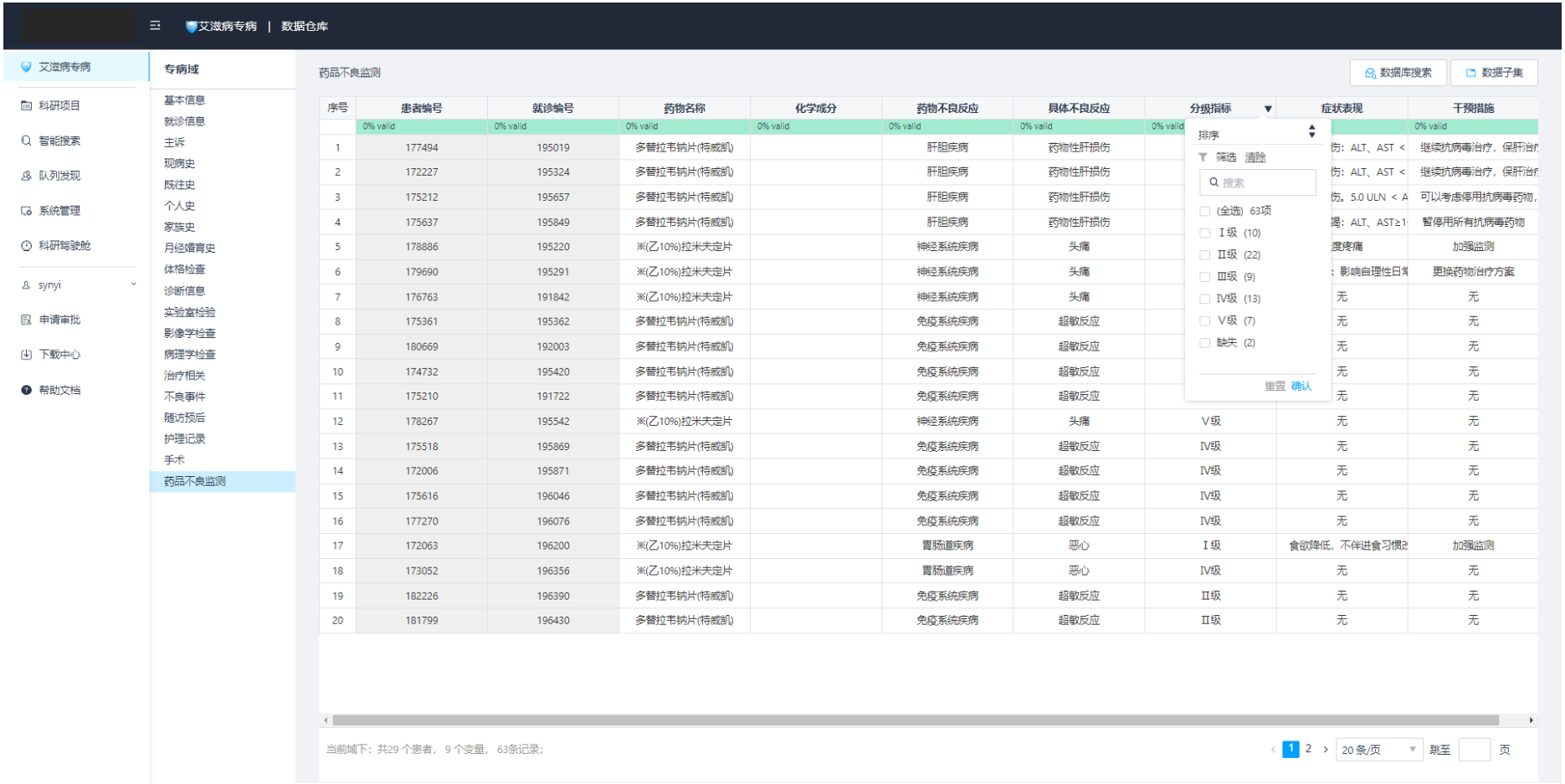
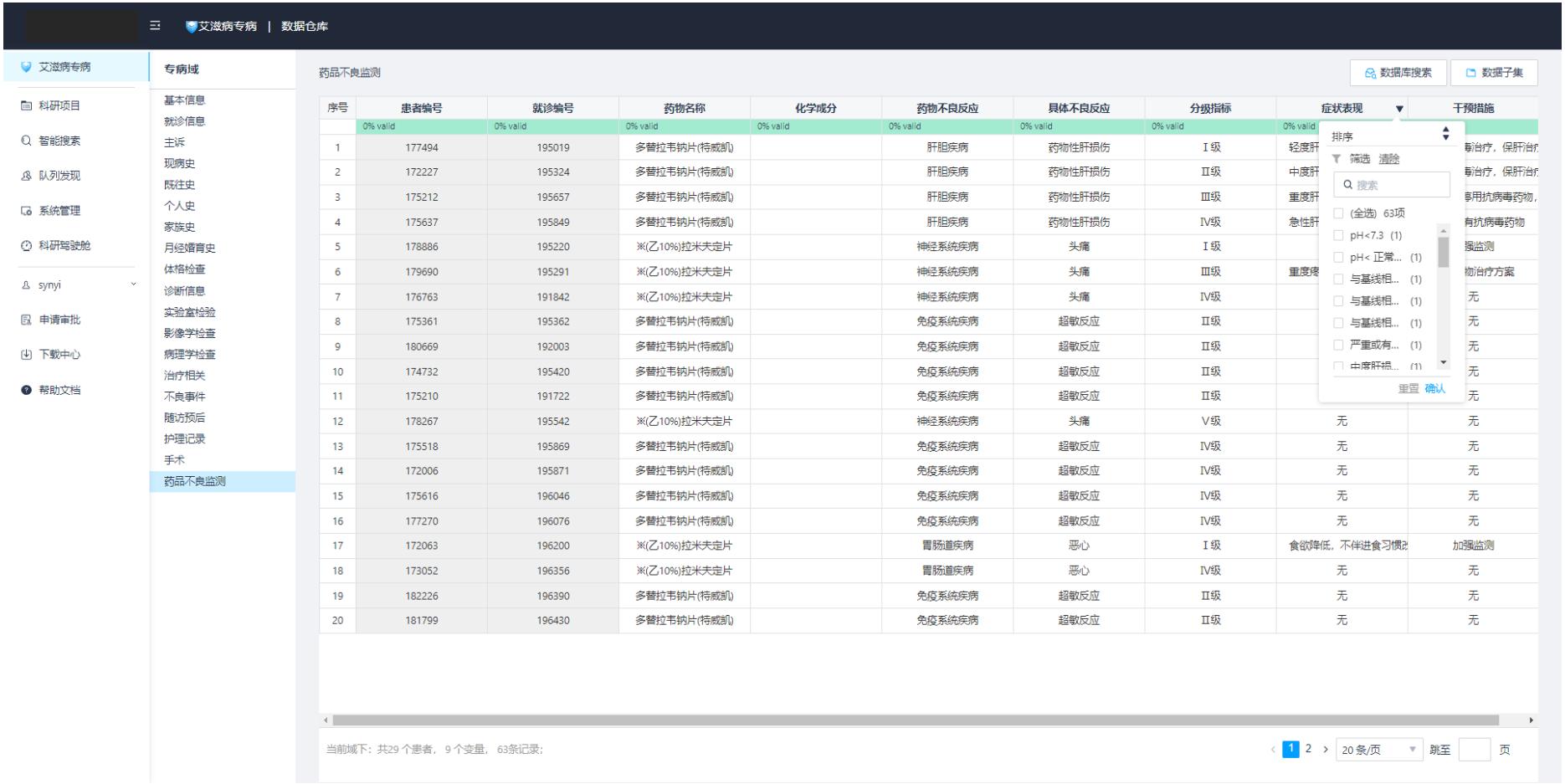


Figure 4-13. Main interface of AE Monitoring View for PLWHIV (3)



序号	患者编号	就诊编号	药物名称	化学成分	药物不良反应	具体不良反应	分级指标	症状表现	干预措施
	0% valid	0% valid	0% valid	0% valid	0% valid	0% valid	0% valid	0% valid	
1	177494	195019	多替拉韦钠片(特威凯)		肝胆疾病	药物性肝损伤	Ⅰ级	轻度肝	毒治疗，保肝治疗
2	172227	195324	多替拉韦钠片(特威凯)		肝胆疾病	药物性肝损伤	Ⅱ级	中度肝	毒治疗，保肝治疗
3	175212	195657	多替拉韦钠片(特威凯)		肝胆疾病	药物性肝损伤	Ⅲ级	重度肝	享用抗病毒药物，
4	175637	195849	多替拉韦钠片(特威凯)		肝胆疾病	药物性肝损伤	Ⅳ级	急性肝	有抗病毒药物
5	178886	195220	※(乙10%)拉米夫定片		神经系统疾病	头痛	Ⅰ级		强监测
6	179690	195291	※(乙10%)拉米夫定片		神经系统疾病	头痛	Ⅲ级	重度疼	物治疗方案
7	176763	191842	※(乙10%)拉米夫定片		神经系统疾病	头痛	Ⅳ级		无
8	175361	195362	多替拉韦钠片(特威凯)		免疫系统疾病	超敏反应	Ⅱ级		无
9	180669	192003	多替拉韦钠片(特威凯)		免疫系统疾病	超敏反应	Ⅱ级		无
10	174732	195420	多替拉韦钠片(特威凯)		免疫系统疾病	超敏反应	Ⅱ级		无
11	175210	191722	多替拉韦钠片(特威凯)		免疫系统疾病	超敏反应	Ⅱ级		无
12	178267	195542	※(乙10%)拉米夫定片		神经系统疾病	头痛	Ⅴ级	无	无
13	175518	195869	多替拉韦钠片(特威凯)		免疫系统疾病	超敏反应	Ⅳ级	无	无
14	172006	195871	多替拉韦钠片(特威凯)		免疫系统疾病	超敏反应	Ⅳ级	无	无
15	175616	196046	多替拉韦钠片(特威凯)		免疫系统疾病	超敏反应	Ⅳ级	无	无
16	177270	196076	多替拉韦钠片(特威凯)		免疫系统疾病	超敏反应	Ⅳ级	无	无
17	172063	196200	※(乙10%)拉米夫定片		胃肠道疾病	恶心	Ⅰ级	食欲降低，不伴进食习惯改	加强监测
18	173052	196356	※(乙10%)拉米夫定片		胃肠道疾病	恶心	Ⅳ级	无	无
19	182226	196390	多替拉韦钠片(特威凯)		免疫系统疾病	超敏反应	Ⅱ级	无	无
20	181799	196430	多替拉韦钠片(特威凯)		免疫系统疾病	超敏反应	Ⅱ级	无	无

Figure 4-14. Main interface of AE Monitoring View for PLWHIV (4)

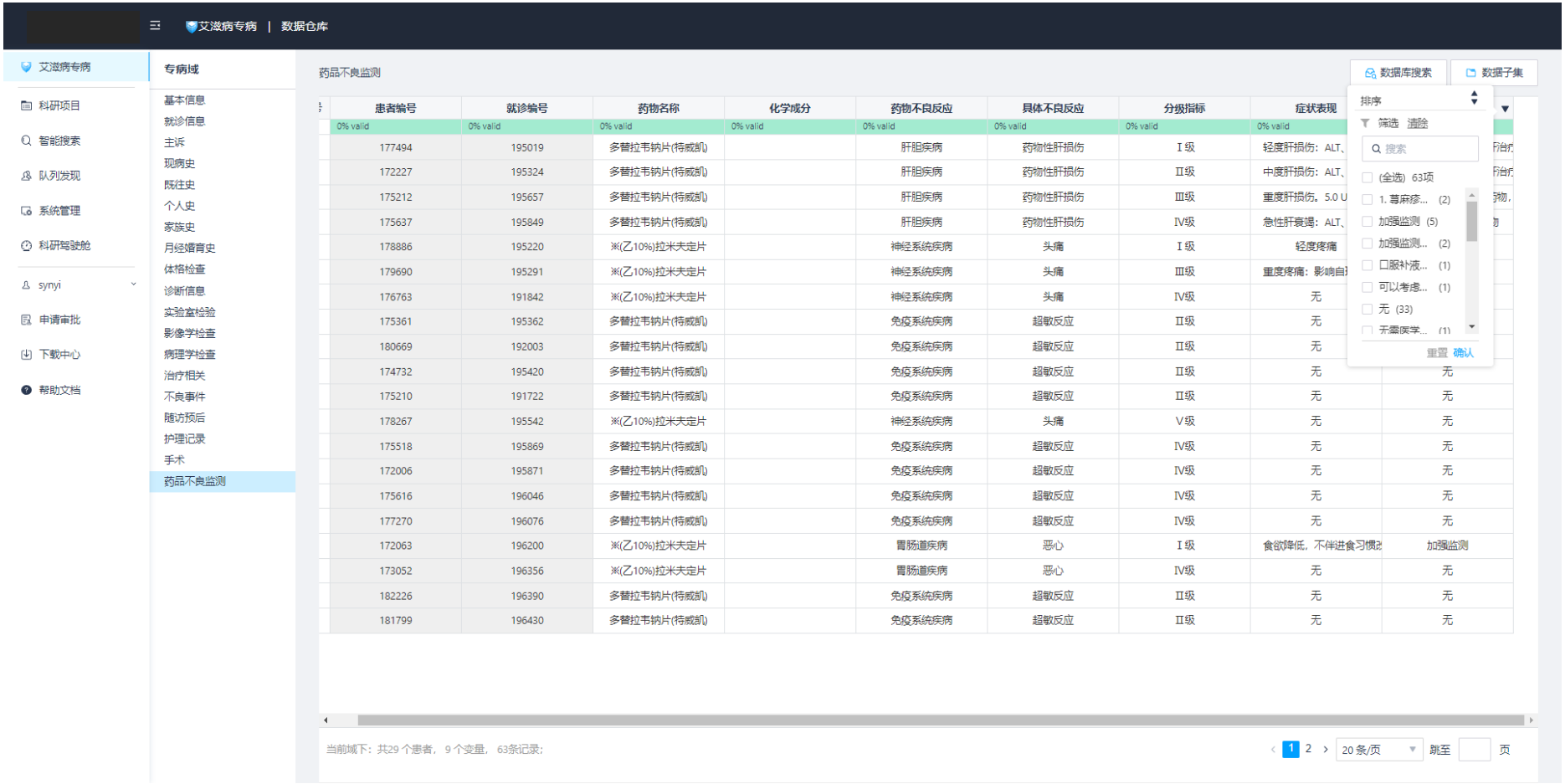


Figure 4-15. Main interface of AE Monitoring View for PLWHIV (5)

4.3.4 Internal pilot-test of usability evaluation results among the research team

"Pilot-test Questionnaire of Internal Usability Evaluation to AE Monitoring View for PLWHIV" was adopted over 11 members of the research team mentioned above in Chapter 3, and their basic information was shown in Table 3-1. Characteristics of research team members (N=11). Table 4-3 shows the scores of the pilot-test. All participants scored 4 and above on all test items, and the mean score for each items is above 4.7, which indicated that participants rated the View's acceptance, convenience, clinical applicability, system stability, and fluency as high, thus the AE Monitoring View for PLWHIV had high usability.

Table 4-3. The scores of the pilot-test (N=11)

Item	Min	Max	Total	Mean	SD
Acceptance					
1. I am satisfied with the overall performance of the view.	4	5	52	4.73	0.467
2. The view gives me a good experience.	4	5	52	4.73	0.467
3. The development and maintenance personnel of this view can sincerely and timely solve the problems I encountered when using the system.	4	5	51	4.64	0.505
4. The view is easy to learn and use	4	5	51	4.64	0.505
Convenience					
5. This view reduces the time it takes me to complete the task.	4	5	53	4.82	0.405
6. This view makes the evaluation and decision-making process more convenient.	4	5	52	4.73	0.467
7. I am satisfied with the efficiency of the view.	4	5	53	4.82	0.405
8. This view reduces the expense of office supplies.	4	5	53	4.82	0.405
Clinical applicability					
9. This view can meet the needs of my actual operation.	4	5	54	4.91	0.302

10. The view played a supporting and auxiliary role in the evaluation and decision-making process.	4	5	52	4.73	0.467
11. The information provided by this view is consistent with the actual situation, and there is no error record.	4	5	53	4.82	0.405
12. The trend chart, evaluation and decision support information provided by this view is valuable and can be used.	4	5	54	4.91	0.302
Stability					
13. Remove the influence of WIFI, the effective response time of this view to complete the command is short, and there are few stalls.	4	5	53	4.82	0.405
14. The view is very stable at runtime.	4	5	54	4.91	0.302
Fluency					
15. The view can be flexibly switched in each interface.	4	5	52	4.73	0.467
16. The view is very smooth at runtime.	4	5	54	4.91	0.302

4.4 Discussion

Since the AE Monitoring View for PLWHIV belongs to the subsystem of the AIDS database, some of its internal search engine functions are related to other subsystems of the database. Therefore, the researcher also connected other subsystems in the process of cooperating with technicians to develop the AE Monitoring View, and internally in the process of functional application testing, all steps including the function of combining with the search engine in other subsystems are listed in turn, and all steps are functionally tested to observe whether there are back-end bugs. The results show that there are no faults or loopholes in the functions of the 58 steps, and each function point that the researcher clicks can successfully complete the task, enter the interface expected by the researcher or search for the target expected by the

researcher. It can be seen through this result that the functional development of the view is successful.

The researcher invited 11 members of the research team to complete the pilot-test of internal usability evaluation. The results of the questionnaire show that the participants have a very high degree of acceptance of the View. It is very convenient and has high clinical application value, and the View itself is stable and smooth. The usability of this View was rated very well by the research team as a whole, as participants tried out the features of the system very highly.

At present, the View is still in the internal testing stage. The research results show that the internal testing of the Monitoring View is successful, and the View will be released simultaneously when the AIDS database goes online. In order to ensure the rigor and scientificity of this View, this research is expected to conduct a formal usability evaluation after the system is released. The researcher plan to invite dozens of clinicians and nurses to use the system according to the instructions within a specified time, and observe their completion degree and speed to judge the effect of use; explore the user's satisfaction through questionnaires and qualitative interviews; These methods can comprehensively evaluate the final usability of the View.

5 Conclusion

5.1 Conclusion

1. The current state of AE monitoring process and the demands of clinicians and nurses for an AE Monitoring View for PLWHIV were investigated through qualitative interviews,
2. Based on AIDS database, the content framework of the AE Monitoring View for PLWHIV was determined through two rounds of Delphi expert consultations based on the existing literature and CTCAE criteria as a guideline,

The AE Monitoring View for PLWHIV was developed and tested after cooperation under technicians and researcher, with a pilot-test of internal usability evaluation over the AE Monitoring View.

5.2 Research innovation

At present, the construction of the domestic special disease database is still in the development stage, and the construction of the clinical information unified view is not yet mature. This research is based on the AIDS database to construct an AE monitoring view for PLWHIV. This research is the first time to subdivide the possible AE of PLWHIV, and propose corresponding intervention measures, which are presented in an interface in the form of an information view, which greatly saves labor costs and improves the efficiency of scientific research.

In fact, the traditional clinical information system also has a list of AE, but according to the researcher's investigation, the functions of these traditional AE systems are very imperfect. This is reflected in the non-standardization of nouns, and imperfect visualization. There is no standardization of traditional AE nouns, resulting in numerous synonyms, and clinicians cannot unify the list of patients with one adverse event, which reduces work efficiency and increases human resource costs. The AE Monitoring View developed combines existing literature, CTCAE, drug description, standardized and unified list of AE determined after integrating expert opinions, all AE can be directly selected in the menu, which greatly shortens the time for clinicians and nurses to improve work efficiency. In addition, traditional AE systems rarely classify and present all patient AE in the same interface, resulting in

low work efficiency for clinicians and nurses, while the View in this research integrates all AE, and setting a search engine guiding user to observe other information corresponding to patients at the same time, and assisting users in judging the occurrence of AE in patients which is of great clinical significance for helping decision-making and intervention.

Finally, the traditional AE system only includes specific AE, while this research proposes a classification of clinical manifestations to judge the degree of AE according to CTCAE, and lists complete corresponding intervention measures accordingly to assist clinicians and nurses in diagnosis and intervention.

5.3 Research limitation

5.3.1 Limited time

Due to time constraints, the formal usability evaluation of this research is not completed yet. Therefore, the researcher will not know the usability of the AE Monitoring View among clinical users in a short time, and there will be usability evaluation in the future if it is allowed. However, the researcher has successfully completed the pilot-test of usability evaluation over AE Monitoring View for PLWHIV by asking the research team members to finish the questionnaire developed by the researcher, and the results show a pilot-test usability of the View.

5.3.2 The contradiction between clinical needs and actual technical capabilities

In this research, a lot of demand information was obtained during the clinical staff demand interviews, but after in-depth communication with technology companies, the researchers found that some demand cannot be realized at the actual technical level. Therefore, the researchers sorted out the clinical requirements that could not be designed to enter the system, such as adding the reminder function on the patient side and linking with the system, and directly popping out the pop-up window next to the abnormal indicators in the trend chart to prompt possible AE and other functions. Although this type of functional requirements cannot be achieved temporarily, the researchers plan to save the sorted data and leave it for subsequent system optimization and iteration.

5.3.3 Limitations of application scenarios

This research is currently an internal beta version and has not been put into formal use, and it is expected to be put into clinical research after use to provide more accurate data and great support for scientific research data.

5.4 Future prospects

5.4.1 Demand for formal usability evaluation

The researcher will not know the usability of the AE Monitoring View in a short time, and there will be usability evaluation in the future if it is allowed. The researcher planned to conduct a one-month test on clinical users in the next phase to understand the usability evaluation, and further obtain the needs of users through the collection of questionnaires and in-depth interviews to optimize the AE Monitoring View.

5.4.2 Demand for more drugs

At present, the researcher selected the most common AIDS drugs as the basis of the content framework. In order to facilitate the presentation of more diverse and targeted opinions in future research, the researcher decide to continue to add more antiviral drugs with common AE into the AE Monitoring View to ensure the integrity and scientificity of system content.

5.4.3 Demand for more concise functions

The researcher sorted out the clinical requirements that could not be designed to enter the system, such as adding the reminder function on the patient side and linking with the system, and directly popping out the pop-up window next to the abnormal indicators in the trend chart to prompt possible AE and other functions. Although this type of functional requirements cannot be achieved temporarily, the researcher plan to save the sorted data and leave it for subsequent system optimization and iteration in the future.

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Appendices

Appendix 1 Informed consent

Research title: Construction of AE Monitoring View for PLWHIV
Researcher: Siyue Ma, postgraduate student, University of Turku
Dear respondent:

Our research team is currently carrying out a study on the construction of drug AE (AE) monitoring view for people living with HIV (PLWHIV) based on AIDS database, which is applied to the clinical AE of PLWHIV, while assisting health professionals in the trend prediction, clinical diagnosis / nursing diagnosis of the condition to PLWHIV in order to take corresponding treatment and nursing intervention measures in time. This study is approved by the research ethics committee of Shanghai Public Health Clinical Center. The research process will not bring any risk or physical and mental harm to you and your family. The research process includes: (1) filling in a general questionnaire; ② This study requires you to accept an interview, and the whole process will take you about 30 ~ 60 minutes of valuable time. For the convenience of recording, the content of the whole interview will be recorded. After converting the recorded data into text data, the recorded data will be deleted.

You have the right to decide whether or not to participate in the study, and you have the right to decide when and where to receive the interview. You can also withdraw from the study at any time, which will not affect you in any way. Your name will be coded instead. Your name will not be mentioned when the research is in progress or when the research paper is published or published. All interview materials will be kept safe and strictly confidential. They will only be used for this study and will not be told to anyone without your permission. I hope to get your support.
If you have any questions about this research, you can contact me by phone or e-mail.
Tel: 18701799671 e-mail: 20211170063@fudan.edu.cn
I have read this consent form and voluntarily agreed to participate in this study.
Subject signature:_____ Date:_____
I have explained the research content to the interviewee and have obtained his / her understanding of informed consent.
Signature of researcher:_____ Date:_____

Appendix 2 Questionnaire on general situation of health professionals

Questionnaire on general situation of health professionals

Please fill in according to your actual situation, thank you!

1. Gender: 1) ☐male 2) ☐Female
2. Year of birth:
3. Education level:

☐graduate or above

☐bachelor degree

☐junior college

☐senior high school or technical secondary school

4. Working years:

☐＜2 years

☐2-5 years

☐5-10 years

☐10-20 years

☐> 20 years

5. Years of work related to AIDS: _____years
6. title:
7. Work Place:

Appendix 3 Interview outline of demand exploration on AE Monitoring View for PLWHIV among clinicians and nurses

Interview outline of demand exploration on AE Monitoring View for PLWHIV among clinicians and nurses

Opening remarks:

Hello, our research team is currently carrying out a study on construction of drug AE (AE) monitoring view for people living with HIV (PLWHIV) based on AIDS database, which is applied to the clinical AE monitoring for PLWHIV, and assist health professionals in the trend prediction, clinical diagnosis / nursing diagnosis of the physical condition among PLWHIV at the same time in order to take corresponding treatment and nursing intervention measures in time. The whole process of this interview will take you about 30 ~ 60 minutes of valuable time, and it needs to be recorded at the same time. The content of the interview will be strictly confidential! To ensure the effectiveness of the interview, please answer each question truthfully. If you have no questions, let's start!

1) What do you think are the most common and rare AE among PLWHIV and which should be noticed and found as soon as possible?
2) How do you carry out the clinical monitoring of AE and what is the effect?
3) What is your experience in monitoring AE among PLWHIV?
4) Do you have any opinions or suggestions on the improvement of AE monitoring methods for PLWHIV?
5) What do you think of using IT/digital methods for AE monitoring?
6) What are your thoughts and suggestions on presenting clinical data of patients in the form of a unified trend view according to the time axis to monitor AE?
7) What do you think about the decision support function of AE monitoring view?

Appendix 4 First round of expert inquiry form

First round of expert inquiry form

Construction of AE monitoring view for PLWHIV

—— Expert inquiry form

Part Ⅰ Forward

Dear experts

Hello!

Thank you for taking the time to fill in this questionnaire. Thank you for your support! Our team is currently working on the construction of a monitoring view of adverse drug reactions (ADR) for people living with HIV (PLWHIV) based on the AIDS database. In this study, Delphi method will be used to construct a unified view of clinical AE monitoring for PLWHIV, and to assist health professionals in trend prediction, clinical diagnosis and nursing diagnosis of PLWHIV so as to take corresponding treatment and nursing intervention measures in time.

1. Background of the research

Acquired immunodeficiency syndrome (AIDS), is a global malignant infectious disease with extremely high fatality rate caused by human immunodeficiency virus (HIV). Since the first case of AIDS reported in China in 1985, it has always been one of the most difficult medical problems. Despite the improvement of medical standards in recent years with AIDS epidemic prevention and control work obtained remarkable achievements, the current epidemic situation is still relatively highly severe. By the end of 2019, there were a total of 963000 survival people living with HIV(PLWHIV)in China，and 316000 cases of death were reported. In case people living with HIV received standardized treatment in time, their expected longevity will not be affected. However, late detection of AIDS is regarded as the main cause of death in China at present. As of the end of 2020, there were still 30% of HIV-infected people in China that had not been detected, while 30% of those who had been diagnosed as being infected were found in late-stage infections, which could increase mortality. According to the 2020 national statutory infectious disease report morbidity and death statistics released by the Chinese National Bureau of Disease Control and Prevention, in the year 2020, 62167 cases of AIDS and 18819 deaths were reported. AIDS has become the statutory infectious disease with the highest number of reported deaths in China in 2020. The prevalence of the AIDS epidemic

in China mainly presents four characteristics currently: (1) It is at a low epidemic level regarding AIDS epidemic in China in the world as a whole, with dramatic differences in epidemic areas, among which the epidemic situation in some parts is fairly serious; (2) The number of reported surviving HIV/AIDS cases continues to increase with the number of reports of new infections and newly discovered diagnoses being rose up at the same time year by year; (3) PLWHIV have gradually entered the stage of disease, which resulted in an significant increase on the number of AIDS patients, while the number of deaths from all causes has tended to be stable; (4) Sexual contact is regarded as the predominant driver of transmission, in which homosexual transmission among men who have sex with men (MSM) has played an increasingly significant role recently.

Regarding there is still no AIDS vaccine or cure in the world so far, the usage of Highly Active Anti -Retroviral Therapy (HAART), which is a treatment regimen typically comprised of a combination of three or more antiretroviral drugs, is currently the most effective way to suppress viral replication and also the current basic therapy, due to the fact that it can significantly control viral load(how much virus is in the blood), delay the onset of progression to AIDS, and prolong life expectancy of PLWHIV. According to the recommendation of Chinese Guidelines for Diagnosis and Treatment of HIV/AIDS (2018), HAART is mostly composed of two nucleoside reverse transcriptase inhibitors (NRTIs) plus one non-nucleoside reverse transcriptase inhibitors (NNRTIs) or an enhanced protease inhibitor (PIs) plus ritonavir or integrase Inhibitor (INIs) composition. However, drug resistance and different degrees of adverse drug reactions (AE) on PLWHIV could occur due to the need for lifelong antiviral therapy and poor compliance with medications, including skin reactions, myelosuppression, metabolic disorders, gastrointestinal intolerance, liver toxicity, renal impairment and peripheral neuropathy. HAART adverse reaction prevalence always varies from regions and countries, with the severity and profile of it varies from patients and drug regimen at the same time. According to a study from India, the incidence of AE among PLWHIV who receive HAART globally ranges between 11% and 35.9%, among whom opportunistic infection occurrence rate being as high as 54%. These unexpected and unwanted AE caused by HAART are often soft, but sometimes getting more severe with leading to increased economic burden, a major impact on health and quality of life for PLWHIV in case of being not noticed in time, including but not limited to prolong

of hospital stay, a variety of complications and other opportunistic infections happening, and even death. Therefore, continuous monitoring and evaluation of HAART AE plays a key role for PLWHIV who are receiving HAART to get all the help they need to minimize the impact of AE.

At present, according to the patient's self-reported symptoms and the observation from health professionals themselves with health records of PLWHIV are still the most common ways to monitor AE for PLWHIV. A study from South Ethiopia reported that an AE monitoring center was established to collect, compile and analyze all the information about AE occurred to PLWHIV who received HAART which was reported by doctors and nurses in the hospital, based on which those unnecessary harm would be avoided as possible throughout risk assessment and clinical intervention. Nevertheless, information on the types and severity of HAART AE is still inadequate in the study area and risk factors for AE have also been controversial. It is reported that gender, age, drug regimens, CD4+ T lymphocyte count, quality of life, and the use of illicit drugs by individuals could all be associated with AE, which means health professionals need to observe the necessary data from different places such as the patient's medical record and clinical examination report to determine whether the patient has a trend of AE. In addition, clinicians need to synthesize the combination of different clinical indicators in the patient report to determine the probability of the patient's AE or the cause of them in the patient who has already had AE. Decentralized clinical data are suggested to be a major problem during AE monitoring process, which could result in incomplete consideration and extension of diagnosis time, thus digital unified view of AE monitoring is asked for badly from health professionals to simplify the tedious process of clinical data collection in order to make timely adoption of appropriate treatment plans and nursing measures via more efficient monitoring and decision-making.

Special disease database refers to an information software system for centralized management of case information of a single disease, which conducts systematic and standardized management of clinical case information data of a large number of relevant cases with scientific research significance and practical value in order to realize rapid query of past case information of the disease and statistical data analysis, thereby conducting clinical research, giving clinical diagnosis and treatment with providing valuable information or meet the needs of clinical teaching.

At present, a huge amount of medical information is generated in the process of clinical AIDS diagnosis and treatment, including clinical data such as clinical features, drug treatments, tests, imaging treatments, and disease outcomes, as well as epidemiological and economic data, which will be of great value for optimizing diagnosis and treatment when being used scientifically and rationally. However, lack of structure and not able to form a standardized data set leads to problems such as heavy workload, low efficiency, high error rate, and difficulty in sharing and using collected data when conducting AIDS research. Therefore, it is urgent to build an integrated AIDS database in the medical big data environment. Clinical information unified view means that clinical medical workers and scientific researchers can consult the patient's medical information through a clear and friendly unified view so that they can have an overall understanding of the patient's medical condition in a short time. A Chinese company has already constructed a clinical information unified view called patient 360 unified view which organized patients' basic information, medical information, health problems, medication information, allergy information, surgery information, inspection reports, past medical history and other information for use by clinicians in the hospital with being provided to health management cloud platform throughout big data platform in order to satisfy patients' requirements for clinical information demands. The unified view of clinical information highly summarizes the patient's full life cycle data to make the treated data more valuable, meanwhile the data is integrated and labeled to provide individual patient conditions and recovery prediction analysis, which is beneficial to provide assistance to clinicians' decision support and help managers better identify risks with realizing timely intervention and control.

However, current domestic and foreign research still lacks a unified view of AIDS-specific clinical information. The complexity of HAART AE monitoring urgently requires highly concentrated patient clinical data to be presented in a unified view to assist health professionals in observation and decision-making to take corresponding intervention measures so that the quality of life for PLWHIV could be improved. Therefore, this study intends to design and construct an AE monitoring view for PLWHIV who receive HAART based on AIDS database, through which doctors and nurses are able to independently select clinical indicators and keep them in a unified view. The AE monitoring view will be displayed in a

chronological order in a trend chart to assist health professionals in clinical decision-making, nursing diagnosis as well as timely corresponding intervention measures.

2. Research method

In this study, Delphi method will be used to seek your opinions and suggestions on the construction of AE monitoring view for PLWHIV. Delphi method refers to the method of consulting experts' opinions and feedback through several rounds of questionnaires to reach a consensus on a certain topic or matter. In this study, researchers set up a research group to construct the framework of AE monitoring view for PLWHIV, compile a questionnaire, conduct several rounds of letters to expert group members by back-to-back communication, and finally determine the content system of AE monitoring view for PLWHIV according to the comprehensive opinions of experts. Therefore, your opinions are very important in the formation of the final plan.

3. Human rights protection & contact information

1) This research promises that your personal information will never be leaked, and all the consultation results obtained will only be used for academic research.

2) To ensure the smooth progress of the project, please try your best to return within one month after receiving the questionnaire. Thank you very much!

3) Contact address: School of nursing, Fudan University, 200031, name: Siyue Ma, Tel: 18701799671, Wechat: msy132426, e-mail: 20211170063@fudan.edu.cn

Finally, thank you again for your guidance and help in our research!

Chen Jun, head of AIDS database project

This study was conducted as a sub item of the AIDS special database.

July, 2021

Part II Expert consultation form

According to the Likert 5 scale method, the expert opinion score is divided, that is, 5 = completely suitable, 4 = relatively suitable, 3 = average, 2 = not very suitable, and 1 = totally unsuitable. Please rate each item according to its scientificity, rationality and applicability, and tick "√" in the corresponding column. In order to facilitate you to modify and supplement the content, an expert opinion column is set up after each item. If you have any remarks, please fill in the expert opinion column.

Item	5/ completely suitable	4/ relatively suitable	3/ average	2/ not very suitable	1/ totally unsuitable	Expert opinion column

1.						
2.						
3.						
4.						
...						

Part Ⅲ Expert information questionnaire

(Please tick "√" in the appropriate information option box☐ or fill in the relevant contents in the blank)

Gender	☐Male ☐Female	Work place	
Contact information (Tel/E-mail)			
Date of birth		Working years	
Technical title	☐Intermediate ☐Deputy senior ☐Senior ☐Others	Highest education	☐PhD ☐MD ☐Bachelor ☐Others
Education background	☐Clinical medicine ☐Public health ☐Nursing ☐Others（Please indicate）		
Current job	☐Clinical medicine☐Medical education☐Clinical nursing ☐Nursing education☐Others（Please indicate）		

Part IV Questionnaire on experts' familiarity with research questions and their judgment basis

(Please tick "√" in the appropriate information box "☐")

Familiarity with the research issues	☐Very familiar ☐familiar ☐general familiar ☐unfamiliar ☐very unfamiliar		
Judgment basis	Influence degree		
	Large	Medium	Small
Practical experience			
Theoretical analysis			
Reference domestic and foreign literature			
Intuitive feeling			

Appendix 5 Pilot-test Questionnaire of Internal Usability Evaluation to AE Monitoring View for PLWHIV

According to the Likert 5-point metric, 5=strongly agree, 4=agree, 3=relatively agree, 2=inappropriate, and 1=strongly disagree. Please rate each item according to your degree of recognition, and tick "√" in the corresponding column.

	Item	5/strongly agree	4/agree	3/relatively agree	2/disagree	1/strongly disagree
Acceptance	1. I am satisfied with the overall performance of the view.					
	2. The view gives me a good experience.					
	3. The development and maintenance personnel of this view can sincerely and timely solve the problems I encountered when using the system.					
	4. The view is easy to learn and use					
Convenience	5. This view reduces the time it takes me to complete the task.					
	6. This view makes the evaluation and decision-making process more convenient.					
	7. I am satisfied with the efficiency of the view.					
	8. This view reduces the expense of office supplies.					
Clinical applicability	9. This view can meet the needs of my actual operation.					
	10. The view played a supporting and auxiliary role in the evaluation and decision-making process.					
	11. The information provided by this view is consistent with the actual situation, and there is no error record.					
	12. The trend chart, evaluation and decision support information provided by this view is valuable and can be used.					
Stability	13. Remove the influence of WIFI, the effective response time of this view to complete the command is short, and there are few stalls.					
	14. The view is very stable at runtime.					
Fluency	15. The view can be flexibly switched in each interface.					
	16. The view is very smooth at runtime.					

Appendix 6 The approval of the Ethics Committee of Shanghai Public Health Clinical Center

项目参加单位遵守医学科研伦理准则和医疗和科技安全法律法规的承诺

本单位依据上海申康医院发展中心“第二轮《促进市级医院临床技能与临床创新三年行动计划(2020-2022 年)》”项目申报指南的任务需求，严格履行法人负责制，自愿提交项目任务书，**在此郑重承诺：**

1、项目按照《国务院办公厅关于促进和规范健康医疗大数据应用发展的指导意见》(国办发[2016]47 号)、《国家卫生健康委员会关于印发国家健康医疗大数据标准、安全和服务管理办法（试行）的通知》(国卫规划发[2018]23 号)、《上海市公共数据和一网通办管理办法》(沪府令 9 号）等文件和管理办法执行。

2、建立完善的医学科研伦理、医疗和科技安全审查机制，防范伦理和安全风险。按照有关法律法规和伦理准则，建立健全医学科研伦理、医疗和科技安全管理制度；加强伦理审查和过程监管，加强生物安全、信息安全等医疗和科技安全责任制。项目开展所涉及的研究方案符合伦理学要求，有符合研究方案及伦理要求的知情同意书，并经过项目申请单位伦理委员会审核，项目启动实施前获得单位伦理委员会审批，并获得正式伦理批件。

项目责任单位单位（公章）：
项目依托单位（公章）：
项目参与单位（公章）：
日期：

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Where of what's past is prologue.

Statement of originality of dissertation

Fudan University
Statement of originality of dissertation

I solemnly declare that the dissertation submitted is the result of my independent research work under the guidance of my supervisor. Except for the specially marked content, the paper does not contain any research results that have been published or written by other individuals or institutions. Individuals and collectives who have made important contributions to this research have made clear statements in the paper and expressed their gratitude. Legal consequences of this statement shall be borne by himself.

Author signature：马恩玥 Date：2022.05.17

Fudan University
Dissertation authorization statement

I fully understand the regulations of Fudan University on the collection and use of doctoral and master's theses, that is, the school has the right to collect, use and send the printed and electronic versions of the thesis to relevant state departments or institutions; allow the thesis to be consulted and borrowed; all or part of the content of the thesis can be published by school, and the thesis can be preserved by photocopying, reduction printing or other reproduction methods. Confidential dissertations shall comply with this requirement after decryption.

Author signature：马恩玥 Supervisor signature：[illegible] Date：2022.05.17