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Waste-minimising measures to achieve sustainable supply and use of medication

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ABSTRACT

Medication waste has a high impact on the healthcare budget and detrimental effects on the environment. Therefore, preventing medication from remaining unused through the pharmaceutical chain forms an interesting approach to achieve sustainable supply and use of medication. This scoping review focusses on how stakeholders involved can prevent the waste of potentially viable medication.

Manufacturers can contribute to sustainable supply and use of medication by extending medications' shelf-life, choosing the most sustainable storage conditions and adjusting package sizes. The role of distributors involves stock management optimisation and loosening shelf-life policies. In turn, prescribers can commit to rational prescribing practices, including consideration of prescription quantities and prescriptions for shorter durations. Pharmacists can contribute via appropriate stock management, enhancing medication preparation processes, optimising dispensing processes, and redispensing unused medication. Patients' awareness of medication waste must be increased to stimulate conscious medication-ordering and to create willingness for participation in waste-minimising interventions. Finally, health authorities can contribute to sustainability by creating awareness and enforcing waste-minimising measures. Due to the multiple causes of medication waste at all levels of the pharmaceutical supply and use chain, no single intervention is sufficient to overcome the problem of medication waste, thus a joint responsibility of all stakeholders is needed.

1. Introduction

Medication waste refers to any pharmaceutical product that remains unused or is not fully consumed throughout the pharmaceutical supply and use chain (West et al., 2015; World Health Organization, 2014). Waste of potentially viable medication jeopardises the budget of pharmaceuticals, causing an annual loss up to $5.4 B in the United States (Law et al., 2015), around £300 M in the United Kingdom (Trueman et al., 2010) and at least €100 M in the Netherlands (Bouvy et al., 2006). Furthermore, pollution of the aqueous environment with pharmaceuticals can have detrimental effects to its ecosystems (Majumder et al., 2019), while it can also be hazardous to humans via incomplete removal by conventional drinking water plans (Kaushik and Thomas, 2019; Kostich et al., 2013). The majority of pharmaceutical pollution is caused by human excreta as a consequence of medication use itself (Nikolaou et al., 2007). Still, the contribution of improper disposal of unused medication cannot be underestimated (Tischler et al., 2013). For example, in many countries the toilet, drain or household trash is still used as disposal route for leftover medication, resulting directly in accumulation of pharmaceuticals in the environment (Kusturica et al., 2016). Accordingly, to protect the healthcare budget and the environment, the supply and use of medication must be arranged in a sustainable manner.

Sustainability is a major global challenge, that can only be overcome

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by taking responsibility and joining forces. Therefore, all member states of the United Nations (UN) endorsed a set of goals for sustainable human development by the year 2030, including responsible production and consumption patterns (UN General Assembly, 2015). This also applies for the supply and use of medication. Moreover, within the pharmaceutical field, the International Pharmaceutical Federation (FIP) invoke all stakeholders involved to minimise their contribution to pollution (International Pharmaceutical Federation, 2015). Green pharmaceutical practices include environmental research on medicinal products, minimising environmental contamination, waste disposal management and a greener community pharmacy (Toma and Crişan, 2018). Although waste disposal management is extensively explored, it would be more effective to prevent occurrence of leftover medication in the first place to achieve a sustainable supply and use of medication.

Causes for medication waste are diverse and can derive among the various stakeholders involved in the pharmaceutical chain, including end-users: patients. For example, by patients not using all medication that is dispensed to them, due to (early) treatment discontinuation resulting from adverse events, lack of efficacy or resolution of the condition (Reitsma et al., 2013; West et al., 2014). Unused medication that is returned unopened to the pharmacy, must generally be disposed of (World Health Organization, 2011), resulting in waste of potentially viable medication. To restrict the problem of medication waste, a transition towards a sustainable practice of manufacturing, distributing, prescribing, dispensing and using medication is needed. Accordingly, this scoping review aims to give an overview of potential waste-minimising measures that can contribute to sustainable supply and use of medication.

2. Methods

Potential waste-minimising measures in the pharmaceutical chain were explored via a literature search over one month in June 2020. Electronic databases searched comprised of PubMed/Medline and Embase. drug OR pharmaceutical, and 3) prevent OR sustainable OR sustainability OR green OR solution OR intervention OR program OR management. A filter was applied to select articles published between 2000 and 2020. Only studies published in either English or Dutch were included in the review. Articles related to different industries, including veterinary medicine, cosmetics, food and chemistry, were excluded. In addition to the electronic database search, bibliographies of retrieved references were searched for additional articles describing waste-minimising measures in the pharmaceutical chain.

Abstracts of publications were screened for waste-minimising measures. Subsequently, the most relevant and potent waste-minimising measures in the pharmaceutical supply and use chain were selected. This resulted in waste-minimising measures derived from 73 publications described in this review.

3. Waste-minimising measures in the pharmaceutical chain

Medication waste can derive in all stages of the pharmaceutical chain, hence minimisation of redundant medication can be achieved via a range of strategies within the supply and use of medication (Fig. 1).

3.1. Manufacturers

The pharmaceutical chain starts with the manufacturing of medication. The manner in which manufacturers develop, produce and distribute pharmaceuticals can affect medication waste in all subsequent stages of the pharmaceutical chain.

For example, if the storage conditions are limited, medication is more likely to expire before it reaches the patient. However, long term storage tests are not a requirement for a medication's authorisation, thus many medications are labelled with a relatively short shelf-life compared to their stability (Diven et al., 2015). For instance, research showed that the majority of EpiPens are potent to treat severe allergic reactions up to 50 months after the labelled expiration date (Cantrell et al., 2017). Moreover, stability data demonstrated that the expiry dates of almost 90% of 112 different medications could have been extended (Lyon et al., 2006), hence further studying the quality of expired medication can help to reduce medication waste. Likewise, explicating

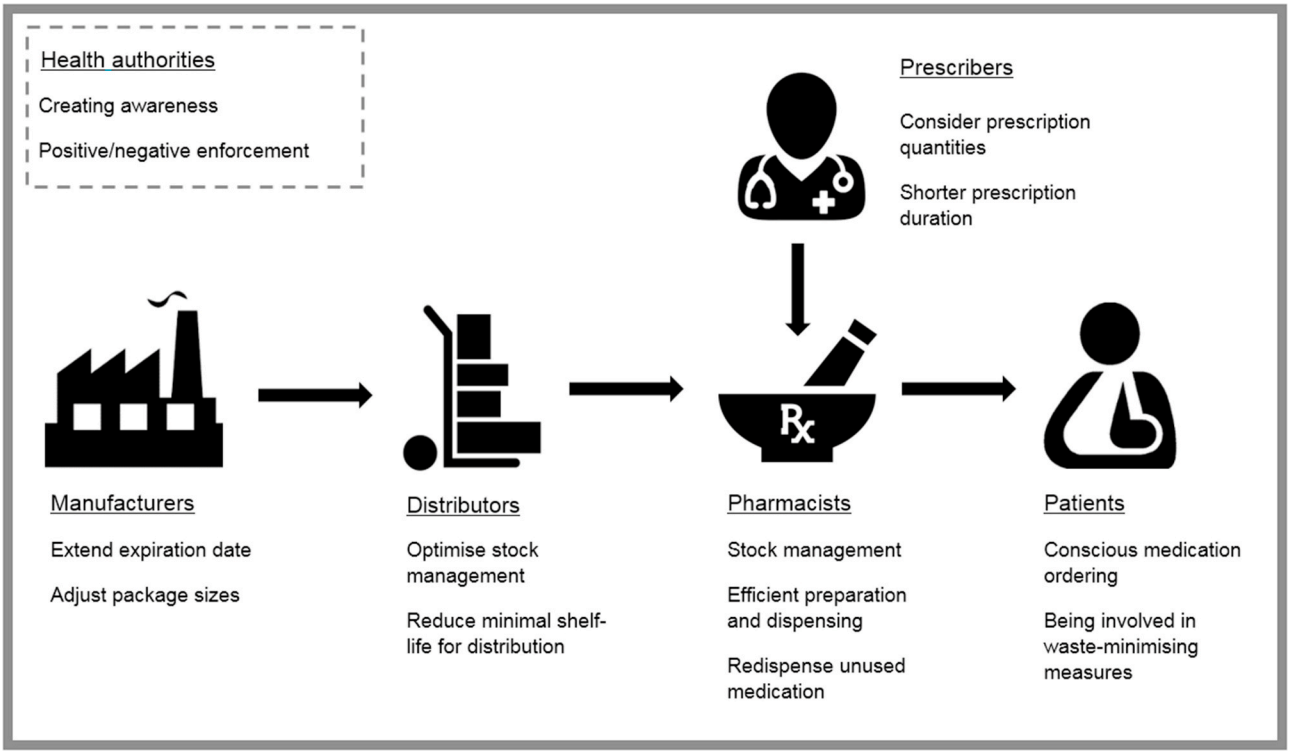

Fig. 1. Impression of waste-minimising measures to achieve sustainable supply and use of medication.

stability of refrigerated medication at ambient conditions can help to avoid waste due to improper storage (Cohen et al., 2007). One question that needs to be asked, however, is how prolonged shelf-life influences the biodegradability of medication. For this purpose, there is a need for the development of pharmaceuticals that can be fully mineralized, while maintaining clinical properties (i.e. toxicity, efficacy, efficiency) and shelf-life stability (Kümmerer, 2019).

Furthermore, medication package sizes regularly deviate from the appropriate dose and quantity required for patients' treatment. In several countries pharmacists are not allowed to split medication packages into smaller quantities, causing a medication over-supply to patients (Bekker et al., 2018a). Furthermore, medication that is dosed based on patient's weight or body size, is often wasted due to the required dose not matching the vial size. As a consequence, up to $1.8 billion of anticancer medication was wasted in 2016 in the United States (Bach et al., 2016). Therefore, to encounter medication waste, manufacturers should facilitate more variety in package sizes and avoid large packages. With the aid of modelling, optimum vial size can be calculated based on the patient population (Hatswell and Porter, 2019). Policy-makers can urge manufacturers to stimulate a reasonable set of size options by requiring a maximum percentage of waste or obliging refunds for leftovers medication (Bach et al., 2016).

3.2. Distributors

The role of distributors involves warehousing and distribution of medication stocks to pharmacies. During these processes medication waste can derive as a consequence of expiration of the medication. To prevent expiration during supply, warehouses utilise shelf-life criteria to manage their stocks. In the Netherlands, it is estimated that on daily basis 4500 packages of generic medication are disposed by warehouses, which can be reduced by 39% if the shelf-life criterium to distribute medication to pharmacies would be condensed from 12 months to 9 months (Soest-Segers et al., 2019). Accordingly, to combat medication waste on the warehouse level, distributors must first restrict the current internal shelf-life criteria.

Subsequently, to guarantee the use of these medications before expiration, effective inventory policies must be established. The debate of pharmaceutical stock management is ongoing. Enlargement of medication stock volumes can help to avoid medication shortages (Lücker and Seifert, 2017), while reduction of stock volume can counteract medication waste and accompanied costs (Sepassi A., 2020). This indicates the need for advanced logistic systems in pharmacies, for example with the aid of mathematical optimisation frameworks (Saedi et al., 2016). Distributors could use their extensive knowledge of logistics and their established logistics network to support pharmacies in appropriate management of their stocks. Particularly for medication with a short expiry date or medication that is rarely used, distributors should support pharmacies, for example by educating inventory policies. Considering inventory policies, besides calculation of optimal stock volumes, the first-in-first-out principle could be utilised (Budiawan et al., 2019). Another interesting opportunity for distributors is to function as a regional storage location for medication or to facilitate exchange of medication that is approaching its expiration date, as inventory pooling may counteract both medication waste and shortages (Saedi et al., 2016).

3.3. Prescribers

Accumulation of medication in a patient's home is associated with an increased risk of misuse (Brat et al., 2018) and medication waste (Trueman et al., 2010). Around 40% of the medication waste is preventable (Bekker et al., 2018b; Trueman et al., 2010), with dispensing medication for a longer period (>3 months) being a significant risk factor for unnecessary medication waste (Bekker et al., 2018b). Thus, regulating the amount of medication that is dispensed to a patient is a particularly valuable waste-preventive strategy. For this purpose, various approaches in the prescribing stage can be used.

One way to address redundant medication prescriptions is by thoroughly considering prescriptions and their quantities, based on patient and treatment related factors (Bettington et al., 2018). Shared decision-making could help prescribers to tailor pharmacotherapy to patient's individual preferences, which can include their need for and attitude towards pharmaceutical treatment, thereby preventing the dispensing of unneeded or unwanted medication. During this consultation, the quantities of previous prescriptions that patients have stored at home could also be addressed in order to prevent an oversupply. Moreover, prescription refills should regularly be evaluated to support patients in understanding their therapy, contributing to improved adherence and a reduction of avoidable waste. Accordingly, sustainable prescribing can contribute to improved therapeutic outcomes and decreased waste (Daughton and Ruhoy, 2011).

Another way to minimise medication waste is by restricting medication supplies. Despite the waste-minimising potential of such programs being demonstrated for several therapeutic classes (Doble et al., 2017; Domino et al., 2004; Murphy et al., 2012), the negative impact on patients' satisfaction and adherence due to the time consumption of regular pharmacy visits must be taken into account (King et al., 2018; Miani et al., 2017; Taitel et al., 2012). This barrier could be overcome by delivering medication to the patient's home or by distributing medication via a continuously accessible locker system. Still, the increase of costs related to the pharmacy dispensing and patients' obtaining their medication must be considered, thus, restricting prescription quantities is presumably attractive for high-cost medication. This is the case for oral anticancer drugs, in which tailored prescribing interventions have proven to be beneficial (Khandelwal et al., 2012). Likewise, prescription quantities should be restricted for patients that are prone to frequent treatment modifications, such as patients in the end-of-life phase and patients who start new therapies.

3.4. Pharmacists

Pharmacists can use a range of approaches to minimise medication waste, depending on the setting and country of employment (Afanasjeva and Gruenberg, 2019; Bekker et al., 2018a). Particularly, these approaches regard to stock management, including effective purchasing, preparation of (compounded) medication and dispensing processes. In addition, medication waste can be mitigated in the leftover stage via the redispensing of unopened medication packages.

Firstly, appropriate stock management is essential for managing internal waste in pharmacies. This can be established via automatized expiry date checks followed by accelerated dispensing of medication close to their expiration date (Respaud et al., 2014). Moreover, exchange with other pharmacies could help to prevent disposal of medication that are not often distributed. In the Netherlands, the online platform PharmaSwap has been established for this purpose, thereby the initiative has prevented 175 medication packages from being wasted to date (Faber and Oosterhof, 2020). Additionally, pharmacists can mediate in achieving efficient packaging and purchasing. For instance, research showed that single-dose vials caused a waste of up to 60% of ephedrine, while phenylephrine, that was used in the same amount of cases but was distributed in pre-filled syringes, only caused a waste of 3% (Atcheson et al., 2016). Other measures that can help to create a more sustainable pharmaceutical assortment include the choice of smaller-sized vials and products with longer expiration dates (Afanasjeva and Gruenberg, 2019). A note of caution is due here since national policies might contain legislative constraints impeding the switch to a therapeutic alternate or another dosage form (Bekker et al., 2018a). Still, we would like to encourage pharmacists to consider sustainability within local formulary decisions and purchasing policies where possible.

Furthermore, optimising process flows of medication preparation and distribution can reduce waste. One source of waste comprises of

compounded medication, as leftovers are usually being discarded due to a short shelf-life after preparation. Predominantly, unnecessary preparation of medication must be avoided. To minimise the chance of treatment modifications after preparation of compounded medication, the frequency of preparing batches of preparations could be increased (Abbasi and Gay, 2017; Toerper et al., 2014). Still, in some regimens, treatment modifications occur frequently, with the potential consequence that compounded medication is no longer required. This is the case for some cancer therapies, and therefore, intensively checking treatment regimens prior to preparation could reduce waste of these medications (Yamada et al., 2020). Additionally, by rounding the dose to a 'flat' or 'fixed' dose (Lindsey et al., 2018; Winger et al., 2011), which can be automatized (Fahey et al., 2019), can help to prevent leftovers. Finally, if leftovers are inevitable, medication (Fasola et al., 2008) and vaccine (Lee et al., 2010) distributions can be clustered by scheduling patients that receive the same medication simultaneously to prevent leftovers from being discarded.

Particularly in hospitals and care homes, medication preparation and distribution processes could be optimised, to avoid accumulation of unused medication. For example, this can be achieved by bulk prescribing medication for occasional use (Hazell and Robson, 2015). In this way, supplies of occasional medication can be bundled for multiple residents, instead of having a single package per resident of which the remainders have to be thrown away (Hazell and Robson, 2015). In hospitals, remainders of medication have to be thrown away after a patients is discharged. Alternatively, patients could bring their own medication, obtained from the community pharmacy, into the hospital when admitted. By using patient's own medication during hospitalisation, the economic value of inpatient medication waste could be reduced by 40% (van Herpen-Meeuwissen et al., 2019).

Patients often have unused medication due to being oversupplied, which may be attributable to a lack of evaluation of their medication. Therefore, an important opportunity lies with discussing required medication quantities with the patient prior to dispensing them (Brown, 2018). Particularly, during treatment initiation, it might be beneficial to adjust medication quantities, as discontinuation occurs more frequently in this stage (Paterson and Anderson, 2002). Consequently, a split-fill program, that dispensed oral anticancer drugs for fourteen days in the first six months of treatment, demonstrated reduced pharmacy costs and potential waste (Staskon et al., 2019). To facilitate the dispensing of limited quantities without increasing internal waste, pharmacists should consider dispensing opened medication packages or using dose-dispensing systems.

When medication waste occurs despite preventative measures, proper disposal routes can help to mitigate downstream environmental effects. Indubitably this includes the collection of unused medication by the pharmacy to avoid disposal via household garbage or the sewage (Smolen, 2011). Additionally, research showed that one-fifth of the returned medication is unopened, undamaged and has a remaining shelf-life exceeding 6 months, making it eligible for redispensing (Bekker et al., 2018b). Furthermore, redispensing is found to be cost-beneficial for expensive medication (Bekker et al., 2019a) and the results appeared to be promising in pilot studies (Bekker et al., 2019b; Toh and Chew, 2017). However, despite the general support of stakeholders (Bekker et al., 2017), including pharmacists (McRae et al., 2016), patients (Alhamad et al., 2018a; Bekker et al., 2019c) and the general public (Alhamad et al., 2018b), concerns regarding counterfeits and quality assurance give rise to legal constrictions. Still, these barriers can be overcome by enhancing pharmaceutical packages with modern sensing technologies (Hui et al., 2020a), guaranteeing quality and safety of redispensed medication (Hui et al., 2020b).

3.5. Patients

Patients can contribute to medication waste by over-ordering medication, together with abandoning a prescription or not using medication according to the directed regimen, thereby allowing the stored medication to expire. An important facilitator for the over-ordering of medication is the inconvenience of picking-up medication regularly experienced by chronic patients (P. M. Wilson et al., 2013). When patients would be more aware of the consequences of medication waste, they might be willing to overcome such barriers. Awareness of medication waste can also help to motivate patients to engage in disposal programs (Seehusen and Edwards, 2006). If patients would return unused medication to the pharmacy, the medication could for example be used for so-called drug donations (World Health Organization, 2011). Accordingly, it is important to increase patients' awareness of medication waste and possibilities for counteracting it.

One way to create this awareness of medication waste is by increasing patients' consciousness of the treatments' costs. This can be achieved by labelling medication with price tags (Torjesen, 2015). A major drawback of this approach is that price tags can be misinterpreted and make patients feel guilty for receiving medication in the first place (Yemm et al., 2017). Still, increasing patients' consciousness of unused medication can increase patients' commitment to sustainable medication use, hence discussions about medication waste should be conducted, but in a careful and understanding way.

A behavioural change is required for patients to take the responsibility for a sustainable healthcare system, hence patient-tailored interventions can be utilised to achieve waste minimisation at patient level (L. M. West et al., 2018). One example of such an intervention is improving patients' medication taking behaviour (Law et al., 2015), as non-adherence is a risk factor for wasting medication (Hovstadius and Petersson, 2011). Moreover, shared decision-making between prescribers and patients could help to tailor pharmacotherapy to patient's individual preferences, thereby improving patients' adherence and reducing medication waste (S. R. Wilson et al., 2010). In conclusion, knowledge of medication waste and opportunities to reduce medication waste may empower patients into commitment to waste-minimising programs.

3.6. Health authorities

Health authorities could enforce waste-minimisation by creating awareness, providing guidelines on waste-minimising measures or stimulating collaborations and alliances.

Education is seen as a key strategy to decrease medication waste (Afanasjeva and Gruenberg, 2019). For example, an important cause of incorrect medication disposal is unawareness of appropriate disposal routes (Kinrys et al., 2018). Accordingly, educating patients (Botelho, 2012; Maughan et al., 2016) and healthcare workers (Ikeda, 2014; Mosquera et al., 2014; Tisdall et al., 2019) proved a successful tool for establishing proper disposal of medication. Similarly, health authorities could stimulate education on the possibilities to prevent medication waste. This could be achieved by national awareness campaigns, but should also be incorporated in the educational programs for healthcare workers, such as pharmacists (Eissen and Backhaus, 2011; Yang et al., 2010), pharmacy technicians and prescribers. Subsequently, healthcare professionals will be more conscious about their decisions, and could be empowered to make more sustainable choices. For example, prescribers could get involved in eco-directed sustainable prescribing (Daughton, 2014) or pharmacists could take a leading role in educating patients about sustainable pharmaceutical practices (Jarvis et al., 2009; Singleton et al., 2018; Tai et al., 2016).

Opportunities for waste-minimising measures differ significantly between countries. In some countries wide implementation of waste-minimising measures is counteracted by policy regulations or the lack thereof (Amster, 2016). This is illustrated by medication redispensing, with projects operating successfully in the United States (SafeNetRx, 2020) and Greece (GIVMED, 2020), whereas in other countries redispensing medication is limited by law or lack of clinical guidelines (Connelly, 2018; Doyle, 2010). Here lies an important role for

policy-makers in providing clear guidelines on waste-minimising initiatives. Moreover, cooperative research and innovation underly sustainable development (UN General Assembly, 2015). Consequently, an interesting strategy for healthcare authorities would be to invest in global partnerships in which expertise and knowledge of stakeholders is bundled to achieve innovation.

4. Discussion

This scoping review showed how all stakeholders of the pharmaceutical chain can contribute to minimising the waste of unused medication. Nevertheless, the multifactorial causes of medication waste imply that no single intervention is sufficient to overcome the problem and thus a multitude of approaches is needed.

Cooperation of all stakeholders is a prerequisite to ensure that efforts promoting sustainability are being made (UN General Assembly, 2015). Health authorities could have a pivotal role in motivating shareholders to take their responsibility, but, to facilitate this, medication waste must be prioritized on their agendas first. This is illustrated by the restriction on redispensing and donating unused medication (World Health Organization, 2011). Despite the public advocating the redispensing of unused medication and the research available to support the practice, national policies limit its implication in clinical practice (Connelly, 2018; Doyle, 2010). However, during the COVID-19 pandemic policy-makers in the United Kingdom showed that necessity knows no law, by temporarily approving the redispensing of medication in home care settings in case of shortages (NHS England and NHS Improvement, 2020). Thereby they demonstrated that the sustainable supply and use of medication not only restrains medication waste, but also counteracts medication shortages (Donyai et al., 2020). With this being said, it is time to prioritize sustainability in the pharmaceutical chain on the agenda of policy-makers, thereby forcing the design of clear policies and implementation of waste reduction practices.

This review discussed numerous waste-minimising interventions, indicating the willingness of stakeholders to contribute to a more sustainable supply and use of medication. Still, a topic of concern includes their cost-effectiveness. Although some interventions, such as reticence in prescribing, directly save money for the healthcare system, other interventions, such as limiting prescription quantities, require an investment due to increased frequency in dispensing and associated pharmacy costs. Nevertheless, in order to achieve the sustainable development goals, a change of policy is needed sooner rather than later. To achieve this change, policy-makers must focus on investing in interventions with high potential to reduce the environmental burden of medication waste. Accordingly, based on cost-effectiveness, potential worthwhile interventions within the given context of a healthcare system should be explored. However, currently comparison of waste-reducing studies is limited due to the use of different methods and outcomes. Future research could therefore elucidate a standardized set of outcomes for waste-minimising interventions, allowing a focus on environmental gain rather than financial resources in political decision-making.

To achieve a sustainable pharmaceutical supply and use chain, not only the problem of medication waste should be tackled, but complete preservation of resources and minimisation of environmental footprint of the pharmaceutical sector should be set as goal. One strategy to achieve a sustainable medication policy is via the circular economy principle, a framework that utilizes a multitude of approaches to manage resources (Alshemari et al., 2020). The strategies utilised within in a circular economy should at least include reducing, reusing and recycling waste, with the minimisation of waste set as a priority (Kirchherr et al., 2017). If translated to the pharmaceutical chain, prevention of waste in the prescribing and dispensing stage is the most preferable, followed by redispensing and recycling medication that remains unused throughout the supply and use chain. Only medication that still has a good-quality can be redispensed. For medication that does not meet the quality requirements of redispensing, recycling could be an option. Specifically, the inner and outer packaging, such as components of inhalers (Wilkinson and Anderson, 2020), could be reprocessed, as well as the active pharmaceutical ingredients that can be extracted from unused dosages, purified and repacked (Hsieh et al., 2017). In addition, pharmaceutical pollution could be further reduced by using biodegradable chemicals and environment-friendly packaging materials, that could be recycled or are produced from recycled materials. In this way, when medication waste is inevitable, its negative environmental impact can still be diminished.

5. Conclusion

Medication waste is a burden to society, due to its destructive impact on the healthcare budget and the environment. Particularly, minimising the avoidable waste of medication forms an interesting approach to encounter medication waste. Manufacturers, distributors, prescribers, pharmacists and patients are jointly responsible for implementing waste-minimising measures. Health authorities should enforce stakeholders to take their responsibility and cooperate in order to achieve a sustainable supply and use of medication.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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