

Management of Cancer Survivors in Clinical and Public Health Perspectives: Current Status and Future Challenges in Korea

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The number of cancer survivors is increasing dramatically. Many cancer survivors face lifetime risks associated with their cancer therapy, with a significant proportion at risk for serious morbidity and premature mortality. Concerns regarding the long-term physical, psychosocial, and economic effects of cancer treatment on cancer survivors and their families are increasingly being recognized and addressed by public and private sector. This article summarizes economic burden of cancer survivors, main post-treatment health problems including secondary primary cancer and comorbidities, health behaviors such as smoking, exercise and physical activity, nutrition, and psychosocial problems. Faced with various health and psychosocial problems specific to this population, several healthcare and policy models are being suggested to address these issues, including 'shared care model' and 'integrative supportive care service delivery system for cancer survivors'. More effort is needed to make the cancer survivorship agenda a reality, attended by a wide variety of stakeholders including researchers, patients, providers, and policy makers.

Key Words: Cancer; Survivors; Second Primary Neoplasm; Korea

INTRODUCTION

With the increasing incidence of cancer and improvement in survival (1), the number of cancer survivors in Korea continues to rise, with more than 800,000 Koreans now living with a history of cancer. It is estimated that the number would reach as many as 1 million in the year 2014 (2). Although many people who survived cancer return to normal functioning after the completion of treatment, cancer and its treatment can also result in a wide range of physical and psychological problems which persist in a chronic, long-term manner, leading to increased healthcare cost and productivity loss.

Therefore, increasing attention is paid to such continued health problems and needs of this growing population and its successful management. Understanding issues in cancer survivorship is not only critical for the clinicians to develop follow-up care plans that may allow for adequate surveillance, prevention, and the management of long-term and late effects of cancer, but also is a key to the development of cancer control plan from the public health perspective.

The purpose of this article was to briefly describe the current health problems faced by cancer survivors in Korea and to discuss potential solutions both from clinical and policy perspectives.

To provide a broad perspective on current status and future challenges in management of cancer survivors in Korea, we performed a narrative review. We searched pivotal papers on this topic, and priority was given to literature from Korea. After the literature review, health problems of cancer survivors were categorized into four topics: 1) second primary cancer; 2) comorbidity; 3) poor health behavior; and 4) psychosocial problems. We also looked up examples from other countries to identify gaps in current status in survivorship care and to propose care models in Korea.

SEASONS OF SURVIVORSHIP

A cancer survivor is defined as a person from the moment of diagnosis and then onward for the remainder of his/her life, and cancer survivorship also includes a cancer survivor's family and caregivers. Cancer survivors experience different health and psychosocial problems according to their stage, as described by Mullan (3) as 3 seasons of survival in their journey: 1) acute survivorship; 2) extended survivorship; and 3) permanent survivorship. In acute survivorship when treatment is ongoing, adequate management of pain, fatigue, and psychological distress are of main concern. Extended survivorship is a pe-

riod of transition when physical, psychological, social and financial readjustment is taking place with surveillance for recurrence ongoing. Finally, permanent survivorship is a period when a gradual sense of confidence develops with lowered risk of recurrence. Cancer survivors face various problems during their journey through the different phases of survivorship.

ECONOMIC BURDEN OF CANCER SURVIVORS

To estimate economic burden in cancer survivors, we performed analysis on medical expenses of cancer survivors using the 2001-2010 Korean National Health Insurance claims data. A total of 105,502 cancer survivors who were diagnosed with cancer was compared to that of matched control. The analysis performed for this study was approved by the institutional review board of National Cancer Center (NCCNCS-10-352). Informed consent was waived by the board.

Healthcare cost of cancer survivors jumped at the year of diagnosis, and decreased in the following years. However, it remained 2 to 3 times higher than that of matched control, even at long-term survivorship phase of ≥ 5 yr after diagnosis, suggesting higher healthcare need in this vulnerable population (Fig. 1).

Economic burden incurred by cancer is estimated to be around 14.1 trillion Korean Won (KRW) (13 billion US dollars) as of year 2005 (4). Morbidity costs accounted for 3.2 trillion won, and the proportion from the total burden is very rapidly increasing

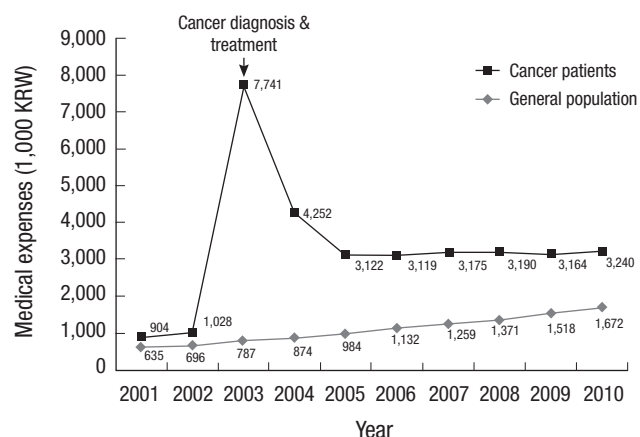


Fig. 1. Trend of medical expenses of cancer survivors compared with general population. Medical expenses covered by the National Health Insurance (not including out-of-pocket payments).

as shown by doubling from 1.6 trillion won in 2002. The relative proportion of morbidity costs in Korea is much higher than that of the US (23% vs 8%), indicating lack of successful rehabilitation programs for cancer survivors can lead to productivity loss and social burden in Korea.

HEALTH PROBLEMS OF CANCER SURVIVORS

Second primary cancer

One of the salient aspects of cancer survivorship is second primary cancer (SPC). SPC is a new primary cancer developing in a person with a history of cancer in a new site or tissue and subsequent to the initial cancer. SPC can occur in concordant (the same type of cancer as the first; e.g. newly developed left breast cancer after right breast cancer), or discordant sites (a different type from the first; e.g. newly developed colon cancer after breast cancer). Genetic predisposition, shared environmental factor, and cancer treatment place cancer survivors at higher risk of developing SPC compared with the general population. Population-based cancer registry data shows overall estimates of relative risk to be 1.1-1.6 (5-8) (Table 1), and SPC comprises a significant portion of all incident cancers (16% in the US, 8.5% for Sweden) (5, 6). To date, there is no official report regarding second primary cancer incidence from Korean Central Cancer Registry.

SPCs can lead to additional mortality (9), and screening for SPC is expected to reduce mortality through early detection at a stage when the SPC is more amenable to treatment. Indeed, earlier and more frequent screening for SPC has been recommended for certain cancer survivor groups (e.g. breast cancer screening for young female Hodgkin's lymphoma survivors who were exposed to chest irradiation). As there is very few data on the effectiveness or cost-effectiveness of second primary cancer screening, no specific evidence-based guideline for SPC screening is available. However, it is well accepted that cancer survivors should receive cancer screening according to general cancer screening guideline, and the US guidelines began to include SPC screening.

In Korea, screening rates among cancer survivors were 48.5%, 54.7%, 34.7%, and 28.6% for breast, cervical, gastric, and colorectal cancer screening, respectively, indicating similar rate with non-cancer control (10). Another study found only 37.7% of survivors had undergone all appropriate SPC screening tests

Table 1. Relative incidence of second primary cancer reported from population cancer registry

Countries	Total	Male	Female	References
United States, SEER (SIR)	1.14*	1.11*	1.17*	Curtis et al. (5)
Sweden, National (SIR)	NR	1.3 (1.2-1.3)	1.6 (1.5-1.6)	Dong et al. (6)
Japan, Osaka (SIR)	1.21 (1.19-1.23)	1.17 (1.14-1.19)	1.31 (1.27-1.35)	Tabuchi et al. (7)
Denmark, National (HR)	1.25 (1.24-1.26)	NR	NR	Nielsen et al. (8)

* $P < 0.05$ (95% confidence interval was not reported). SIR, standardized incidence ratio; HR, hazard ratio; NR, not reported.

(11). When compared to the US, screening rates among Korean cancer survivors is suboptimal, emphasizing the need for a more systematic approach.

A number of barriers have been identified. First, cancer survivors were shown to have limited knowledge about SPC and its screening. Having been not heard of SPC, they were found to be unable to differentiate SPC from 'recurrence' or 'metastasis,' also unaware of their increased risk of SPC (12). They were also found to have difficulty in the distinction between 'cancer screening' and 'routine surveillance test' after cancer treatment (11, 12). Second, oncologists do not consider SPC screening as their responsibility (13). Lack of established guidelines and short consultation time have been shown to further worsen the situation (13). As a result, only 21.5% of survivors were shown to have been recommended for screening for SPC (11). Third, coordination system for personal guidance is lacking. An intervention with an educational material increased knowledge of SPC and its screening, but failed to increase screening rate (14). Therefore, further efforts are needed to increase awareness of SPC risk in cancer survivors and physicians, and to establish proper coordination systems (11-14).

Comorbidity

Comorbidity, i.e., concomitant illness, is another concern for cancer survivors as the cancer is the disease of the elderly (Table 2). Comorbidity can be present at the time of diagnosis and treatment, and often influence the choice of treatment. In addition, comorbidity can also occur as a late effect of cancer treatment, including surgery, radiation, and chemotherapy. For example, breast cancer patients who received adjuvant treatment have higher risk for cardiovascular disease from radiation-related cardiac damage, as well as cardiotoxicity from anthracyclines,

paclitaxel and trastuzumab. Prostate cancer patients who received androgen deprivation therapy are also at risk for cardiovascular disease. Cardiovascular disease is the most common concomitant disease entity, and more attention is being paid to metabolic syndrome and its individual components. Osteoporosis is another common treatment sequelae of cancer treatment, including oophorectomy, androgen deprivation therapy, aromatase inhibitors, and chemotherapy, and can lead to fracture and disability.

Therefore, people diagnosed with cancer suffer from more comorbidities than general population control (15) and have an increased risk of death from non-cancer causes. An investigation in non-cancer death in Korea also revealed 24.0% of long-term cancer survivors died of non-cancer diseases, and excess mortality was observed in younger survivors (16). The proportion of non-cancer death is expected to rise because of improving cancer survival, and appropriate medical attention is warranted to prevent premature deaths from non-cancer causes.

However, it has been noted that cancer survivorship often receive suboptimal care for chronic medical conditions, such as follow-up for heart failure, necessary diabetic care, or recommended preventive services (17). However, survivors who had been followed up by both primary care physicians and oncologists had better care (17), suggesting that disease-specific, narrow specialty model of cancer care may limit appropriate care. In addition, cancer survivors were shown not to adhere to treatment for non-cancer conditions, such as hypertension (18). Future work should examine how to improve screening and treatment of co-morbid disease in Korean healthcare system and how to increase survivors' adherence to them.

HEALTH BEHAVIORS OF CANCER SURVIVORS

Occurrence of cancer is often associated with unhealthy behaviors, such as smoking, poor diet, and sedentary lifestyle. Changing such unhealthy behaviors may help reduce cancer treatment sequelae, recurrence, and risk for other common diseases.

Smoking

Continued smoking after having been diagnosed with cancer has many negative consequences for cancer survivors: 1) diminished effectiveness of anticancer treatment (e.g. head and neck cancer patients who continued smoking during radiotherapy had poor locoregional control, poorer disease-free and overall survival as compared with those who quit before radiation therapy); 2) increased risk of treatment complication (e.g. postoperative pulmonary complications); 3) shortened survival time due to disease progression and recurrence, SPCs, and comorbidity (19). Smoking cessation can ameliorate such negative effects from smoking (20), however, many cancer patients, who

Table 2. Common late effects of cancer treatments

Cancer treatment	Late effect
Bilateral oophorectomy	Cardiovascular disease Osteoporosis
Chest/breast irradiation	Coronary artery disease Cardiomyopathy/Heart failure
Abdominal irradiation	Liver disease
Cisplatin (Platinum agents)	Cardiovascular disease Hypertension Hyperlipidemia Weight gain Impaired renal function/microalbuminuria Gonadal dysfunction Decreased pulmonary function
Anthracycline	Cardiomyopathy Cardiovascular disease
Hematopoietic stem cell transplantation	Diabetes Hypertension Cardiovascular disease
Androgen deprivation therapy	Cardiovascular disease Diabetes
Aromatase inhibitor	Osteoporosis

were smoking prior to their illness, continue to smoke after diagnosis and treatment with a reported prevalence ranging from 7, even to 60%. Therefore, support for cancer patients to stop smoking seems a critical extension of present treatment protocols, and integration of such programs is becoming routine, especially for smoking-related cancer, and 'Stop smoking clinic for cancer survivors' was initiated in many countries, such as by the Netherlands Cancer Institute (21). However, we are not aware of any dedicated program for cancer survivors in Korea.

Exercise and physical activity

Exercise has been shown to improve fitness and physical functioning, reduce fatigue, and modestly decrease weight and body fat in cancer survivors, and may extend survival in cancer survivors (22). Cancer survivors are recommended to avoid inactivity, and recommendation for most exercise is the same as age-appropriate guidelines for the general public (23). However, cancer survivors often remain inactive because of persistent effects of cancer treatments, as well as clinicians' advice that cancer patients should rest and avoid activity (23). There are several points which apply to cancer survivors. Pre-exercise medical assessment and exercise testing is often necessary, considering common toxicities associated with cancer treatments including increased risk for fractures and cardiovascular events with hormonal therapies, neuropathies related to chemotherapy, etc (23). In addition, exercise prescription should be individualized according to cancer survivors' pretreatment fitness, comorbidities, and negative treatment effects. For example, a stationary bike may be preferable over weight bearing exercise for people with peripheral neuropathy (23).

Nutrition

Nutritional issues differ according to phase of cancer trajectories. Symptoms such as anorexia, early satiety, change in taste and smell, and bowel disturbances are common side effects of cancer treatment and can lead to malnutrition and weight loss during cancer treatment. Individual nutritional advice can ameliorate such toxicities. After recovery, dietary patterns and weight management become important to promote overall health, prevent SPCs, and control comorbidities. Obesity is associated with an increased risk of recurrence of breast and other cancers, and avoidance of weight gain and weight maintenance throughout treatment is recommended. While it is not clear that intentional weight reduction can improve prognosis, there is some evidence that a low-fat diet which resulted in 4% weight loss reduced risk of recurrence among breast cancer survivors (24). A dietary pattern high in fruits, vegetables, whole grains, poultry, and fish was found to be associated with reduced mortality in breast and colorectal cancer patients. There are numerous other issues regarding nutrition, including specific dietary composition (e.g. fat in breast cancer), specific food (e.g. toma-

to in prostate cancer), and dietary supplement (e.g. multivitamins). However, drawing conclusion is difficult due to paucity and inconsistency of results.

Health behaviors play a significant role in that they may modify the progression of disease, as well as influence risk for comorbid conditions, such as cardiovascular disease. Patients with "cancer" diagnosis are probably more receptive for lifestyle advice by their physicians, and the diagnosis and treatment period offer a "teachable moment".

Although largely consensus-based because scientific evidences are limited for specific cancer survivors, there are guidelines which provide specific recommendations of health behaviors for survivors with common cancers in the US (23, 25). Given the differences in the epidemiology of cancer, living environment, diet, and culture between the US and Korea, they cannot be directly applicable. Further research efforts are needed to address the unique needs of Korean cancer survivors. In addition, it is not realistic to expect oncologists to give detailed guidance on these complex issues when mean consultation time is very short and insufficient. In the US, there are certifications such as ACSM Cancer Exercise Trainer CertificationSM, Certified Specialists in Oncology Nutrition, and Tobacco Treatment Specialist. It is needed to establish such support systems so that oncologists can refer their cancer patients to support personnel who are certified within the area of cancer supportive care.

PSYCHOSOCIAL PROBLEMS OF CANCER SURVIVORS

Distress and mental health

Cancer diagnosis places significant distress on the patients and their caregivers. Higher level of anxiety and depression is seen with people with cancer. They are also at risk of mental disorders, such as major depression, drug dependence, simple phobia and agoraphobia. As a result, suicide is more common in cancer survivors than in the general population, meaning that cancer diagnosis is a significant risk factor for suicide (26). Clinicians should be alert for signs of clinical depression or anxiety so that appropriate referrals to mental health professionals can be made. Recommendation for distress management in cancer patients has been developed by the National Cancer Center, and includes screening, assessment and triage, pharmacological and non-pharmacological management (27). In addition to medical attention, social support is also helpful for improving mental health and QOL in cancer patients (28).

Employment and work-related difficulty

One study shows that almost half of the cancer patients (47.0%) lost their job after cancer diagnosis, and among those who lost their job in the first year, only 30.5% were re-employed during follow-up (29). Survivors had relatively lower employment rate

than the general population. And those who were working had difficulties such as fatigue and exhaustion (30, 31)

Social stigma

Cancer survivors also suffer from stigma. In general, people have negative attitude toward cancer survivors that cancer patients would not be able to make contributions to society (71.8%), and that they would avoid working with persons who have cancer (23.5%) (32). Social advocacy campaigns for cancer survivors would be necessary to reduce such negative attitude.

MODEL OF CARE DELIVERY FOR CANCER SURVIVORS: SHARED CARE

Cancer diagnosis may shift attention of patients and physicians away from important non-cancer problems, and cancer survivors often underuse other necessary non-cancer-related healthcare, such as treatment for comorbidities or recommended preventive services (17). Development of care models which can ensure quality of comprehensive cancer care is needed, as a narrow subspecialty model of cancer care has led to cancer treatment often being given outside the full medical context of the patient. Oncologists could not identify the needs of the patients as perceived by themselves (33). In 2005, the Institute of Medicine (IOM) (34) described the situation of cancer survivors as “Lost in Transition”, and the President’s Cancer Panel called for the remedy for this “Broken system”.

Various models have been suggested in the US and other

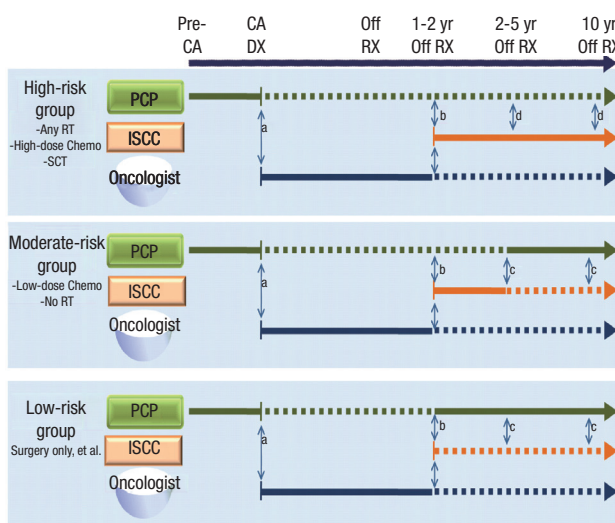


Fig. 2. Model for shared care of cancer survivors. Solid line connotes primary responsibility; Dashed line connotes secondary responsibility. CA, cancer; DX, diagnosis; Off RX, completion of cancer therapy; PCP, primary care physician; ISCC, integrated supportive cancer center. a, cancer diagnosis and planned therapeutic approach; b, cancer summary (care plan), cancer diagnosis, cancer therapy, surveillance recommendations, contact information; c, periodic update with changes in surveillance recommendations and new information regarding potential late effects; d, periodic update of survivor’s health for primary care physician’s record.

countries, including exclusive responsibility for follow-up care by family physicians, shared care with primary care physicians or nurse practitioners, and specialized multidisciplinary survivorship programs (35). Among those, shared care model by both oncologists and primary care physicians has been mostly highlighted as a viable option (35) (Fig. 2) and is also well applicable to the Korean healthcare system and culture. Shared care between oncologists and primary care physicians can enhance quality of non-cancer care (17), and also has a positive influence on patients’ attitudes towards the healthcare system.

However, there are challenges in the successful implementation of shared care model in survivorship care. There is limited information about “the best way to share the care” of these patients. In a study which compared expectations for cancer survivorship care among patients and their physicians, expectations were incongruent regarding the role and responsibilities for primary cancer follow-up, cancer screening, and general preventive health (36). Furthermore, survivors were not confident with their primary care physicians’ ability to deliver cancer-specific survivorship care and worried about poor communication between their oncologists and primary care physicians (37). To improve communication between the physicians, a cancer survivorship care plan including treatment history and follow-up care plan was suggested by the Institute of Medicine and by others (34). However, oncologists felt burdensome to complete it given their busy schedule.

In Korea, an institution-based shared care model was suggested as a potential solution given current oncology practices in Korea (13). It was preferred for the following reasons: easy information sharing by electronic medical record, easy access and communication with primary care physicians if necessary, and patients’ preference for being cared for at the same institution where they undergo cancer treatment (13).

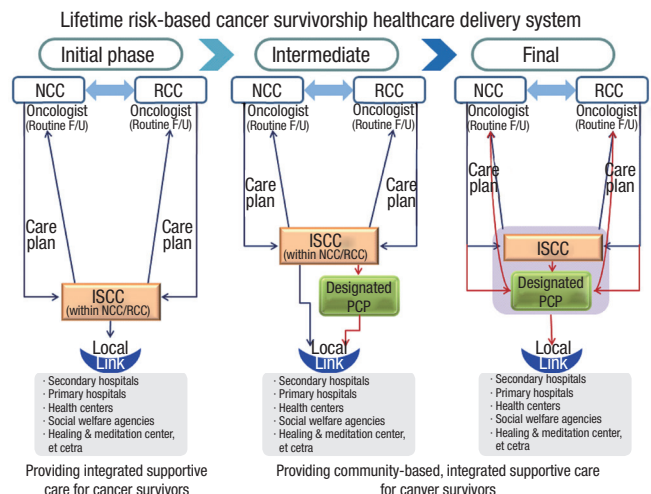


Fig. 3. Lifetime risk-based cancer survivorship healthcare delivery system.

Table 3. Cancer Objectives of Healthy People 2020 in Korea

Indicators	2005	2008	2020
Reduction in overall cancer death rate (per 100,000 population)	112.2	103.8	78.7
Increase in the overall cancer survival rate (%)	50.8	57.1	67.8 ('15)
Increase in the awareness of cancer prevention (%)	NA	51.7	70.0
Increase in cancer screening rate (%)	40.3	50.7	80.0
Increase in the rate of participation in National Cancer Screening Program (%)	19.6	31.7	70.0
Decrease in regional differences in National Cancer Screening Program (%p)	9.4	8.3	5.0
Designation of integrated supportive cancer survivorship center (number)	NA	NA	12
Increase in utilization rate of integrated supportive cancer survivorship center among cancer patients (%)	NA	NA	10.0

NA, not applicable. (Source: Ministry of Welfare and Korean Institute of Health and Social Affairs, 3rd term National Plan for Health Promotion: 2011-2020).

NATIONAL POLICY FOR CANCER SURVIVORSHIP AND FUTURE CHALLENGES

Since 2010, the cancer policy branch of the National Cancer Control Institute has been developing 'integrative supportive care service delivery system for cancer survivors,' which is wider in scope than shared care with primary care physicians (Fig. 3). Composition of integrative supportive care team has been defined, and includes professionals for psycho-oncology, rehabilitation, pain control, nutrition management, social work services, etc. A coordination system has been also established: primary assessment by nurse coordinators, and further evaluation and referral to necessary care by dedicated physicians (i.e. usually family physicians or internists of the cancer center dedicated in survivorship care). Need assessment tools were also developed for both cancer survivors and their caregivers (38, 39). Demonstration projects for shared care between regional cancer centers and public health centers are currently ongoing (40). In the future, community-based models including primary care physicians in the community are to be pursued.

Based on such policy model, integrated supportive cancer survivorship centers were included in the recently announced 'Cancer Objectives of Healthy People 2020 in Korea' The Ministry of Health and Welfare aimed to designate at least 12 integrated supportive cancer survivorship centers at regional cancer centers, and increase its utilization rate up to 10% of cancer patients by the year 2020 (Table 3). By this plan, we expect cancer survivorship care to be systematically developed and disseminated to regional level at a faster rate than ever.

However, there are several challenges for further development of survivorship care from national public health perspectives. First, a legal foundation for cancer survivorship care should be prepared, like the Comprehensive Cancer Care Improvement Act in the US. Second, a reimbursement mechanism is necessary for new items of survivorship care, including treatment summary, need assessment, transition visit, etc. Third, a care delivery system including community resources such as primary care clinics and public health centers, and an information system to support this are limited. Fourth, evidence-based clinical and public health guidance based on more precise sta-

tistics and vigorous research on cancer survivorship in Korea is needed. Finally, training of professionals who will be involved in survivorship care would be necessary.

CONCLUSION

Cancer survivors experience various health and psychosocial problems specific to this population during their cancer care trajectory. Several healthcare and policy models are being suggested to address these issues, including 'shared care model' and 'integrative supportive care service delivery system for cancer survivors.' Above all, there needs to be more effort to make the cancer survivorship agenda a reality, attended by policy makers and a wide variety of stakeholders including researchers, patients, and providers.

DISCLOSURE

The authors have no conflicts of interest to disclose.

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