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Assessment of tissue allograft safety monitoring with administrative healthcare databases: a pilot project using Medicare data

Sanjaya Dhakal · Dale R. Burwen · Laura L. Polakowski · Craig E. Zinderman · Robert P. Wise

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Abstract Assess whether Medicare data are useful for monitoring tissue allograft safety and utilization. We used health care claims (billing) data from 2007 for 35 million fee-for-service Medicare beneficiaries, a predominantly elderly population. Using search terms for transplant-related procedures, we generated lists of ICD-9-CM and CPT® codes and assessed the frequency of selected allograft procedures. Step 1 used inpatient data and ICD-9-CM procedure codes. Step 2 added non-institutional provider (e.g., physician) claims, outpatient institutional claims, and CPT codes. We assembled preliminary lists of diagnosis codes for infections after selected allograft procedures. Many ICD-9-CM codes were ambiguous as to whether the procedure involved an allograft. Among 1.3 million persons with a procedure ascertained using the list of ICD-9-CM codes, only 1,886 claims clearly involved an allograft. CPT codes enabled better ascertainment of some allograft procedures (over 17,000 persons had corneal transplants and over 2,700 had allograft skin transplants). For spinal fusion procedures, CPT codes improved specificity for allografts; of nearly 100,000 patients with ICD-9-CM codes for spinal fusions, more than 34,000 had CPT codes indicating allograft use. Monitoring infrequent events (infections) after infrequent exposures (tissue allografts) requires large study populations. A strength of the large Medicare databases is the substantial number of certain allograft procedures. Limitations include lack of clinical detail and donor information. Medicare data can potentially augment passive reporting systems and may be useful for monitoring tissue allograft safety and utilization where codes clearly identify allograft use and coding algorithms can effectively screen for infections.

Keywords Tissue safety · Allografts · Post-transplant infection · Administrative data

S. Dhakal · D. R. Burwen · L. L. Polakowski · C. E. Zinderman (✉) · R. P. Wise
Division of Epidemiology (DE), Office of Biostatistics and Epidemiology (OBE), Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 1401 Rockville Pike WOC I 441 S, Rockville, MD 20852, USA
e-mail: craig.zinderman@fda.hhs.gov

Present Address:
S. Dhakal
Division of Notifiable Diseases and Healthcare Information, Public Health Surveillance and Informatics Program Office, Office of Surveillance, Epidemiology and Laboratory Services, Centers for Disease Control and Prevention, Atlanta, GA, USA

Present Address:
D. R. Burwen
National Institutes of Health, Bethesda, MD, USA

Present Address:
R. P. Wise
Medimmune LLC, Gaithersburg, MD, USA

Introduction

The U.S. Food and Drug Administration (FDA) protects public health through regulation of food, drugs, devices, and biologics, which include vaccines, blood, and human tissues. There is a growing need for tissue and cell products in the health care industry. A survey of tissue establishments accredited by the American Association of Tissue Banks (AATB) suggested that about 1.5 million human tissue allografts (excluding organ allografts, corneas, sclera, and devices involving human tissue) were distributed in 2007 by United States tissue processors. (AATB 2010) The FDA plays an important role in ensuring the safety of these products through regulations that require donor screening and testing, adequate processing, and reporting of certain infectious adverse reactions. (FDA 2001).

Human cell and tissue products include "any articles containing or consisting of human cells, tissues and cellular and tissue-based products (HCT/Ps) that are intended for implantation, transplantation, or transfer into a human recipient." (FDA 2001) Examples of HCT/Ps include human bone, tendons, corneas, skin, blood vessels, heart valves, and certain reproductive products. By definition, HCT/P excludes whole organs such as heart, liver, lungs, kidney, intestine, thymus, and pancreas. (FDA 2001) A tissue establishment typically recovers tissues from recently deceased individuals in hospital operating rooms, medical examiner's offices, or dedicated recovery sites at the tissue establishment. Since tissue allografts come from other human donors, they have the potential to transmit disease from a donor to the recipient and also have a risk of contamination during recovery, processing, storage, or distribution. (Wang et al. 2007; Mallick et al. 2012) Donors are screened via a donor medical history interview with the donor's next of kin or physician; physical assessment or examination; and review of available relevant medical records for risk factors or clinical evidence of communicable diseases. (Mallick et al. 2012) Donor blood samples are also tested for HIV, viral hepatitis, and other specific communicable diseases. Before distribution, most tissues undergo disinfecting processes to reduce or remove contamination with bacteria, fungi, or viruses. However, these methods can vary by tissue type and processor. Bone allografts often undergo extensive processing with irradiation and removal of fats and blood, while other tissues, such as corneas and musculoskeletal soft tissue, often receive antibiotic soaks and/or chemical treatments with hydrogen peroxide or other detergents. (Boneva et al. 2001; FDA 2005; McAllister et al. 2007; Fishman et al. 2009; Vaishnav et al. 2009; Center for Medicare & Medicaid Services 2010) Some tissues, such as corneas, are used fresh, while others can be preserved by freezing or freeze-drying. Implantation into patients can follow promptly, but preserved tissue products may remain in inventory for months to years (FDA 2005).

FDA monitors HCT/P safety partly through evaluation of communicable disease-related adverse reaction (AR) reports from tissue establishments, health care providers, and consumers. (Wang et al. 2007) According to 21 CFR 1271.3(y) an AR is a noxious and unintended response to any HCT/P for which there is a reasonable possibility that the HCT/P caused the response. (FDA 2001) FDA's Current Good Tissue Practice rule requires manufacturers of tissue products to report serious communicable disease related ARs to FDA (FDA 2005).

Although tissue manufacturers are required to report these ARs, safety surveillance for tissues is fundamentally passive, relying on clinicians to recognize and report infections or other allograft-related problems. Vulnerabilities of passive surveillance systems include under-reporting and reporting biases. Absence of consistently ascertained numerators (total numbers of post-allograft infections) precludes reliable incidence rate calculations, even when denominator estimates can be developed.

Administrative health care databases, in contrast to passive reporting, capture information about product utilization as well as patient outcomes and do not rely on voluntary reporting. Surveillance using administrative data potentially could assess the magnitude of tissue allograft utilization and characterize post-transplant infection rates by type of tissue or organism. Use of these data can complement passive surveillance and provide context for interpreting passively reported infections, thereby helping tissue processors and FDA to continue assuring tissue safety and protecting recipients.

The main objective of this pilot project was to assess whether Medicare claims data from the Centers for Medicare & Medicaid Services (CMS) may be useful for monitoring tissue allograft utilization and

safety. Medicare covers approximately 39 million elderly Americans (age 65 years or older) and 8 million younger Americans with disability or end stage renal disease. (Center for Medicare & Medicaid Services 2010) Of these, approximately 35 million are enrolled in fee-for-service Medicare. The nearly universal medical insurance coverage for persons 65 year old and older results in very large data sets with the potential for evaluation of infrequent to rare adverse outcomes that might escape detection in smaller systems.

Our specific goals were to evaluate whether Medicare data can identify definite or possible tissue allograft procedures through International Classification of Disease, 9th revision, Clinical Modification (ICD-9-CM) codes, Common Procedural Terminology (CPT) codes, and/or Healthcare Common Procedural Coding System (HCPCS) codes; to assess the specificity of each of these coding systems for finding allograft procedures; and then to see if the data can be used to identify post-transplant infections in the same population. Evaluating the circumstances and degree to which these data can identify allograft procedures and potential subsequent infections are important inputs to assess the usefulness of Medicare data for monitoring HCT/P safety.

Methods

CMS uses ICD-9-CM, CPT, and/or HCPCS codes to identify surgical procedures. *Autografts* involve transplantation of a body part from one location to another within the same patient. *Allografts*, or *homografts*, involve transplantation of a body part from one person into another, usually from a deceased cadaver donor into a living patient (e.g., bone allograft), but occasionally from a living donor to a patient (e.g., skin graft). *Heterografts* (*or xenografts*), involve transplantation of a body part from another species into a human, such as a porcine heart valve.

We assessed the feasibility of identifying tissue allograft procedures in Medicare administrative claims data in a two-Step process. In Step 1, we identified ICD-9-CM procedure codes involving tissue grafts in inpatient data and obtained the frequency of each procedure. In Step 2, we examined frequencies of these procedures in additional Medicare data files, including outpatient data, and we evaluated whether the CPT coding system provided more descriptive codes that could help to distinguish tissue allografts from other graft types (e.g., autograft or prosthetic). Part of this work was performed as a collaboration between FDA and CMS within the Safe Rx project (http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FoodandDrugAdministrationAmendmentsActof2007/ucm184271.htm).

Data sources

Step 1 involved the examination of inpatient data from institutional providers. We used the 100 % (i.e., population level) 2007 Medicare Provider Analysis and Review (MedPAR) file. The MedPAR file has inpatient information from claims for service provided to enrollees admitted to CMS-certified hospitals or skilled nursing facilities, including demographics and pertinent clinical information, such as procedure and diagnosis codes. The MedPAR files contain ICD-9-CM procedure codes for up to six procedures per inpatient stay.

Step 2 involved the examination of the 2007 Medicare Carrier and Outpatient Standard Analytical Files, in addition to the MedPAR file. The Carrier file provides data from non-institutional providers, such as physicians, while the Outpatient file contains data for all outpatient encounters in institutional settings, such as ambulatory surgical centers. In both files, procedures are identified with HCPCS codes. Level 1 HCPCS codes are CPT codes published by the American Medical Association. Level 2 HCPCS are national codes created by CMS. Level 3 HCPCS are local and regional codes.

These claims files provide information on health care utilization among approximately 35 million people enrolled in fee-for-service Medicare. Additional files such as the Medicare Denominator file can be used to assess enrollment status of all Medicare beneficiaries.

Search methods

For Step 1, we used relevant terms such as transplant, transposition, graft, and flap to generate a list of ICD-9-CM procedure codes that definitely or possibly involve tissue allografts by searching in:

1. a "Procedure Codes and Abbreviated Titles" document available at the CMS website,

2. ICD-9-CM coding websites, (Chrisendres 2012, Data 2012)
3. national and international tissue bank websites of the American Association of Tissue Banks, the Eye Bank Association of America, the Canadian Tissue Bank, and the European Tissue Bank, and
4. medical literature (PubMed).

We ascertained which inpatient stays in the MEDPAR file had an ICD-9-CM procedure code from the generated list of codes.

For Step 2, we identified a list of CPT codes for procedures that may involve allografts by assembling a list of terms that included arthroplasty, bone chips, excision, implant, replacement, and others. We entered each term into CPT coding software (Current Procedural Coding Expert Package) to obtain a comprehensive list of CPT code ranges that possibly involve tissue allografts. After removing duplicates, we divided the code ranges into individual procedures.

Using the lists of ICD-9-CM and CPT codes, we identified the number of persons in the MedPAR, Outpatient, and Carrier files who had undergone each procedure. If a person had multiple occurrences of the same code in a particular database, the person was only counted once. We evaluated selected examples of tissue allograft procedures that occur with substantial frequency in the Medicare data and represent several body systems (ocular, cardiac, dermatologic, musculoskeletal).

As an additional part of Step 2, we identified ICD-9-CM diagnosis codes for site-specific and general post-operative infections that might follow a tissue allograft procedure. To demonstrate how Medicare data can be used to find infections after a known allograft transplant, we identified potential endophthalmitis infections (identified as ICD-9-CM code series 360.0x) within 6 months after corneal transplant procedures in 2007 (first claim per person). For general infections, we used ICD-9-CM codes for complications of surgical and medical care not elsewhere classified, such as post-operative infection.

Results

Step 1

From over 15.7 million inpatient stays in the 2007 MedPAR data, a subset of 1,339,879 persons had claims that included at least one of the 393 ICD-9-CM codes selected with our search terms. However, many of these ICD-9-CM codes were for procedures that were not specific for tissue allograft use (i.e., may or may not have involved an allograft), or involved autografts, xenografts, mechanical prostheses, or synthetic implants. Based on clinical judgment and the text description of the codes, only a subset of ICD-9-CM codes, corresponding to claims for 1,886 persons, clearly involved a tissue allograft procedure (with or without other graft). These codes included: *Allogeneic Hematopoietic Stem Cell Transplant Without Purging (41.05), Allogeneic Hematopoietic Stem Cell Transplant With Purging (41.08), Allotransplantation Of*

Table 1 Inpatient setting examples of codes specific (corneal transplant) and not specific (heart valve replacement) for allograft procedure, based on ICD-9-CM codes, 2007

ICD-9-CM codes	Name of procedure	Frequencies
Codes specific to allograft procedures[a]		
11.64	Other penetrating keratoplasty with homograft	129
11.60	Corneal transplant, keratoplasty, NOS	28
11.69	Other corneal transplant	24
11.62	Other lamellar keratoplasty	12
11.63	Penetrating keratoplasty with autograft	8
11.72	Keratophakia	16
Codes not specific to allograft procedures		
35.21	Replacement of aortic valve with tissue graft (aortic valve with auto, hetero, or homo grafts)	23,945
35.23	Replacement of mitral valve with tissue graft (mitral valve with auto, hetero, or homo grafts)	5,752

Inpatient data from 2007 Medicare beneficiaries

[a] Indicates allograft (with or without other graft)

Cells Of Islets Of Langerhans (52.85), Homograft To Skin (86.66), Other Penetrating Keratoplasty (11.64), Corneal Transplant, Not Otherwise Specified (11.60), Other Corneal Transplant (11.69), Other Lamellar Keratoplasty (11.62), Keratophakia (11.72), and *Penetrating Keratoplasty With Autograft (11.63)*.

Table 1 illustrates examples of ICD-9-CM procedure codes that are specific for tissue allograft and some that are not, along with corresponding frequencies of unique persons with an inpatient procedure. Corneal transplant procedures are examples of codes that clearly involve an allograft. However, many other ICD-9-CM codes are not specific enough to classify the graft type and only possibly involve the use of an allograft; examples include aortic and mitral valve replacements, which could be either allograft or xenograft. Nearly 24,000 aortic valves and nearly 6,000 mitral valves were replaced with grafts in 2007. Each of these almost 30,000 procedures could have involved an allograft or other type of tissue graft (e.g., xenograft (heterograft).

Step 2

Table 2 indicates that the inclusion of CPT codes improved ascertainment of persons undergoing corneal transplants. Examining the MedPAR data alone, a total of 217 persons received corneal transplants in the inpatient setting as indicated by ICD-9-CM codes. However, CPT codes identify approximately 8,000 persons receiving corneal transplants in the Outpatient file and nearly 17,000 persons in the Carrier (Physician) file. Overall, 17,372 distinct persons received corneal transplants in 2007.

Some skin graft procedure codes specifically identify the type of graft (Table 2). However, for this example, CPT codes in the Physician data file identify more skin allograft procedures than ICD-9-CM procedure codes in the MedPAR data file. CPT codes 15300, 15301, 15320, and 15321 all correspond to skin allograft procedures and identify about 2,700 beneficiaries in the Physician file, while ICD-9-CM procedure code 86.66 for homograft (allograft) to skin finds only 1,337 beneficiaries. After eliminating the overlap between patients in the MedPAR, Physician, and Outpatient datasets (i.e., patients with procedures identified through more than one dataset), we estimated that approximately 3,800 distinct Medicare beneficiaries underwent skin allograft procedures in 2007.

As with skin allograft procedures, the combination of ICD-9-CM codes and CPT codes yielded the greatest number of distinct patients undergoing ACL reconstruction (Table 2). However, codes for ACL

Table 2 Frequency of transplant varies by data source, 2007 (inpatient and outpatient data)

Data source	Code type	Code	Procedure	Frequencies
Corneas				
MedPAR	ICD-9-CM	11.6x[a], 11.72	Corneal transplant	217
Outpatient	CPT	657xx[b]	Keratoplasty	7,892
Physician	CPT	657xx[b]	Keratoplasty	16,787
Skin				
MedPAR	ICD-9-CM	86.66	Homograft to skin	1,337
Outpatient	CPT	153xx	Allograft skin	918
Physician	CPT	153xx	Allograft skin	2,685
MedPAR, outpatient, and physician	ICD-9-CM and CPT	86.66 153xx	Allograft skin	3,774
Anterior cruciate ligament				
MedPAR	ICD-9-CM	81.45	Cruciate ligament repair	217
Outpatient	CPT	29888	ACL repair	1,074
Physician	CPT	29888	ACL repair	1,563
MedPAR, outpatient, and physician	ICD-9-CM and CPT	81.45 29888	ACL repair	1,931

[a] ICD-9 codes: 11.60, 11.61, 11.62, 11.63, 11.64, 11.69

[b] CPT Codes: 65710, 65730, 65750 & 65755

Table 3 Examples comparing frequencies of procedures using CPT versus ICD-9-CM codes, 2007: aortic valve replacement, spine surgery

Data source	Code type	Code	Procedure	Frequencies
Aortic valve replacement				
MedPAR	ICD-9-CM	35.21	Replacement of aortic valve with tissue graft (auto, hetero, homo)	23,945
Physician	CPT	33406	Allograft valve	575
MedPAR and physician	ICD-9-CM and CPT	35.21 33406	Replacement of aortic valve with tissue graft/allograft valve	409
Spine surgery				
MedPAR	ICD-9-CM	81.0x	Spinal fusion (includes procedures with bone graft)	98,753
Physician	CPT	20930	Allograft, morselized[a]	18,177
		20931	Allograft, structural[a]	21,096
MedPAR and physician	ICD-9-CM and CPT	81.0x 20930 20931	Spinal fusion and (morselized or structural allograft)	34,204

Inpatient and outpatient data from 2007 Medicare beneficiaries

[a] Number of persons with either moralized or structural allograft was 37,608

repairs are not specific for allograft tissues; they may employ autografts, allografts, or no graft.

In Table 3, we demonstrate increased specificity with the use of a CPT code compared to an ICD-9-CM procedural code. MedPAR data using ICD-9-CM codes identify approximately 24,000 beneficiaries with aortic valve replacements using tissue grafts. This number includes auto-, hetero-, and homografts (allografts). CPT code 33406, a specific code for aortic valve replacement with an allograft, appears in the Physician file for only 575 beneficiaries, 409 of which were also identified in the MedPAR data.

Similarly, CPT codes for spine surgery more specifically identify allografts than ICD-9-CM codes. Although ICD-9-CM codes from 2007 MedPAR data have over 98,000 beneficiaries with spinal fusions that may have included bone grafts, CPT codes from the Physician data file found about 38,000 beneficiaries with spine surgery involving allografts.

Possible cases of endophthalmitis during months 0–6 after cornea transplant included 58 on the date of corneal transplant and then 22, 21, 12, 15, 8, and 10, respectively, in each of the next 6 months. These preliminary counts indicate that even a single year of data identified a relatively large number of events (146 total), highlighting the advantage of evaluating this issue in the sizable Medicare population and the large number of procedures captured in the database. Additional years of data could be used to augment these numbers if needed. Also, the data demonstrate higher frequency of endophthalmitis diagnoses in earlier months after transplant, as would be expected if infections are associated with the surgical procedure. It should be noted that the events reported here include all endophthalmitis coded in the claims data regardless of the source; they cannot be assumed attributable to the corneal allografts. Indeed, as with any surgery, infections following transplants may occur at some background rate even in the absence of contamination or transmission via the allograft. A variety of data issues would need to be considered before assessing a post-transplant rate of infection, including clarification of the appropriate criteria for counting persons in the numerator and denominator, and analysis of reasons (e.g., coding patterns, clinical issues) for the relatively large number on the day of transplant. Validation with medical chart review would also be needed to confirm cases and evaluate the positive predictive value of diagnostic codes for endophthalmitis. The numbers reported here are intended as a preliminary screening analysis only.

Discussion

This pilot project provides a number of insights about the use of Medicare and potentially other administrative health care databases for monitoring safety and

utilization of tissue allografts. Although infectious hazards from allografts and xenografts may differ, basic safety monitoring principles apply to both. (Boneva et al. 2001; Fishman et al. 2009, 2012) Using multiple Medicare data files improved ascertainment of the number of persons undergoing a variety of allograft procedures. In Step 1, which focused on billing (claims) data from inpatient facilities, we found that only a small proportion of ICD-9-CM procedure codes clearly involved allografts. More often the codes for the procedures were not sufficiently specific to indicate if an allograft was used. Step 2 demonstrated that the use of CPT codes in examination of billing data from physicians and other non-institutional providers increased ascertainment of allograft procedures. For some surgical procedures, CPT codes are more specific in identifying allograft transplant procedures than ICD-9-CM procedural codes. Data from outpatient institutional providers (e.g., ambulatory surgical centers) may be relevant for surgeries that are more frequently performed in an outpatient rather than inpatient setting. A single procedure will often be associated with both a physician bill and a facility bill (inpatient or outpatient institutional provider), so that overlap between databases is expected. Assessing the number of unique patients with a procedure removes the overlap produced by using multiple files together. The value of adding the facility claims (i.e., increase in ascertainment of allograft procedures) varied depending on the example selected. Procedures that have codes specific to allografts and also occur with high frequency in the Medicare data, such as corneal transplant and spine surgery with graft, may be especially useful for evaluating uncommon post-transplant events such as infection. Additional effort will be needed to assess the actual breadth and frequency of allograft types available in the Medicare data.

We initiated work towards identifying potential post-transplant infections using endophthalmitis after corneal transplants. Infection codes can be specific to a surgical site (e.g., endophthalmitis, osteomyelitis) or general (e.g., post-operative infection). Among the types of infections that potentially can be transmitted by tissue allografts, we focused on those that would manifest at the surgical site (e.g., bacterial or fungal infections) and develop rapidly enough to be captured within the data. We did not include viral infections (e.g., cytomegalovirus, hepatitis, HIV) which have longer latency before presentation. In addition, patient risk factors (e.g., IV drug use, sexual behavior, immune status) that suggest etiologies of viral infections other than tissue transmission are often not assessable using claims data alone. Further in-depth assessment will be needed for potential post-transplant infections in each category of allografts.

Some limitations in using Medicare data for tissue safety surveillance require consideration. Medicare claims data are collected for administrative purposes, specifically for billing. Data sets are routinely available yearly from CMS for other analyses beneficial to the Medicare population or program, after sufficient time has elapsed for the claims to accrue. This routine schedule may not be timely enough for some HCT/P surveillance purposes such as detection of rapidly changing trends. These data can also lack clinical details that would be helpful for safety surveillance, such as the specific location of an infection (e.g., superficial wound surface vs. deep joint infection), the onset of signs or symptoms, and often the identity of the infecting organism. Additionally, the Medicare population is predominantly elderly, making our findings less generalizable to the entire U.S. population. Orthopedic procedures for sports injuries in younger patients are not well represented, for example. Finally, many of the CPT and ICD-9-CM procedure codes available in Medicare and other administrative health care databases are not sufficiently specific to identify allograft use. For example, anterior cruciate ligament (ACL) reconstruction is one of the most commonly performed orthopedic procedures in the U.S., and various reports of infections attributed to allografts in medical literature involve ACL repair. (Lutz et al. 2001; Bos et al. 2003; Kainer et al. 2004; Farooq et al. 2007; Mei-Dan et al. 2008; Mouzopoulos et al. 2009) However, codes for ACL repairs are not specific for allograft tissues. The lack of specificity of the codes in claims data could lead to incomplete ascertainment of actual tissue allograft use. Thus, the total number of procedures involving tissue allografts reported here is likely underestimated. However, such coding biases are likely to be consistent over time (in the absence of coding changes), so monitoring the same data source over time could still allow for detection of emerging trends.

To improve the utility of claims data in monitoring tissue allograft utilization and safety, greater granularity of coding systems may add value by

distinguishing allografts. Coding refinements from other biological medical products include a recent revision of approximately twenty ICD-9-CM codes to provide more detail for blood transfusion-related safety outcomes and the creation of HCPCS codes that facilitated safety monitoring of H1N1 pandemic influenza vaccinations during the 2009–2010 influenza season (CMS 2010). Thus, proposing changes to coding systems is a potential avenue to increase data utility. Sufficient justification will be needed, given the complexity and broad use of the billing systems, but these recent examples demonstrate the feasibility of modifying the coding conventions to accommodate evolving surveillance needs.

Medicare data also have several important strengths, beginning with their size. Because of the large number of enrolled persons, some tissue allograft procedures appear with sufficient frequency to allow for evaluation of the adequacy of the codes for identifying allografts. These data could be used to identify infrequent adverse reactions, such as infections associated with tissue transplant procedures which would not be evaluable in some smaller databases. Medicare data can potentially provide national cohort-based information about allograft procedures that are common among the elderly (e.g., corneal transplants, spine surgery with bone grafts). Also, monitoring trends over time may be useful in some instances even when data have imperfect sensitivity or specificity, because these limitations may be fairly constant over time. Another very important aspect is that these databases already exist, so that there is no need to collect new data, allowing for a more efficient use of public health resources.

Given the rigorous screening and testing of prospective tissue donors, as well as the processing of HCT/Ps before implantations, the risk of transmission of infections from donors to recipients is low. However, such transmissions remain possible. (Tugwell et al. 2005; Hassan et al. 2008; Fishman et al. 2009; Pruett et al. 2012) Since dozens of tissues can be recovered from one donor and transplanted into multiple recipients, the risk of disease transmission through allograft tissues is potentially multiplicative in nature. Passive surveillance and investigations of reported infections have traditionally been key tools used by FDA for monitoring HCT/P safety. This system relies on clinicians to recognize and spontaneously report post-transplant infections leading to under-reporting and biases (e.g., infections with shorter onset or uncommon organisms are more likely to be reported). However, investigations of reported infections, conducted by the establishment distributing the tissue, and by FDA, include assessment of the tissue donor and processing. This assessment provides an advantage over claims data, which do not include donor information. Linking infections after tissue transplants with information about the tissue donors would allow detection of clusters of infections in multiple recipients of tissues from a particular donor. Information about the tissue bank source of an HCT/P may be identified from the lot or graft identification number recorded in the recipient's medical record (Brubaker and Wilson 2010; Strong et al. 2010). Efforts currently under development to standardize terminology and coding for tissue allografts may help link implanted tissues to information about the tissue donor (Ashford et al. 2010; Strong and Shinozaki 2010). Such information is not currently reported on claims, but health care database systems that include access to medical records can potentially take advantage of this information. The Notify Library (www.notifylibrary.org), an international project coordinated by the World Health Organization in collaboration with other international public health agencies, is an effort currently under development to establish a standardized, searchable database of documented adverse outcomes in transplantation. This project could complement both passive and claims-based surveillance by identifying general principles supporting detection and investigation of post-transplant infections.

An early FDA Sentinel Initiative contract examined the breadth of potential sources for computerized information about tissue and blood products (Cupryk 2009). This project surveyed a variety of commercial U.S. health care settings (e.g., large integrated health care delivery systems and health maintenance organizations) and found that while encounter data with additional clinical details or electronic medical records are available in some health care systems, their relatively small size and regional scope diminish the capability to evaluate tissue allograft safety. The usefulness of administrative health care databases can be augmented if additional clinical details are available, such as laboratory results or medical records. Eventually, the growing use of electronic medical records and related computerized information flows

may facilitate systematic surveillance of infections. For example, it would seem promising to harness automated data from microbiology laboratories to recognize positive bacterial cultures from wounds, joint aspirates, or blood within appropriate intervals after surgical procedures that involve allograft implantations. However, this type of linkage may only be possible within health care delivery systems, and additional clinical data may be needed to confirm infection (as opposed to colonization or contamination).

Conclusion

Currently no single data source provides an ideal surveillance system with the breadth and depth of desirable information to monitor tissue allograft safety, yet a variety of data sources may be useful. Our pilot project suggests the potential for Medicare data to complement passive surveillance with additional methods development. Desirable features to augment the utility of claims data would include specific allograft codes for procedures in which codes are currently ambiguous or nonexistent, and validated coding algorithms to identify relevant post-surgical infections. Health care database systems that include or link to detailed clinical data that can confirm infections and provide tissue allograft specifications (including source information about the tissue bank and donor) would be the most useful for safety surveillance.

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