Shandera. Clin Diabetes Res 2017, 1(1):35-39
DOI: 10.36959/647/491 | Volume 1 | Issue 1

Clinical Diabetes and Research

Review Article Open Access

Ethical Issues Attendant with the Current Pandemic of Diabetes

Wayne X Shandera*

Assistant Professor of Medicine, Division of General Medicine, Baylor College of Medicine, Texas, USA

Introduction and Rationale

The International Diabetes Foundation (IDF) estimates that 415 million of the 7 billion global inhabitants have diabetes and this number is estimated to surge to 642 million by 2040 [1]. The rising tide of cases is particularly troublesome among low- and middle-income countries, areas which comprise 80% of all global diabetes. The current WHO global prevalence is 8.8% [2]. Prevalences approach 9% and 10% respectively in India and China and higher values are estimated in Mexico (13%) and Egypt (17%) [3]. In wealthier nations the rates are burdensomely elevated, with Saudi Arabia showing one of the highest global prevalences at 24% [1].

The economic consequences of this transition are devastating. The current IDF estimates for the costs of the outbreak are 376 billion United States Dollars (USD), increasing by 2030 to 490 billion USD, with already over 12% of the global health care budget being spent on diabetes [4]. These values appear low when one considers that one rickettsial outbreak among 201 American Indians in Arizona was associated with indirect and direct costs of over 12 million USD [5].

The current surge in prevalence of diabetes is occurring at a time when new pathways for control of the disease and new medications are increasingly available. The renowned Joslin Center in Boston, for example, now lists fifteen medications (including two derivatives) among seven major categories of oral medications for management of diabetes (biguanides, sulfonylureas, meglitinides including D-phenylalanine derivatives, thiazolidinediones, Dipeptidyl Dipeptidase (DPP)-4 inhibitors, alpha-glucosidase inhibitors, and bile acid sequestrants with seven combinations of these agents also available [6].

Currently nine classes of oral medications are listed as used for diabetes by the American Diabetes Association [7]. These include sulfonylureas (limited in usefulness because of hypoglycemia especially when combined with insulin), biguanides (of which metformin has received particular recognition as a leading and also cost-effective agent in diabetes control by the United Kingdom Prospective Diabetes Study), [8] meglitinides (also complicated by hypoglycemia), thiazolidinediones whose two leading compounds have had restricted use because of concerns regarding bladder cancer (pioglitazone) and increased cardiovascular disease risk (rosiglitazone), dipeptidyl peptidase-4 DPP-4 inhibitors (some of whom worsen heart failure, and among which there is a unproven risk of pancreatic cancer), sodium glucose cotransporter-2 SGLT2 inhibitors (glifozins), alpha glucosidase inhibitors (alpha-glucosidase), and bile acid sequestrants (such as cholestyramine, not very effective in diabetes control) [7].

The continued investigative merit of pharmacologic studies into the pathogenesis of diabetes occurs at a time when the prevalence dictates a need for such work as well as unique, novel approaches.

Methods

A PubMed search was performed using the terms "ethics" and "diabetes", the number of peer-reviewed articles written between 1996 and 2015 were assessed and a similar count was established using Google Scholar. Other relevant recent articles that pertain to the quality or ethical control of diabetes were assessed. Major articles and trends were assessed in light of ethical principles of autonomy, beneficence, and distributive justice.

Additional ethical topics were obtained by PubMed and by Google Scholar, using the terms, insulin and monopo-

***Corresponding author:** Wayne X Shandera, M.D., Assistant Professor of Medicine, Division of General Medicine, Baylor College of Medicine, Houston TX 77030, Texas, USA, Tel: 713-873-3389, E-mail: shandera@bcm.edu

Received: July 29, 2017; **Accepted:** September 21, 2017;

Published online: September 23, 2017

Citation: Shandera WX (2017) Ethical Issues Attendant with the Current Pandemic of Diabetes. Clin Diabetes Res 1(1):35-39

ly, cholesterol and diabetes, and statin and diabetes, using preferentially reviews and articles from the last five years.

Results

Using these strict criteria, between the interval 1996 and 2015, the limited (ten) Pub Med articles generated included a diverse set of ethical and legal issues. There were three peer-reviewed articles on the ethics of prevention and screening including screening of newborns [9-11], three articles on research ethics [12-14], and one each on hematopoietic stem cell transplants [15], on driving motor vehicles [16], on needs for cardiovascular prevention [17], and on ethics of a particular drug trial [18]. Articles matched highly through Google Scholar for the same time interval also dealt with ethical or quality issues and eldercare [19], consumer protection [19,20], and diabetes and fertility [21].

Discussion

Investigative work on diabetes including basic investigative studies, is carried out with a basic ethical underpinning toward these activities with resultant publications may not appear using the above literature search command. Other salient aspects of diabetes and ethical issues are notable only as part of a broader review of ethical considerations, for example as part of the revolution in direct-to-consumer testing with personal genomics companies [20,22]. Alternatively, the ethical aspect may be ensconced under a term such as "quality", and important ethical research in diabetes care may as well not be detected with a restrictive search command. An example would be an article reviewing the quality of on-line sites for diabetes care [23] or the important interactions now being uncovered between statins and diabetogenicity [24,25].

Diabetes thus is infrequently the target of ethical challenges or dilemmas when one assesses the disease from the individual patient perspective. The importance of examining diseases from a societal perspective is however receiving increasing recognition in medicine. The importance of societal ethical challenges was the topic of a keynote address at a major international seminar on global inequities in disease [26] and is the theme of a new textbook on social ethics in medicine [27].

Why does the current outbreak of diabetes continue to rampage societies globally while at the same time newer and ostensibly more effective therapies are being produced, basic science and epidemiologic investigations provide new means of control and prevention, and international guidelines are promulgated which should control the disease? Why is the prevalence of diabetes increasing white at the same time a record number of investigations and creative public health interventions are underway? The discord is striking and a theme of this paper is to better understand this gap between knowledge and societal impact. The core ethical issues are those of distributive justice. An international debate is needed to understand this ethical tension and ascertain why current endocrinologists and primary care physicians are failing to make a public health impact.

Why many new medications appear at a time when diabetes control is clearly worsening questions their efficacy. Insulin, the original hypoglycemic, now available, in short- and long-acting forms, dispensed by injection or by formulated pens (which are shown to increase adherence) was itself the subject of a monopoly discussion reported in JAMA in 1941 [28]. Its many formulations represent a type of "evergreening", in which new compounds are given patents (as a biologic the ethical issues associated with patency merit a separate discussion) and prevent the decline in price [29]. This oligopolization of insulin is especially a product for the developing world.

Another ethical dilemma confronted by the investigator, the public health and the clinical physician is the issue or drug interactions. Concomitant medications such as antihypertensives (e.g., thiazides) and statins complicated diabetes control. Only recently is it recognized that statins may in the elderly induce the development of diabetes [24,25,30]. The mechanisms for this are multiple and include impact on beta cell apoptosis, transport proteins, glucokinase concentrations, and LDL levels and calcium channel-dependent insulin secretion [31]. While statins themselves very significantly reduce cardiovascular risk, the ethical dilemma is the extent to which this reduction is canceled by a diabetogenic effect. Preliminary studies suggest that the diabetogenic effect is small but it is worth following the literature for the results of future long-term, prospective studies [32].

The waxing and waning of philosophies and the ethical dilemmas attendant with them is reflective of the controversies regarding cholesterol, whose values were allowed to plummet to untenable values, and within the U.S. at least the current recognition that some cholesterol is needed for multiple biologic functions including neurosynthesis and that levels of serum cholesterol need not be controlled as tightly as has been done in the past [33].

The ethical issues with the medications and their effects on blood lipids and blood sugars are the basis for many pharmacologic studies, but seldom do they specifically enter the arena of pure ethical discussions and manifest themselves in a restrictive ethical search command as above.

The investigative work on such studies hopefully forms the basis for future societal control and public health programs and hopefully creative new investigations will yield unexpected results. Alternative theories, for example, for the development of diabetes currently have acquired scientific respectability including recognition of the role of altered microbiome among diabetics [34] and the role of lactation in preventing diabetes [35]. Also, in animal mod-

els, it is long recognized that certain viruses such as the encephalomyocarditis virus and other enteroviruses such as Coxsackie B virus are diabetogenic [36]. If exposure to such viruses is a significant cofactor for disease, maybe newer case-control studies assessing serologic exposure are indicated.

If such alternative theories have legitimacy, statements that only altering diet and exercise as the only modes to control type 2 disease, for example, have limited validity. When the acquisition of a diabetogenic flora or a virus, or the absence of lactation may be significant cofactors in the development of diabetes our dilemmas in treatment may move from the examination room to the epidemiologist or the public health office.

What is the major ethical issues attendant with the societal need for better diabetes control? The decades-honored reliance on patient autonomy appears to be relatively ineffective and appeals to monetary control are unproven [37]. When autonomy fails, beneficence and the paternalism of traditional medicine become the traditional standards.

The patient must nonetheless recognize the importance of adherence. In the diabetes literature, patients who are more self-sufficient and who show higher levels of autonomy in their care improve their long term control as shown by falling levels of hemoglobin A1C [38]. The provider needs to keep abreast of the new developments in diabetology, the guidelines regarding statins and cholesterol levels, and the optimal frequency for monitoring of glucose control. Investigators are encouraged to find creative new pathways for diabetes control, assess in large prospective studies the interactions between statins and diabetes incidence and also develop translational methodologies for new findings on microbiome data and on the importance of neonatal lactation. Public health leaders should support the development of studies and models which assess control policies such as the new sugar tax now being implemented in Philadelphia. Such taxes should preferentially be used for funding prevention of diabetes activities. Pharmaceutical companies are advised to find means to make insulin more affordable to the enlarging number of diabetics. International agencies must respect the limitations of local budgets in making broad recommendations for surgery among those with diabetes as a consequence of morbid obesity.

Ethical issues in the control of diabetes are perhaps particularly important at the community level. That community behavior is important is recognized from the past studies of American Southwest Pima Indians whose rates of diabetes soared after emigration to the United States [39]. Currently the body of prevention recommendations includes frequent determinations of hemoglobin A1C, often every 3-4 months, from the serum of known diabetes, as a monitor for control, a monitoring system attendant with complications of largely co-morbid disease states [40]. Borrowing from HIV medicine, where community HIV "viral loads" are used to assess the degree to which control is being achieved, largely through antiretroviral therapy, in a given community [41] might not similar control be achieved with community monitoring of an equivalent measure for diabetes, such as the concentration of hemoglobin A1Cl among diabetic populations? Using such monitors suggest that certain communities are better at sustaining a modifying diet and exercise among their members.

The cautionary factors associated with wide scale use of a hemoglobin A1C for community assessment are patient compliance with testing, the lower accuracy of the assays among populations with hemoglobinopathies and among patients with altered red blood cell production from recent transfusions or blood loss (again producing elevated values) and among patients affected by the ingestion of substances from chronic alcohol to opioids and vitamin C or E, or salicylates [42].

The ethics of preventing diabetes at the social level is the basis for several types of legislation.

Woodrow Wilson established the first sugar tax, but for political, not health, reasons. More recently taxes on sugar-sweetened beverages have become increasingly popular. The rationale is explained in a meta-analysis of eight articles for diabetes and three for the metabolic syndrome showing a 26% and 20% increase respectively in the prevalence of these entities associated with increased consumption of such beverages [43]. A US-based (Centers for Disease Control and Prevention) analysis, based on the Coronary Heart Disease Policy Model, finds that a penny-per-ounce tax on sale of sugar-sweetened beverages would reduce consumption 15% and prevent 2.4 million diabetes-years over an 11 year interval [44]. Sugar taxes have been attempted, largely unsuccessfully, in a number of communities including Philadelphia, USA. Philadelphia is the latest community to embark on a rather stringent soda tax, an amount equal to 0.015 USD per ounce at the distributor level, which went into effect January 1, 2017 [45]. The cost of a sweetened tea in Philadelphia now costs the consumer over twice as much. Berkeley, California, a far smaller community, also has such a tax and this tax is estimated to have reduced sweetened beverage consumption over 20%. To date, no studies however have proven an impact on health indices, despite experience with such taxes in Mexico, Norway, and the United Kingdom. Especially interesting would be the impact of prevention programs funded by such taxes.

Distributive justice is perhaps the greatest ethical principle challenged by the current societal dilemma of the increased prevalence of diabetes. The increasing resources attendant with the control and treatment of diabetes will require financial and administrative sources whose benefit is

deemed better spent elsewhere. This can be said about virtually any disease state, such as HIV or many forms of cancer, which are in large part preventable. As scientific advances eliminate individual culpability for disease (for reasons listed above), the ethical dilemmas will transfer potentially more into the societal level.

A review of the Portuguese experience contrasting diabetes with AIDS is illustrative. The review emphasizes a relative equivalence between the two for expenses, prevalence and mortality, but the official attention afforded to AIDS is ostensibly greater while long-term consequences for society may be greater associated with diabetes [46]. AIDS has evolved into a more chronic disease so such comparisons are not completely valid, although the inequity in attention between the two states underscores the problems with distributive justice when using other diseases as a barometer for comparison.

The monetary crisis attendant with diabetes is especially apparent when one considers the impact of the latest International Society of Diabetes recommendation regarding bariatric surgery for the morbidly obese [47]. The costs for such surgery are high, with an average of $23,000 USD for gastric bypass surgery (less for lap banding, more for gastric sleeves) [48]. Despite ostensible long-term cost benefits, the procedures have limited usefulness among the poor and in financially-strapped health agencies. Recognizing the importance of control and prevention of this major societal epidemic is effective only when the control of diabetes is addressed and carried out at many levels beyond the community.

In the end a teamwork approach is increasingly recognized as a stimulant to better health and improved mortality [49,50] could perhaps be translated to the community level. With a disease such as diabetes with its increasing prevalence and high morbidity, coordinated efforts are required to control this individual, societal, and now global scourge.

Conclusions

Limited number traditional studies assess the diabetic care using the traditional principles of ethics including autonomy, beneficence, and distributive justice. The investigative and public health activities that assist in the control of diabetes are executed independent of such ethical discussion. Despite the proliferation of new agents and technologies, diabetes prevalence continues to grow and this increase in prevalence will in the future especially impact highly populated developing and middle income nations. New theories regarding the pathogenesis exonerate some of the individual culpability for diabetes. To close the gap between increasing knowledge of the pathogenesis and the increasing prevalence of the disease, it is hoped that ethical principles will help bridge this discrepancy. The control of adult-onset diabetes will be achieved only when the importance and implications of its control are understood by the individual, the provider, the community, the investigator, the pharmaceutical industry, and diverse national and international agencies but societal ethical control is perhaps foremost using measures such as surveillance, taxes, citizen initiatives to lower the costs of insulin, and reasonable policy guidelines for surgery, as a means to restrain the growth in this current societal scourge.

References

1. International Diabetes Foundation (2016) IDF Diabetes Atlas. (7th edn).
2. World Health Organization (2016) Global report on diabetes.
3. Seuring T, Archangelidi O, Suhrcke M (2015) The Economic costs of type 2 Diabetes: A global systematic review. Pharmacoeconomics 33: 811-831.
4. Zhang P, Zhang X, Brown J, et al. (2010) Global healthcare expenditure on diabetes for 2010 and 2030. Diabetes Res Clin Pract 87: 293-301.
5. Drexler NA, Traeger MS, McQuiston JH, et al. (2015) Medical and indirect costs associated with a rocky mountain spotted fever epidemic in Arizona, 2002-2011. Am J Trop Med Hyg 93: 549-551.
6. Joslin Diabetes Center (2015) Oral diabetes medications summary chart.
7. American Diabetes Association (2017) What Are My Options?
8. Clarke P, Gray A, Adler A, et al. (2001) Cost-effectiveness analysis of intensive blood-glucose control with metformin in overweight patients with type II diabetes (UKPDS No. 51). Diabetologia 44: 298-304.
9. Nordenfelt L (1996) Prevention and ethics in medicine: the case of diabetes prevention. J Pediatr Endocrinol Metab 9: 381-386.
10. Ross LF (2003) Minimizing risks: the ethics of predictive diabetes mellitus screening research in newborns. Arch Pediatr Adolesc Med 157: 89-95.
11. Ross LF (2003) The ethics of type 1 diabetes prediction and prevention research. Theor Med Bioeth 24: 177-197.
12. Misbin RI (1999) Comment on the ethics of placebo-controlled trials in patients with type 2 diabetes mellitus. J Clin Endocrinol Metab 84: 823-824.
13. Macaulay AC, Cross EJ, Delormier T, et al. (1998) Developing a code of research ethics for research with a native community in Canada: A report from the kahnawake schools diabetes prevention project. Int J Circumpolar Health 57: 38-40.
14. Henriksen H (1993) Are principles of ethics observed in new discoveries on diabetes? Lakartidningen 90: 4413-4414.
15. Ross LF, Philipson LH (2007) Ethics of hematopoietic stem cell transplantation in type 1 diabetes mellitus. JAMA 298: 285.
16. Cox DJ, Singh H, Lorber D (2013) Diabetes and driving safety: Science, ethics, legality and practice. Am J Med Sci 345: 263-265.
17. Scheen AJ (2003) Clinical study of the month. Premature interruption of ASCOT and CARDS clinical trials of cardio-

vascular prevention with atorvastatin in patients with arterial hypertension or diabetes mellitus: compromise between ethics and statistics in evidence-based medicine. Rev Med Liege 58: 585-590.

18. Mudur G (2002) Researchers question ethics of diabetes drug trial. BMJ 325: 353.
19. Fahey T, Montgomery AA, Barnes J, et al. (2003) Quality of care for elderly residents in nursing homes and elderly people living at home: Controlled observational study. BMJ 326: 580.
20. Hogarth S, Javitt G, Melzer D (2008) The current landscape for direct-to-consumer genetic testing: Legal, ethical, and policy issues. Annu Rev Genomics Hum Genet 9: 161-182.
21. Ethics Committee of the American Society for Reproductive Medicine (2016) Electronic address, A.a.o. and M. Ethics Committee of the American Society for Reproductive, Provision of fertility services for women at increased risk of complications during fertility treatment or pregnancy: An Ethics Committee opinion. Fertil Steril.
22. Bunnik EM, Schermer MH, Janssens AC (2012) The role of disease characteristics in the ethical debate on personal genome testing. BMC Med Genomics 5: 4.
23. Weitzman ER, Cole E, Kaci L, et al. (2011) Social but safe? Quality and safety of diabetes-related online social networks. J Am Med Inform Assoc 18: 292-297.
24. Corrao G, Ibrahim B, Nicotra F, et al. (2014) Statins and the risk of diabetes: evidence from a large population-based cohort study. Diabetes Care 37: 2225-2232.
25. Park ZH, Juska A, Dyakov D, et al. (2014) Statin-associated incident diabetes: A literature review. Consult Pharm 29: 317-334.
26. Braun F (2016) Global bioethics and inequities, in Ethics and Social Determinants of Health. Zagreb, Croatia.
27. Shandera WX (2016) Expanding our calling: Social ethics in medical education. Ethical Issues in the 21st Century, 147.
28. Manson-Bahr P (1941) The Insulin Monopoly. JAMA 117: 112.
29. Greene JA, Riggs KR (2015) Why is there no generic insulin? Historical origins of a modern problem. N Engl J Med 372: 1171-1175.
30. Corrao G, Monzio Compagnoni M, Rea F, et al. (2017) Clinical significance of diabetes likely induced by statins: Evidence from a large population-based cohort. Diabetes Res Clin Pract 133: 60-68.
31. Sampson UK, Linton MF, Fazio S (2011) Are statins diabetogenic? Curr Opin Cardiol 26: 342-347.
32. Rajpathak SN, Kumbhani DJ, Crandall J, et al. (2009) Statin therapy and risk of developing type 2 diabetes: A meta-analysis. Diabetes Care 32: 1924-1929.
33. Kratz M (2005) Dietary cholesterol, atherosclerosis and coronary heart disease. Handb Exp Pharmacol 195-213.
34. Tamburini S, Shen N, Wu HC, et al. (2016) The microbiome in early life: Implications for health outcomes. Nat Med 22: 713-722.
35. Stuebe AM, Rich-Edwards JW, Willett WC, et al. (2005) Duration of lactation and incidence of type 2 diabetes. JAMA 294: 2601-2610.
36. Craighead JE, McLane MF (1968) Diabetes mellitus: Induction in mice by encephalomyocarditis virus. Science 162: 913-914.
37. Pellegrino ED (1984) Autonomy and coercion in disease prevention and health promotion. Theor Med 5: 83-91.
38. Williams GC, Freedman ZR, Deci EL (1998) Supporting autonomy to motivate patients with diabetes for glucose control. Diabetes Care 21: 1644-1651.
39. Cummings DJ, Bull J (2015) Type 2 Diabetes in the Pima Indians of Arizona - a Review. Health Behavior and Policy Review 2: 485-492.
40. Gallagher EJ, Le Roith D, Bloomgarden Z (2009) Review of hemoglobin A(1c) in the management of diabetes. J Diabetes 1: 9-17.
41. Das M, Chu PL, Santos GM, et al. (2010) Decreases in community viral load are accompanied by reductions in new HIV infections in San Francisco. PLoS One 5: e11068.
42. Larese J (2012) When is hemoglobin A1c inaccurate in assessing glycemic control? Clinical Correlations.
43. Malik VS, Popkin BM, Bray GA, et al. (2010) Sugar-sweetened beverages and risk of metabolic syndrome and type 2 diabetes: A meta-analysis. Diabetes Care 33: 2477-2483.
44. Wang YC, Coxson P, Shen YM, et al. (2012) A penny-per-ounce tax on sugar-sweetened beverages would cut health and cost burdens of diabetes. Health Aff (Millwood) 31: 199-207.
45. National Public Radio (2016) Philadelphia becomes 1st major U.S. City to pass a Tax on Soda, in The two-way, breaking news.
46. Oliveira SL, Lunardi Filho WD (2004) [AIDS and diabetes mellitus versus distributive justice in the public health system]. Rev Bras Enferm 57: 750-753.
47. Rubino F, Nathan DM, Eckel RH, et al. (2016) Metabolic Surgery in the Treatment Algorithm for Type 2 Diabetes: A Joint Statement by International Diabetes Organizations. Diabetes Care 39: 861-877.
48. (2017) Weight loss surgery insurance and costs.
49. Baker DP, Salas E, King H, et al. (2005) The role of teamwork in the professional education of physicians: current status and assessment recommendations. Jt Comm J Qual Patient Saf 31: 185-202.
50. Baker DP, Gustafson SB, Salas E (2005) Medical teamwork and patient safety: The evidence-based relations, Health and Human Services, Editor. 2005, U.S. Government: Agency for Healthcare Research and Quality, 1-64.